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(54) BETACORONAVIRUS MRNA VACCINE

- (71) Applicant: ModernaTX, Inc., Cambridge, MA (US)
- (72) Inventors: Giuseppe Ciaramella, Sudbury, MA (US); Sunny Himansu, Winchester, MA (US)
- (73) Assignee: ModernaTX, Inc., Cambridge, MA (US)
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Primary Examiner — Nicole Kinsey White (74) Attorney, Agent, or Firm — Wolf, Greenfield & Sacks, P.C.

(57) ABSTRACT

The disclosure relates to respiratory virus ribonucleic acid (RNA) vaccines and combination vaccines, as well as methods of using the vaccines and compositions comprising the vaccines.

26 Claims, 24 Drawing Sheets

Specification includes a Sequence Listing.

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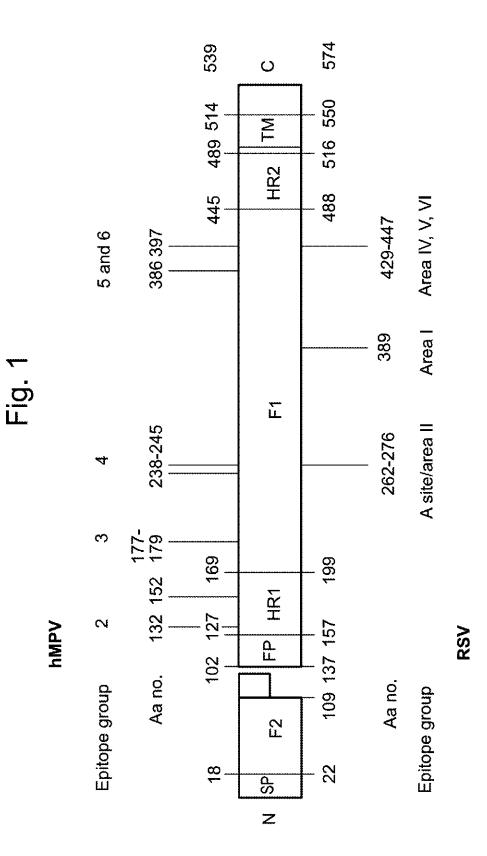
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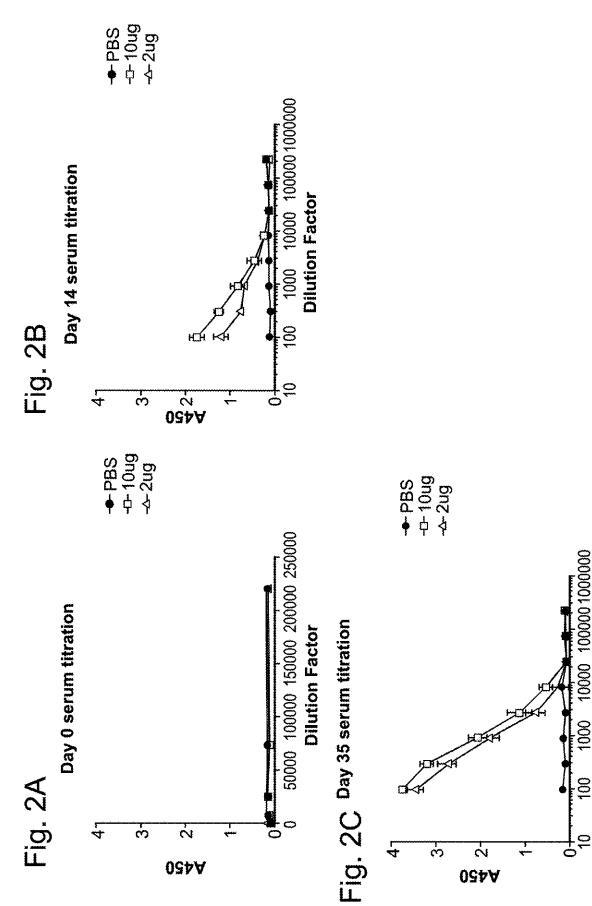
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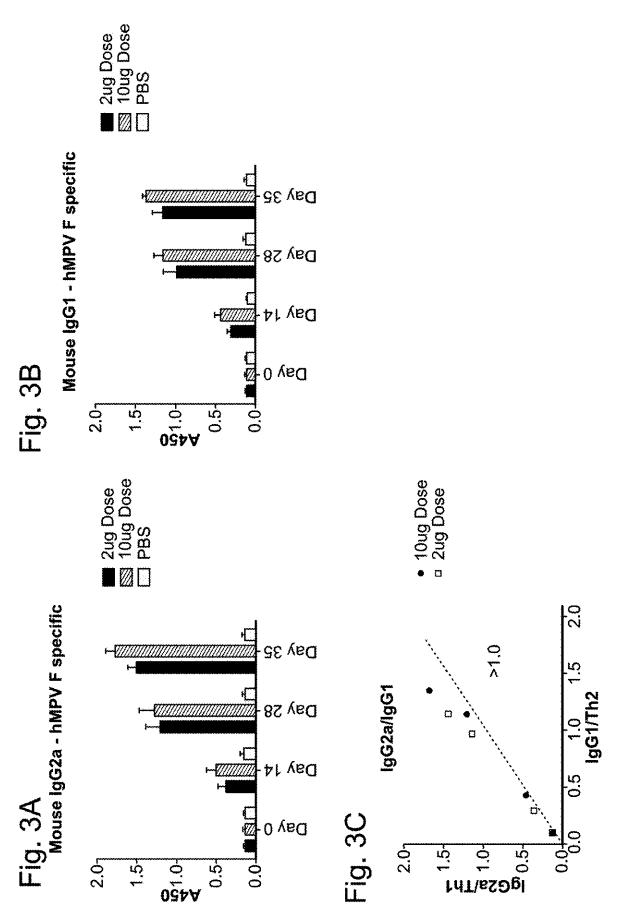
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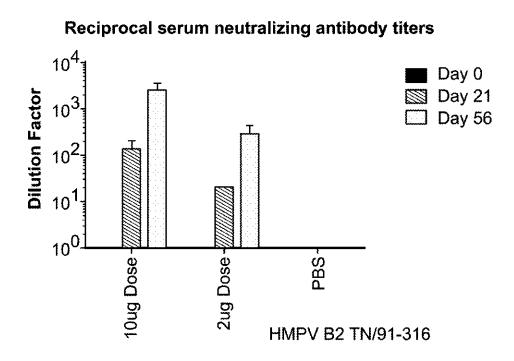
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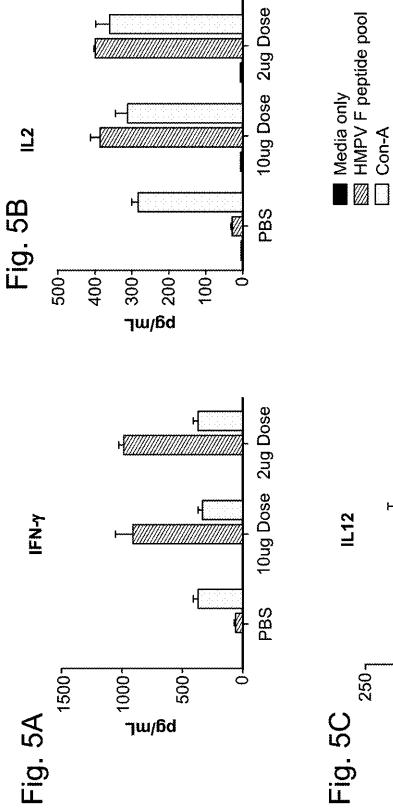


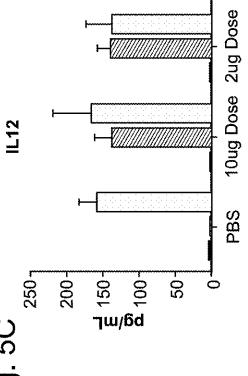
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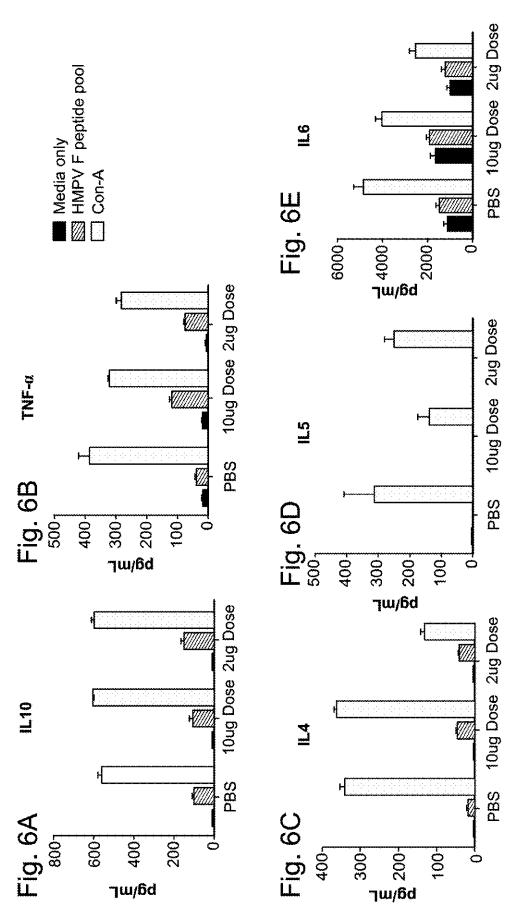


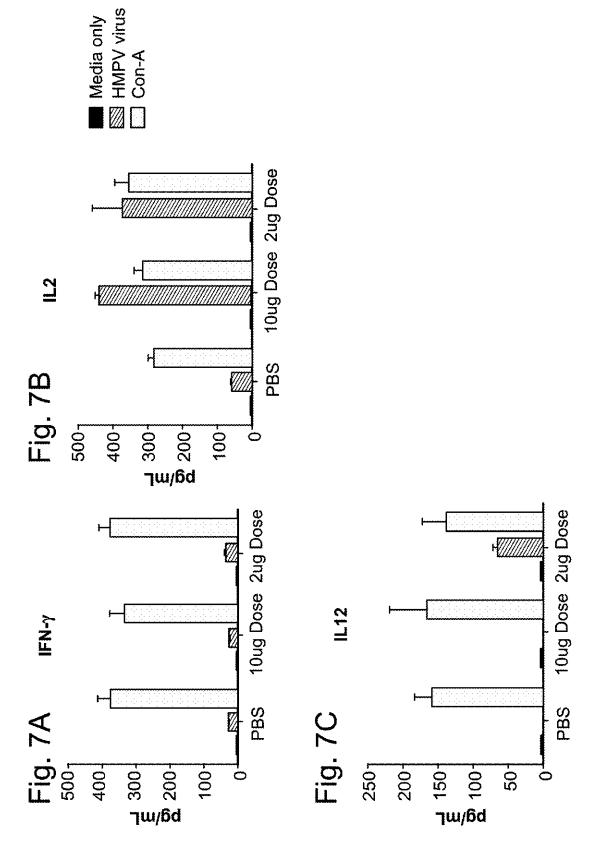


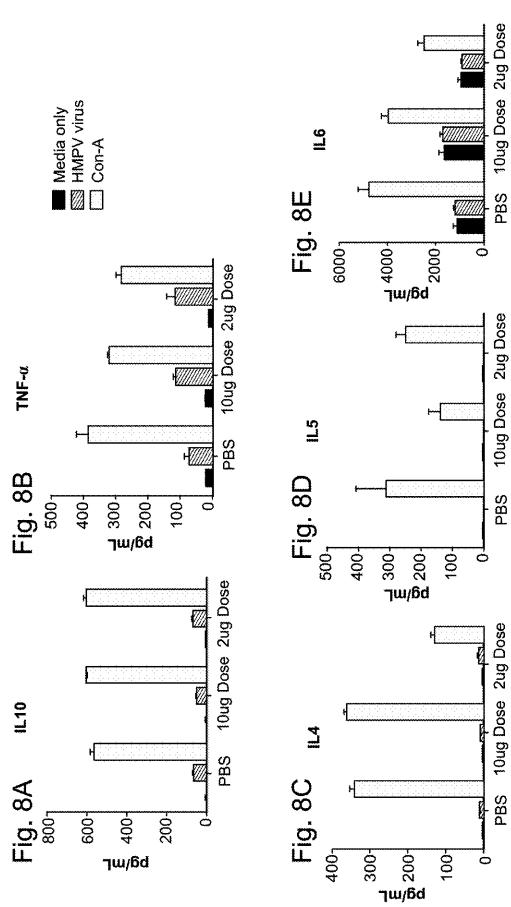


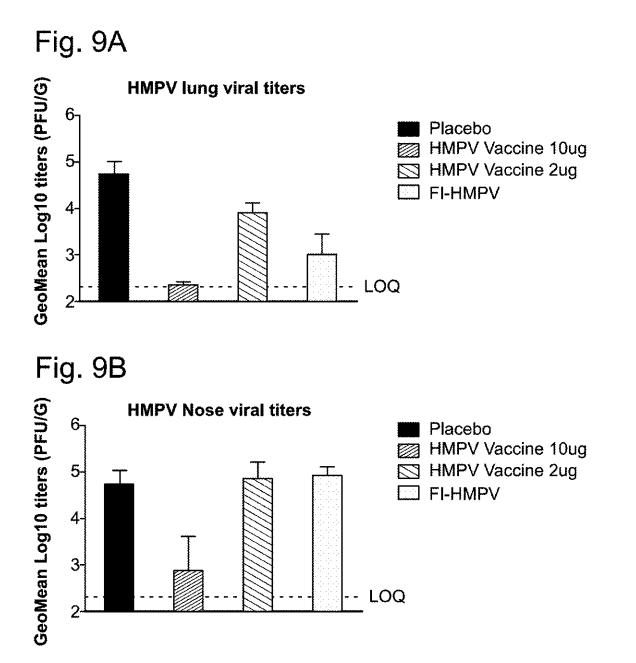


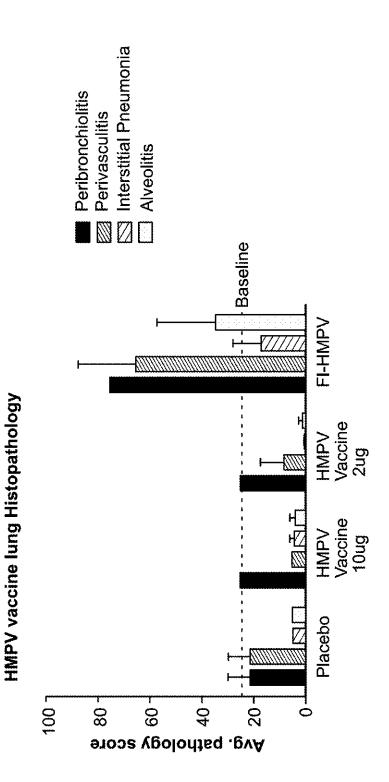


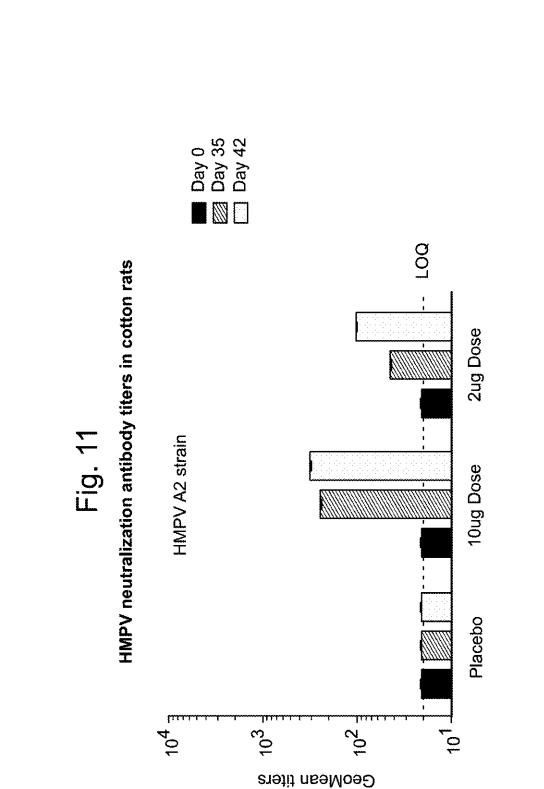


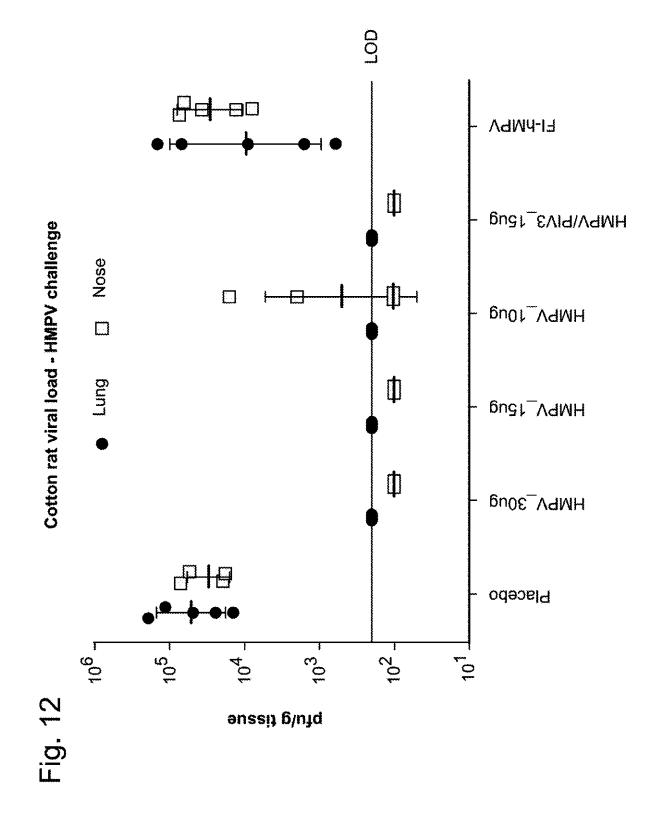


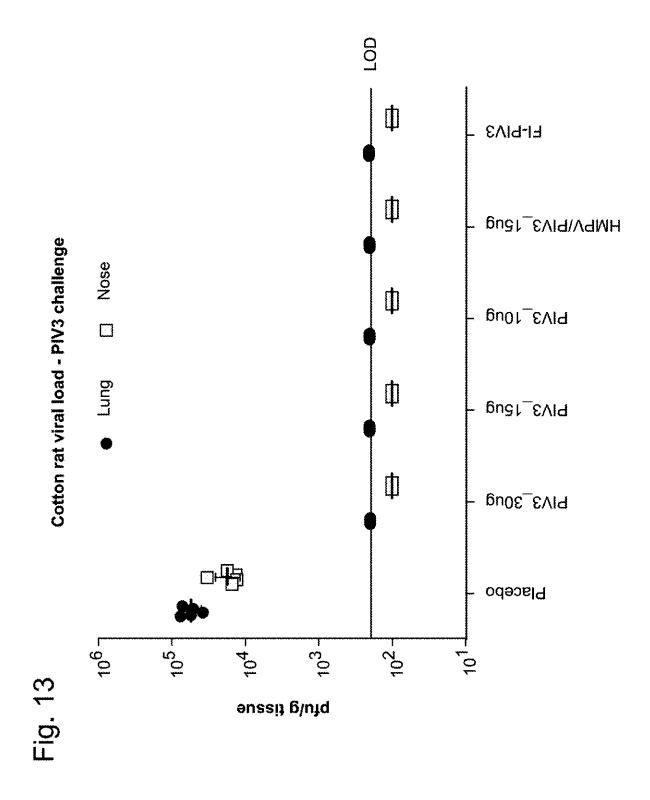


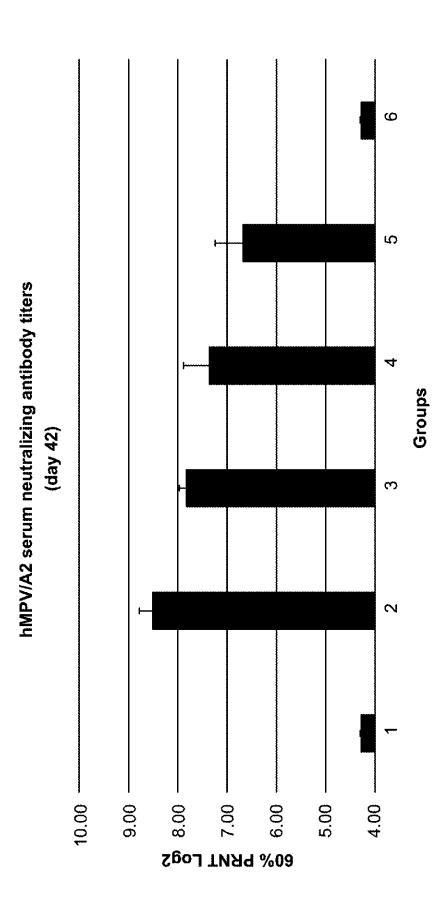


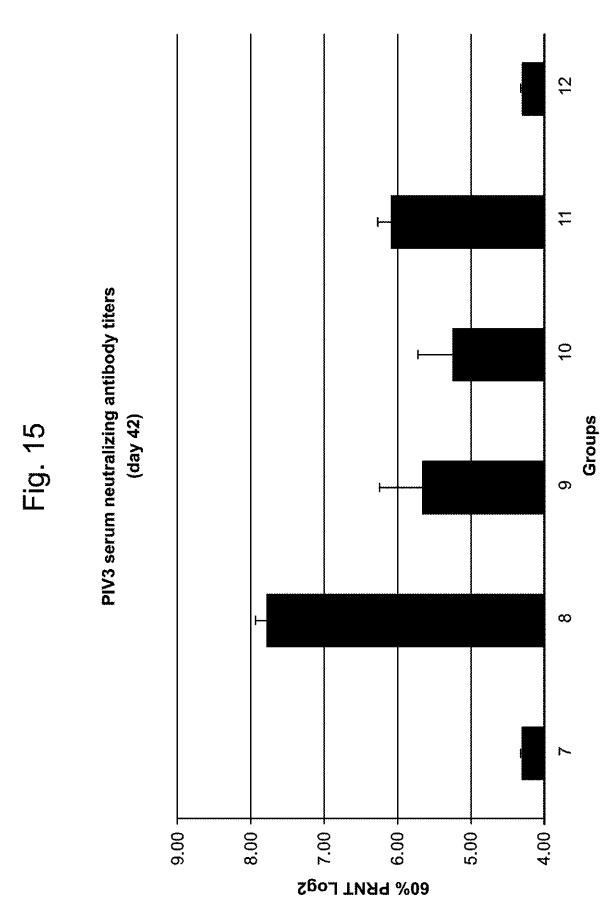




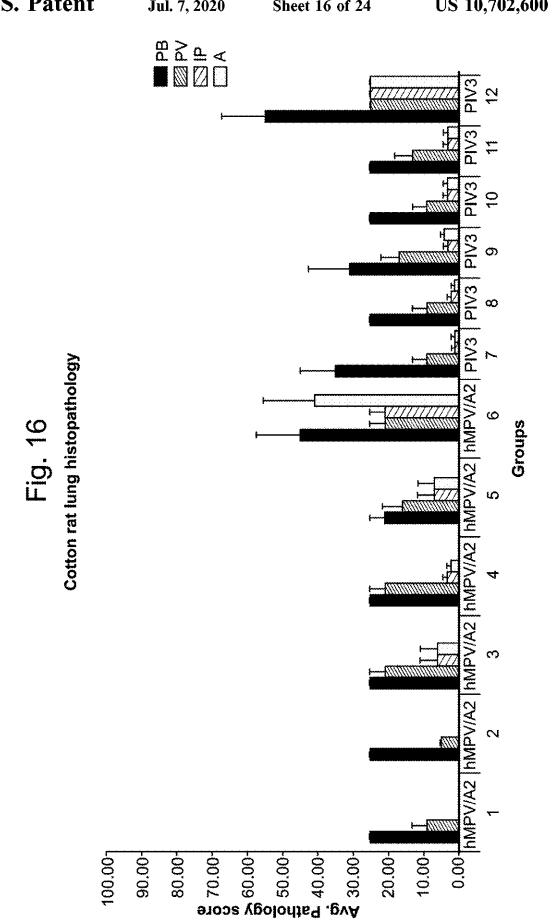








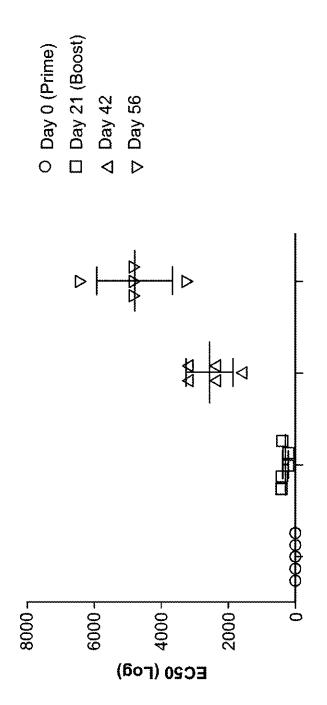
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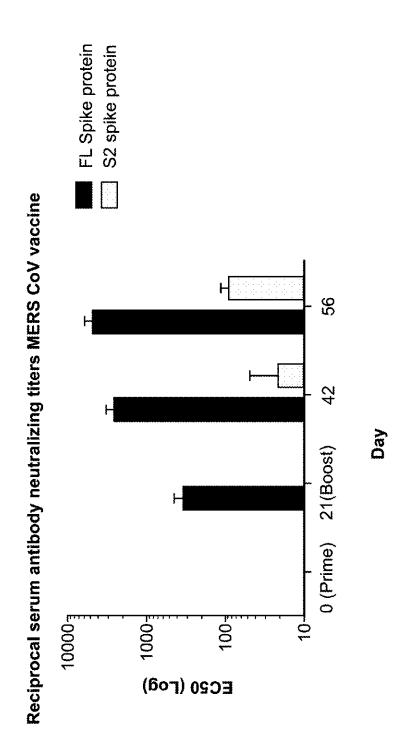






Reciprocal serum antibody neutralizing titers MERS CoV FL vaccine





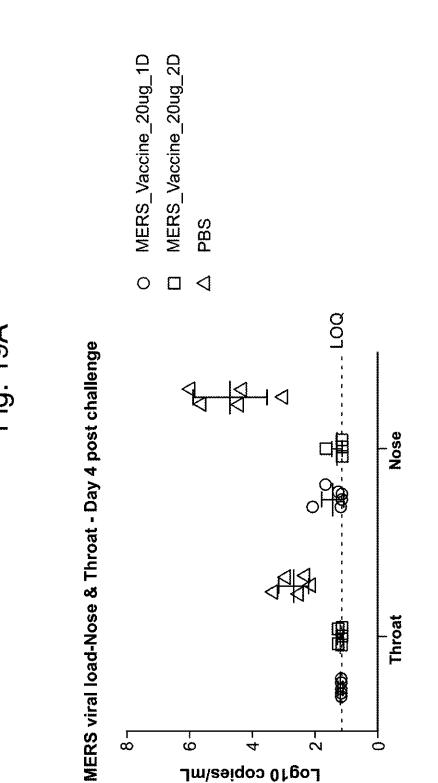


Fig. 19A

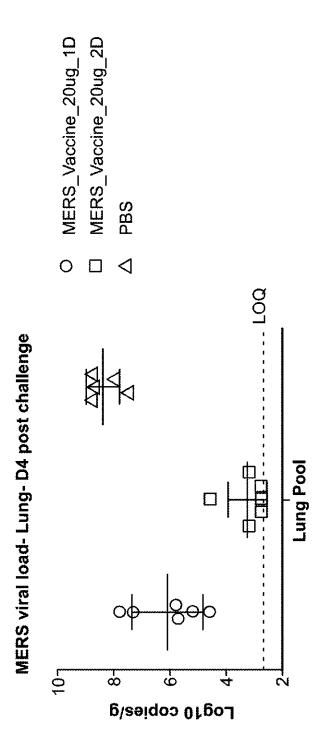
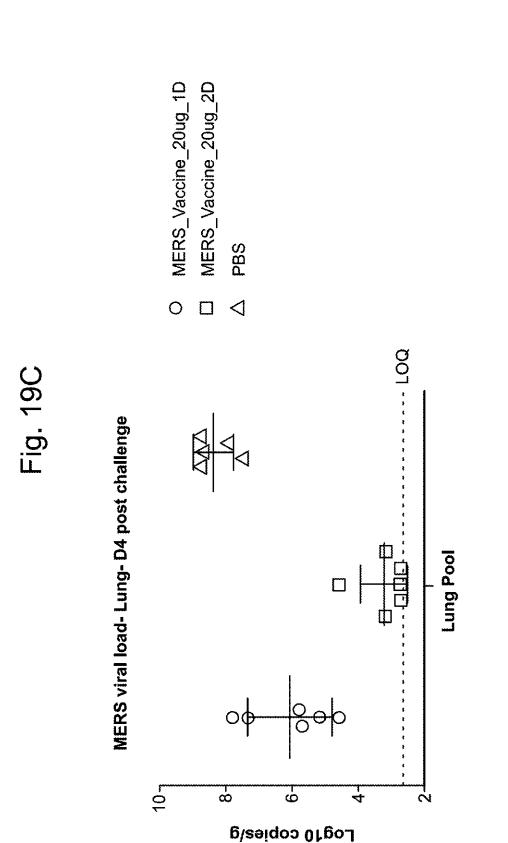
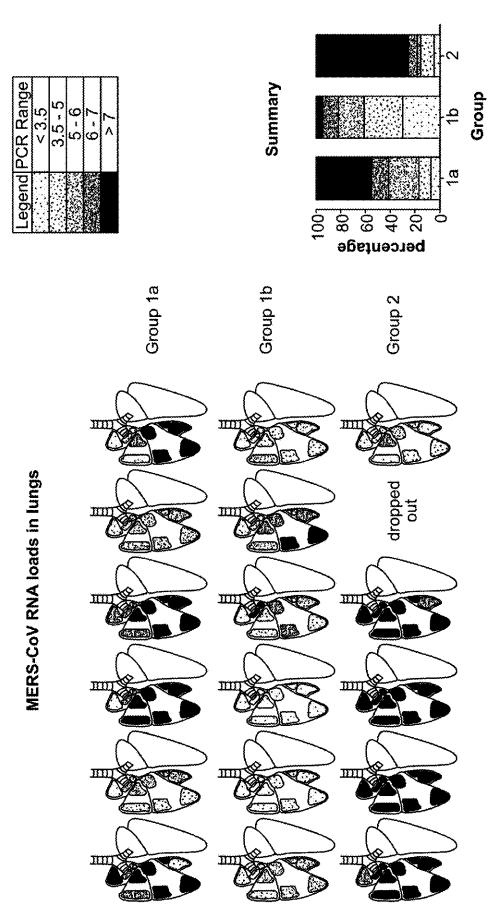
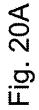


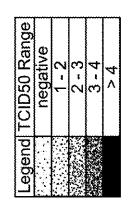
Fig. 19B

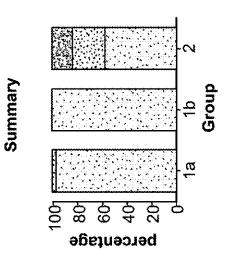


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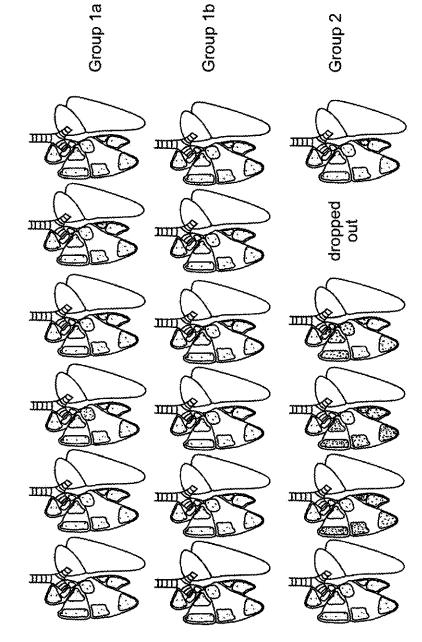






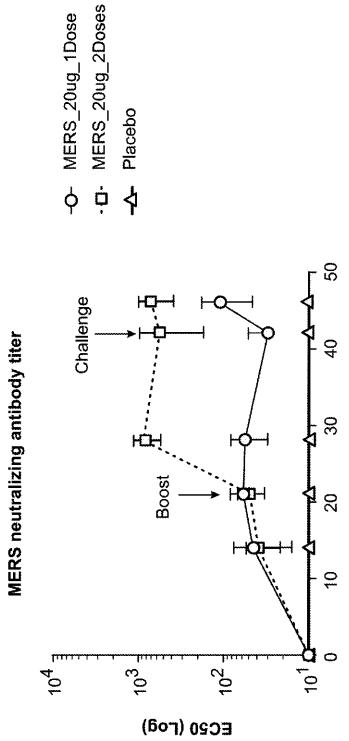


MERS-CoV replication in lungs





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BETACORONAVIRUS MRNA VACCINE

RELATED APPLICATIONS

This application is a continuation of U.S. application Ser. 5 No. 16/368,270, filed Mar. 28, 2019, which is a continuation of Ser. No. 16/040,981, filed Jul. 20, 2018, now U.S. Pat. No. 10,272,150, which is a continuation of U.S. application Ser. No. 15/674,599, filed Aug. 11, 2017, now U.S. Pat. No. 10,064,934, which is a continuation of International appli-10 cation number PCT/US2016/058327, filed Oct. 21, 2016, which claims the benefit under 35 U.S.C. § 119(e) of U.S. provisional application No. 62/244,802, filed Oct. 22, 2015, U.S. provisional application No. 62/247,297, filed Oct. 28, 2015, U.S. provisional application No. 62/244,946, filed 15 Oct. 22, 2015, U.S. provisional application No. 62/247,362, filed Oct. 28, 2015, U.S. provisional application No. 62/244, 813, filed Oct. 22, 2015, U.S. provisional application No. 62/247,394, filed Oct. 28, 2015, U.S. provisional application No. 62/244,837, filed Oct. 22, 2015, U.S. provisional appli- 20 cation No. 62/247,483, filed Oct. 28, 2015, and U.S. provisional application No. 62/245,031, filed Oct. 22, 2015, each of which is incorporated by reference herein in its entirety.

BACKGROUND

Respiratory disease is a medical term that encompasses pathological conditions affecting the organs and tissues that make gas exchange possible in higher organisms, and includes conditions of the upper respiratory tract, trachea, 30 bronchi, bronchioles, alveoli, pleura and pleural cavity, and the nerves and muscles of breathing. Respiratory diseases range from mild and self-limiting, such as the common cold, to life-threatening entities like bacterial pneumonia, pulmonary embolism, acute asthma and lung cancer. Respiratory 35 disease is a common and significant cause of illness and death around the world. In the US, approximately 1 billion "common colds" occur each year. Respiratory conditions are among the most frequent reasons for hospital stays among children. 40

The human metapneumovirus (hMPV) is a negativesense, single-stranded RNA virus of the genus Pneumovirinae and of the family Paramyxoviridae and is closely related to the avian metapneumovirus (AMPV) subgroup C. It was isolated for the first time in 2001 in the Netherlands by using 45 the RAP-PCR (RNA arbitrarily primed PCR) technique for identification of unknown viruses growing in cultured cells. hPMV is second only to RSV as an important cause of viral lower respiratory tract illness (LRI) in young children. The seasonal epidemiology of hMPV appears to be similar to that 50 of RSV, but the incidence of infection and illness appears to be substantially lower.

Parainfluenza virus type 3 (PIV3), like hMPV, is also a negative-sense, single-stranded sense RNA virus of the genus Pneumovirinae and of the family Paramyxoviridae 55 and is a major cause of ubiquitous acute respiratory infections of infancy and early childhood. Its incidence peaks around 4-12 months of age, and the virus is responsible for 3-10% of hospitalizations, mainly for bronchiolitis and pneumonia. PIV3 can be fatal, and in some instances is 60 associated with neurologic diseases, such as febrile seizures. It can also result in airway remodeling, a significant cause of morbidity. In developing regions of the world, infants and young children are at the highest risk of mortality, either from primary PIV3 viral infection or a secondary conse-65 quences, such as bacterial infections. Human parainfluenza viruses (hPIV) types 1, 2 and 3 (hPIV1, hPIV2 and hPIV3,

respectively), also like hMPV, are second only to RSV as important causes of viral LRI in young children.

RSV, too, is a negative-sense, single-stranded RNA virus of the genus Pneumovirinae and of the family Paramyxoviridae. Symptoms in adults typically resemble a sinus infection or the common cold, although the infection may be asymptomatic. In older adults (e.g., >60 years), RSV infection may progress to bronchiolitis or pneumonia. Symptoms in children are often more severe, including bronchiolitis and pneumonia. It is estimated that in the United States, most children are infected with RSV by the age of three. The RSV virion consists of an internal nucleocapsid comprised of the viral RNA bound to nucleoprotein (N), phosphoprotein (P), and large polymerase protein (L). The nucleocapsid is surrounded by matrix protein (M) and is encapsulated by a lipid bilayer into which the viral fusion (F) and attachment (G) proteins as well as the small hydrophobic protein (SH) are incorporated. The viral genome also encodes two nonstructural proteins (NS1 and NS2), which inhibit type I interferon activity as well as the M-2 protein.

The continuing health problems associated with hMPV, PIV3 and RSV are of concern internationally, reinforcing the importance of developing effective and safe vaccine candidates against these virus.

Despite decades of research, no vaccines currently exist (Sato and Wright, *Pediatr: Infect. Dis. J.* 2008; 27(10 Suppl): S123-5). Recombinant technology, however, has been used to target the formation of vaccines for hPIV-1, 2 and 3 serotypes, for example, and has taken the form of several live-attenuated intranasal vaccines. Two vaccines in particular were found to be immunogenic and well tolerated against hPIV-3 in phase I trials. hPIV1 and hPIV2 vaccine candidates remain less advanced (Durbin and Karron, Clinical infectious diseases: an official publication of the Infectious Diseases Society of America 2003; 37(12):1668-77).

Measles virus (MeV), like hMPV, PIV3 and RSV, is a negative-sense, single-stranded RNA virus that is the cause of measles, an infection of the respiratory system. MeV is of the genus Morbillivirus within the family Paramyxoviridae. Humans are the natural hosts of the virus; no animal reservoirs are known to exist. Symptoms of measles include fever, cough, runny nose, red eyes and a generalized, maculopapular, erythematous rash. The virus is highly contagious and is spread by coughing

In additional to hMPV, PIV, RSV and MeV, betacoronaviruses are known to cause respiratory illnesses. Betacoronaviruses (BetaCoVs) are one of four genera of coronaviruses of the subfamily Coronavirinae in the family Coronaviridae, of the order Nidovirales. They are enveloped, positive-sense, single-stranded RNA viruses of zoonotic origin. The coronavirus genera are each composed of varying viral lineages, with the betacoronavirus genus containing four such lineages. The BetaCoVs of the greatest clinical importance concerning humans are OC43 and HKU1 of the A lineage, SARS-CoV of the B lineage, and MERS-CoV of the C lineage. MERS-CoV is the first betacoronavirus belonging to lineage C that is known to infect humans.

The Middle East respiratory syndrome coronavirus (MERS-CoV), or EMC/2012 (HCoV-EMC/2012), initially referred to as novel coronavirus 2012 or simply novel coronavirus, was first reported in 2012 after genome sequencing of a virus isolated from sputum samples from a person who fell ill during a 2012 outbreak of a new flu. As of July 2015, MERS-CoV cases have been reported in over 21 countries. The outbreaks of MERS-CoV have raised

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serious concerns world-wide, reinforcing the importance of developing effective and safe vaccine candidates against MERS-CoV.

Severe acute respiratory syndrome (SARS) emerged in China in 2002 and spread to other countries before brought ⁵ under control. Because of a concern for reemergence or a deliberate release of the SARS coronavirus, vaccine development was initiated.

Deoxyribonucleic acid (DNA) vaccination is one technique used to stimulate humoral and cellular immune responses to foreign antigens, such as hMPV antigens and/or PIV antigens and/or RSV antigens. The direct injection of genetically engineered DNA (e.g., naked plasmid DNA) into a living host results in a small number of its cells directly producing an antigen, resulting in a protective immunological response. With this technique, however, comes potential problems, including the possibility of insertional mutagenesis, which could lead to the activation of oncogenes or the inhibition of tumor suppressor genes.

SUMMARY

Provided herein are ribonucleic acid (RNA) vaccines that build on the knowledge that RNA (e.g., messenger RNA 25 (mRNA)) can safely direct the body's cellular machinery to produce nearly any protein of interest, from native proteins to antibodies and other entirely novel protein constructs that can have therapeutic activity inside and outside of cells. The RNA (e.g., mRNA) vaccines of the present disclosure may 30 be used to induce a balanced immune response against hMPV, PIV, RSV, MeV, and/or BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1), or any combination of two or more of the foregoing viruses, comprising 35 both cellular and humoral immunity, without risking the possibility of insertional mutagenesis, for example, hMPV, PIV, RSV, MeV, BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) and combinations thereof are 40 referred to herein as "respiratory viruses." Thus, the term "respiratory virus RNA vaccines" encompasses hMPV RNA vaccines, PIV RNA vaccines, RSV RNA vaccines, MeV RNA vaccines, BetaCoV RNA vaccines, and any combination of two or more of hMPV RNA vaccines, PIV RNA 45 vaccines, RSV RNA vaccines, MeV RNA vaccines, and BetaCoV RNA vaccines.

The RNA (e.g., mRNA) vaccines may be utilized in various settings depending on the prevalence of the infection or the degree or level of unmet medical need. The RNA (e.g. 50 mRNA) vaccines may be utilized to treat and/or prevent a hMPV, PIV, RSV, MeV, a BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1), or any combination of two or more of the foregoing viruses, of various geno- 55 types, strains, and isolates. The RNA (e.g., mRNA) vaccines have superior properties in that they produce much larger antibody titers and produce responses earlier than commercially available anti-viral therapeutic treatments. While not wishing to be bound by theory, it is believed that the RNA 60 (e.g., mRNA) vaccines, as mRNA polynucleotides, are better designed to produce the appropriate protein conformation upon translation as the RNA (e.g., mRNA) vaccines co-opt natural cellular machinery. Unlike traditional vaccines, which are manufactured ex vivo and may trigger 65 unwanted cellular responses, RNA (e.g., mRNA) vaccines are presented to the cellular system in a more native fashion.

In some aspects the invention is a respiratory virus vaccine, comprising at least one RNA polynucleotide having an open reading frame encoding at least one respiratory virus antigenic polypeptide, formulated in a cationic lipid nanoparticle.

Surprisingly, in some aspects, it has also been shown that efficacy of mRNA vaccines can be significantly enhanced when combined with a flagellin adjuvant, in particular, when one or more antigen-encoding mRNAs is combined with an mRNA encoding flagellin.

RNA (e.g., mRNA) vaccines combined with the flagellin adjuvant (e.g., mRNA-encoded flagellin adjuvant) have superior properties in that they may produce much larger antibody titers and produce responses earlier than commer-15 cially available vaccine formulations. While not wishing to be bound by theory, it is believed that the RNA (e.g., mRNA) vaccines, for example, as mRNA polynucleotides, are better designed to produce the appropriate protein conformation upon translation, for both the antigen and the adjuvant, as the RNA (e.g., mRNA) vaccines co-opt natural cellular machinery. Unlike traditional vaccines, which are manufactured ex vivo and may trigger unwanted cellular responses, RNA (e.g., mRNA) vaccines are presented to the cellular system in a more native fashion.

Some embodiments of the present disclosure provide RNA (e.g., mRNA) vaccines that include at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide or an immunogenic fragment thereof (e.g., an immunogenic fragment capable of inducing an immune response to the antigenic polypeptide) and at least one RNA (e.g., mRNA polynucleotide) having an open reading frame encoding a flagellin adjuvant.

In some embodiments, at least one flagellin polypeptide (e.g., encoded flagellin polypeptide) is a flagellin protein. In some embodiments, at least one flagellin polypeptide (e.g., encoded flagellin polypeptide) is an immunogenic flagellin fragment. In some embodiments, at least one flagellin polypeptide and at least one antigenic polypeptide are encoded by a single RNA (e.g., mRNA) polynucleotide. In other embodiments, at least one flagellin polypeptide and at least one antigenic polypeptide are each encoded by a different RNA polynucleotide.

In some embodiments at least one flagellin polypeptide has at least 80%, at least 85%, at least 90%, or at least 95% identity to a flagellin polypeptide having a sequence identified by any one of SEQ ID NO: 54-56.

Provided herein, in some embodiments, is a ribonucleic acid (RNA) (e.g., mRNA) vaccine, comprising at least one (e.g., at least 2, 3, 4 or 5) RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, or a BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide, or any combination of two or more of the foregoing antigenic polypeptides. Herein, use of the term "antigenic polypeptide" encompasses immunogenic fragments of the antigenic polypeptide (an immunogenic fragment that is induces (or is capable of inducing) an immune response to hMPV, PIV, RSV, MeV, or a BetaCoV), unless otherwise stated.

Also provided herein, in some embodiments, is a RNA (e.g., mRNA) vaccine comprising at least one (e.g., at least 2, 3, 4 or 5) RNA polynucleotide having an open reading frame encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, and/or a BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63,

HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, linked to a signal peptide.

Further provided herein, in some embodiments, is a nucleic acid (e.g., DNA) encoding at least one (e.g., at least 5 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, and/or a BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) RNA (e.g., mRNA) polynucleotide.

Further still, provided herein, in some embodiments, is a 10 method of inducing an immune response in a subject, the method comprising administering to the subject a vaccine comprising at least one (e.g., at least 2, 3, 4 or 5) RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, 15 RSV, MeV, and/or a BetaCoV (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide, or any combination of two or more of the foregoing antigenic polypeptides. 20

hMPV/PIV3/RSV

In some embodiments, a RNA (e.g., mRNA) vaccine comprises at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3 or RSV antigenic polypeptide. In some embodiments, 25 at least one antigenic polypeptide is a hMPV, PIV3 or RSV polyprotein. In some embodiments, at least one antigenic polypeptide is major surface glycoprotein G or an immunogenic fragment thereof. In some embodiments, at least one antigenic polypeptide is Fusion (F) glycoprotein (e.g., 30 Fusion glycoprotein F0, F1 or F2) or an immunogenic fragment thereof. In some embodiments, at least one antigenic polypeptide is major surface glycoprotein G or an immunogenic fragment thereof and F glycoprotein or an immunogenic fragment thereof. In some embodiments, the 35 antigenic polypeptide is nucleoprotein (N) or an immunogenic fragment thereof, phosphoprotein (P) or an immunogenic fragment thereof, large polymerase protein (L) or an immunogenic fragment thereof, matrix protein (M) or an immunogenic fragment thereof, small hydrophobic protein 40 (SH) or an immunogenic fragment thereof nonstructural protein1 (NS1) or an immunogenic fragment thereof, or nonstructural protein 2 (NS2) and an immunogenic fragment thereof.

In some embodiments, at least one hMPV antigenic 45 polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 (Table 3; see also amino acid sequences of Table 4). In some embodiments, the amino acid sequence of the hMPV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% 50 (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 5-8 (Table 3; see also amino acid sequences of Table 4).

In some embodiments, at least one hMPV antigenic polypeptide is encoded by a nucleic acid sequence identified by any one of SEQ ID NO: 1-4 (Table 2). In some embodiments, at least one MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 4.4 (Table 2).

In some embodiments, at least one hMPV RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 1-4 (Table 2). In some embodi-60 ments, at least one hMPV RNA (e.g., mRNA) polynucle-otide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 57-60 (Table 2).

In some embodiments, at least one antigenic polypeptide 65 is obtained from hMPV strain CAN98-75 (CAN75) or the hMPV strain CAN97-83 (CAN83).

In some embodiments, at least one PIV3 antigenic polypeptide comprises hemagglutinin-neuraminidase, Fusion (F) glycoprotein, matrix protein (M), nucleocapsid protein (N), viral replicase (L), non-structural V protein, or an immunogenic fragment thereof.

In some embodiments, at least one PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 (Table 6; see also amino acid sequences of Table 7). In some embodiments, the amino acid sequence of the PIV3 antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 12-13 (Table 6; see also amino acid sequences of Table 7).

In some embodiments, at least one PIV3 antigenic polypeptide is encoded by a nucleic acid sequence identified by any one of SEQ ID NO: 9-12 (Table 5; see also nucleic acid sequences of Table 7).

In some embodiments, at least one PIV3 RNA (e.g., 20 mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 9-12 (Table 5; see also nucleic acid sequences of Table 7). In some embodiments, at least one PIV3 RNA (e.g., mRNA) polynucleotide comprises a 25 nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 61-64 (Table 5).

In some embodiments, at least one antigenic polypeptide is obtained from PIV3 strain HPIV3/Homo sapiens/PER/ FLA4815/2008.

In some embodiments, at least one RSV antigenic polypeptide comprises at least one antigenic polypeptide that comprises glycoprotein G, glycoprotein F, or an immunogenic fragment thereof. In some embodiments, at least one RSV antigenic polypeptide comprises at least one antigenic polypeptide that comprises glycoprotein F and at least one or at least two antigenic polypeptide selected from G, M, N, P, L, SH, M2, NS1 and NS2.



In some embodiments, a RNA (e.g., mRNA) vaccine comprises at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one MeV antigenic polypeptide. In some embodiments, at least one antigenic polypeptide is a hemagglutinin (HA) protein or an immunogenic fragment thereof. The HA protein may be from MeV strain D3 or B8, for example. In some embodiments, at least one antigenic polypeptide is a Fusion (F) protein or an immunogenic fragment thereof. The F protein may be from MeV strain D3 or B8, for example. In some embodiments, a MeV RNA (e.g., mRNA) vaccines comprises a least one RNA polynucleotide encoding a HA protein and a F protein. The HA and F proteins may be from MeV strain D3 or B8, for example.

In some embodiments, at least one MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 (Table 14). In some embodiments, the amino acid sequence of the MeV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 47-50 (Table 14).

In some embodiments, at least one MeV antigenic polypeptide is encoded by a nucleic acid sequence of SEQ ID NO: 35-46 (Table 13).

In some embodiments, at least one MeV RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified

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by any one of SEQ ID NO: 35-46 (Table 13). In some embodiments, at least one MeV RNA (e.g., mRNA) polynucleotide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 69-80 (Table 13).

In some embodiments, at least one antigenic polypeptide is obtained from MeV strain B3/B3.1, C2, D4, D6, D7, D8, G3, H1, Moraten, Rubeovax, MVi/New Jersey.USA/45.05, MVi/Texas.USA/4.07, AIK-C, MVi/New York.USA/26.09/ 3, MVi/California.USA/16.03, MVi/Virginia.USA/15.09, MVi/California.USA/8.04, or MVi/Pennsylvania.USA/ 20.09.

BetaCoV

In some embodiments, a RNA (e.g., mRNA) vaccine comprises at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one Beta-CoV antigenic polypeptide. In some embodiments, the Beta-CoV is MERS-CoV. In some embodiments, the BetaCoV is SARS-CoV. In some embodiments, the BetaCoV is HCoV- 20 OC43. In some embodiments, the BetaCoV is HCoV-229E. In some embodiments, the BetaCoV is HCoV-NL63. In some embodiments, the BetaCoV is HCoV-HKU1. In some embodiments, at least one antigenic polypeptide is a betacoronavirus structural protein. For example, a betacorona- 25 virus structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, a betacoronavirus structural protein is a spike protein (S). In some embodiments, a betacoronavirus structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

BetaCoV RNA (e.g., mRNA) polynucleotides of the vaccines provided herein may encode viral protein components 35 of betacoronaviruses, for example, accessory proteins, replicase proteins and the like are encompassed by the present disclosure. RNA (e.g., mRNA) vaccines may include RNA polynucleotides encoding at least one accessory protein (e.g., protein 3, protein 4a, protein 4b, protein 5), at least one 40 is a SARS-CoV structural protein. For example, a SARSreplicase protein (e.g., protein 1a, protein 1b), or a combination of at least one accessory protein and at least one replicase protein. The present disclosure also encompasses RNA (e.g., mRNA) vaccines comprising RNA (e.g., mRNA) polynucleotides encoding an accessory protein and/or a 45 replicase protein in combination with at least one structural protein. Due to their surface expression properties, vaccines featuring RNA polynucleotides encoding structural proteins are believed to have preferred immunogenic activity and, hence, may be most suitable for use in the vaccines of the 50 present disclosure.

Some embodiments of the present disclosure provide betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1 or a combination thereof) vaccines that 55 include at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide. Also provided herein are 60 pan-betacoronavirus vaccines. Thus, a betacoronavirus vaccine comprising a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding any one, two, three or four of MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, and HCoV-HKU1, for example, may be effec- 65 tive against any one of, any combination of, or all of, MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E,

HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1. Other betacoronaviruses are encompassed by the present disclosure.

In some embodiments, at least one antigenic polypeptide is a MERS-CoV structural protein. For example, a MERS-CoV structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the MERS-CoV structural protein is a spike protein (S) (see, e.g., Coleman C M et al. Vaccine 2014; 32:3169-74, incorporated herein by reference). In some embodiments, the MERS-CoV structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof (Li J et al. Viral Immunol 2013; 26(2):126-32; He Y et al. Biochem Biophys Res Commun 2004; 324(2):773-81, each of which is incorporated herein by reference).

In some embodiments, at least one MERS-CoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-28 or 33 (Table 11). In some embodiments, the amino acid sequence of the MERS-CoV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 24-28 or 33 (Table 11).

In some embodiments, at least one MERS-CoV antigenic polypeptide is encoded by a nucleic acid sequence identified by any one of SEQ ID NO: 20-23 (Table 10).

In some embodiments, at least one MERS-CoV RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 20-23 (Table 10). In some embodiments, at least one MERS-CoV RNA (e.g., mRNA) polynucleotide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 65-68 (Table 10).

In some embodiments, at least one antigenic polypeptide is obtained from MERS-CoV strain Rivadh 14 2013, 2cEMC/2012, or Hasa_1_2013.

In some embodiments, at least one antigenic polypeptide CoV structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the SARS-CoV structural protein is a spike protein (S). In some embodiments, the SARS-CoV structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

In some embodiments, at least one SARS-CoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 29, 32 or 34 (Table 11). In some embodiments, the amino acid sequence of the SARS-CoV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 29, 32 or 34 (Table 11).

In some embodiments, at least one antigenic polypeptide is a HCoV-OC43 structural protein. For example, a HCoV-OC43 structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the HCoV-OC43 structural protein is a spike protein (S). In some embodiments, the HCoV-OC43 structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

In some embodiments, at least one HCoV-OC43 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 30 (Table 11). In some embodiments, the amino acid sequence of the HCoV-OC43 antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 30 (Table 11).

In some embodiments, an antigenic polypeptide is a HCoV-HKU1 structural protein. For example, a HCoV-HKU1 structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodi-10 ments, the HCoV-HKU1 structural protein is a spike protein (S). In some embodiments, the HCoV-HKU1 structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

In some embodiments, at least one HCoV-HKU1 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 31 (Table 11). In some embodiments, the amino acid sequence of the HCoV-HKU1 antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 20 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 31 (Table 11).

In some embodiments, an open reading frame of a RNA (e.g., mRNA) vaccine is codon-optimized. In some embodiments, at least one RNA polynucleotide encodes at least one 25 antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and is codon optimized mRNA.

In some embodiments, a RNA (e.g., mRNA) vaccine 30 further comprising an adjuvant.

Tables 4, 7, 12 and 15 provide National Center for Biotechnology Information (NCBI) accession numbers of interest. It should be understood that the phrase "an amino acid sequence of Tables 4, 7, 12 and 15" refers to an amino 35 acid sequence identified by one or more NCBI accession numbers listed in Tables 4, 7, 12 and 15. Each of the amino acid sequences, and variants having greater than 95% identity or greater than 98% identity to each of the amino acid sequences encompassed by the accession numbers of Tables 40 4, 7, 12 and 15 are included within the constructs (polynucleotides/polypeptides) of the present disclosure.

In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 45 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 80% identity to wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 50 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 75%, 85% or 95% identity to a wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of 55SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 50-80%, 60-80%, 40-80%, 30-80%, 70-80%, 75-80% or 78-80% identity to wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is 60 encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 40-85%, 50-85%, 60-85%, 30-85%, 70-85%, 75-85% or 80-85% identity to wild-type mRNA 65 sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence

identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 40-90%, 50-90%, 60-90%, 30-90%, 70-90%, 75-90%, 80-90%, or 85-90% identity to wild-type mRNA sequence.

In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to wild-type mRNA sequence, but does not include wild-type mRNA sequence.

In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and has less than 95%, 90%, 85%, 80% or 75% identity to wild-type mRNA sequence.

In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and has 30-80%, 40-80%, 50-80%, 60-80%, 70-80%, 75-80% or 78-80%, 30-85%, 40-85%, 50-805%, 60-85%, 70-85%, 75-85% or 78-85%, 30-90%, 40-90%, 50-90%, 60-90%, 70-90%, 75-90%, 80-90% or 85-90% identity to wild-type mRNA sequence.

In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15). In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having 95%-99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15).

In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and having membrane fusion activity. In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having 95%-99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and having membrane fusion activity.

In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) that attaches to cell receptors.

In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) that causes fusion of viral and cellular membranes.

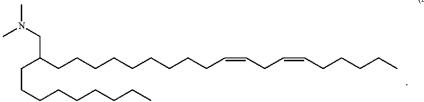
In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic

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a cationic lipid is selected from the group consisting of 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), (12Z,15Z)—N,N-dimethyl-2-nonylhenicosa-12,15-dien-1amine (L608), and N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]heptadecan-8-amine (L530).

In some embodiments, the lipid is (L608). In some embodiments, the lipid is

(L608)



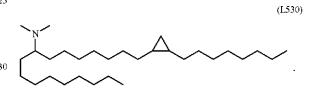
polypeptide, at least one RSV antigenic polypeptide, at least ²⁵ one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) ³⁰ that is responsible for binding of the virus to a cell being infected.

Some embodiments of the present disclosure provide a vaccine that includes at least one ribonucleic acid (RNA) (e.g., mRNA) polynucleotide having an open reading frame 35 encoding at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, 40 SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides), at least one 5' terminal cap and at least one chemical modification, formulated within a lipid nanoparticle.

In some embodiments, a 5' terminal cap is 7mG(5')ppp (5')NlmpNp.

In some embodiments, at least one chemical modification is selected from pseudouridine, N1-methylpseudouridine, 2-thiouridine, N1-ethylpseudouridine, 4'-thiouridine, 50 5-methylcytosine, 5-methyluridine, 2-thio-1-methyl-1deaza-pseudouridine, 2-thio-1-methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thiodihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thiopseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl- 55 pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyl uridine. In some embodiments, the chemical modification is in the 5-position of the uracil. In some embodiments, the chemical modification is a N1-methylpseudouridine. In 60 some embodiments, the chemical modification is a N1-ethylpseudouridine.

In some embodiments, a lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a noncationic lipid. In some embodiments, a cationic lipid is an 65 ionizable cationic lipid and the non-cationic lipid is a neutral lipid, and the sterol is a cholesterol. In some embodiments,



In some embodiments, a lipid nanoparticle comprises compounds of Formula (I) and/or Formula (II), discussed below.

In some embodiments, a repiratory virus RNA (e.g., mRNA) vaccine is formulated in a lipid nanoparticle that comprises a compound selected from Compounds 3, 18, 20, 25, 26, 29, 30, 60, 108-112 and 122, described below.

Some embodiments of the present disclosure provide a vaccine that includes at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides), wherein at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) of the uracil in the open reading frame have a chemical modification, optionally wherein the vaccine is formulated in a lipid nanoparticle (e.g., a lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid).

In some embodiments, 100% of the uracil in the open reading frame have a chemical modification. In some embodiments, a chemical modification is in the 5-position of the uracil. In some embodiments, a chemical modification is a N1-methyl pseudouridine. In some embodiments, 100% of the uracil in the open reading frame have a N1-methyl pseudouridine in the 5-position of the uracil.

In some embodiments, an open reading frame of a RNA (e.g., mRNA) polynucleotide encodes at least two antigenic polypeptides (e.g., at least two hMPV antigenic polypeptides, at least two PIV3 antigenic polypeptides, at least two

RSV antigenic polypeptides, at least two MeV antigenic polypeptides, or at least two BetaCoV antigenic polypeptides, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the 5 foregoing antigenic polypeptides). In some embodiments, the open reading frame encodes at least five or at least ten antigenic polypeptides. In some embodiments, the open reading frame encodes at least 100 antigenic polypeptides. In some embodiments, the open reading frame encodes 10 2-100 antigenic polypeptides.

In some embodiments, a vaccine comprises at least two RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one 15 PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or 20 any combination of two or more of the foregoing antigenic polypeptides). In some embodiments, the vaccine comprises at least five or at least ten RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide or an immunogenic fragment 25 thereof. In some embodiments, the vaccine comprises at least 100 RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide. In some embodiments, the vaccine comprises 2-100 RNA (e.g., mRNA) polynucleotides, each having an 30 open reading frame encoding at least one antigenic polypeptide.

In some embodiments, at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic 35 methods of inducing an antigen specific immune response in polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic 40 polypeptides) is fused to a signal peptide. In some embodiments, the signal peptide is selected from: a HulgGk signal peptide (METPAQLLFLLLWLPDTTG; SEQ ID NO: 15); IgE heavy chain epsilon-1 signal peptide (MDWTWIL-FLVAAATRVHS; SEQ ID NO: 16); Japanese encephalitis 45 PRM signal sequence (MLGSNSGQRVVFTILLLLVA-PAYS; SEQ ID NO: 17), VSVg protein signal sequence (MKCLLYLAFLFIGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWLVSLAIVTA-CAGA; SEQ ID NO: 19). 50

In some embodiments, the signal peptide is fused to the N-terminus of at least one antigenic polypeptide. In some embodiments, a signal peptide is fused to the C-terminus of at least one antigenic polypeptide.

In some embodiments, at least one antigenic polypeptide 55 (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, 60 HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) comprises a mutated N-linked glycosylation site.

Also provided herein is a RNA (e.g., mRNA) vaccine of 65 any one of the foregoing paragraphs (e.g., a hMPV vaccine, a PIV3 vaccine, a RSV vaccine, a MeV vaccine, or a

BetaCoV vaccine, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing vaccines), formulated in a nanoparticle (e.g., a lipid nanoparticle).

In some embodiments, the nanoparticle has a mean diameter of 50-200 nm. In some embodiments, the nanoparticle is a lipid nanoparticle. In some embodiments, the lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid. In some embodiments, the lipid nanoparticle comprises a molar ratio of about 20-60% cationic lipid, 0.5-15% PEG-modified lipid, 25-55% sterol, and 25% non-cationic lipid. In some embodiments, the cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid, and the sterol is a cholesterol. In some embodiments, the cationic lipid is selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319).

In some embodiments, a lipid nanoparticle comprises compounds of Formula (I) and/or Formula (II), as discussed below.

In some embodiments, a lipid nanoparticle comprises Compounds 3, 18, 20, 25, 26, 29, 30, 60, 108-112, or 122, as discussed below.

In some embodiments, the nanoparticle has a polydispersity value of less than 0.4 (e.g., less than 0.3, 0.2 or 0.1).

In some embodiments, the nanoparticle has a net neutral charge at a neutral pH value.

In some embodiments, the respiratory virus vaccine is multivalent.

Some embodiments of the present disclosure provide a subject, comprising administering to the subject any of the RNA (e.g., mRNA) vaccine as provided herein in an amount effective to produce an antigen-specific immune response. In some embodiments, the RNA (e.g., mRNA) vaccine is a hMPV vaccine, a PIV3 vaccine, a RSV vaccine, a MeV vaccine, or a BetaCoV vaccine, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1 vaccines. In some embodiments, the RNA (e.g., mRNA) vaccine is a combination vaccine comprising a combination of any two or more of the foregoing vaccines.

In some embodiments, an antigen-specific immune response comprises a T cell response or a B cell response.

In some embodiments, a method of producing an antigenspecific immune response comprises administering to a subject a single dose (no booster dose) of a RNA (e.g., mRNA) vaccine of the present disclosure. In some embodiments, the RNA (e.g., mRNA) vaccine is a hMPV vaccine, a PIV3 vaccine, a RSV vaccine, a MeV vaccine, or a BetaCoV vaccine, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1 vaccines. In some embodiments, the RNA (e.g., mRNA) vaccine is a combination vaccine comprising a combination of any two or more of the foregoing vaccines.

In some embodiments, a method further comprises administering to the subject a second (booster) dose of a RNA (e.g., mRNA) vaccine. Additional doses of a RNA (e.g., mRNA) vaccine may be administered.

In some embodiments, the subjects exhibit a seroconversion rate of at least 80% (e.g., at least 85%, at least 90%, or at least 95%) following the first dose or the second (booster)

dose of the vaccine. Seroconversion is the time period during which a specific antibody develops and becomes detectable in the blood. After seroconversion has occurred, a virus can be detected in blood tests for the antibody. During an infection or immunization, antigens enter the 5 blood, and the immune system begins to produce antibodies in response. Before seroconversion, the antigen itself may or may not be detectable, but antibodies are considered absent. During seroconversion, antibodies are present but not yet detectable. Any time after seroconversion, the antibodies can 10 be detected in the blood, indicating a prior or current infection.

In some embodiments, a RNA (e.g., mRNA) vaccine is administered to a subject by intradermal or intramuscular injection.

Some embodiments, of the present disclosure provide methods of inducing an antigen specific immune response in a subject, including administering to a subject a RNA (e.g., mRNA) vaccine in an effective amount to produce an antigen specific immune response in a subject. Antigen- 20 PIV3, RSV, MeV and/or BetaCoV vaccine, or a hMPV, specific immune responses in a subject may be determined, in some embodiments, by assaying for antibody titer (for titer of an antibody that binds to a hMPV, PIV3, RSV, MeV and/or BetaCoV antigenic polypeptide) following administration to the subject of any of the RNA (e.g., mRNA) 25 vaccines of the present disclosure. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by at least 1 log relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by 1-3 log relative 30 to a control.

In some embodiments, the anti-antigenic polypeptide antibody titer produced in a subject is increased at least 2 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the 35 subject is increased at least 5 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased at least 10 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is 40 increased 2-10 times relative to a control.

In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has not been administered a RNA (e.g., mRNA) vaccine of the present disclosure. In some embodiments, the control is an 45 anti-antigenic polypeptide antibody titer produced in a subject who has been administered a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine (see, e.g., Ren J. et al. J of Gen. Virol. 2015; 96: 1515-1520), or wherein the control is an anti-antigenic polypeptide 50 antibody titer produced in a subject who has been administered a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a hMPV, 55 PIV3, RSV, MeV and/or BetaCoV virus-like particle (VLP) vaccine (see, e.g., Cox R G et al., J Virol. 2014 June; 88(11): 6368-6379).

A RNA (e.g., mRNA) vaccine of the present disclosure is administered to a subject in an effective amount (an amount 60 effective to induce an immune response). In some embodiments, the effective amount is a dose equivalent to an at least 2-fold, at least 4-fold, at least 10-fold, at least 100-fold, at least 1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV 65 protein vaccine, wherein the anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an

anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a live attenuated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, an inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, or a hMPV, PIV3, RSV, MeV and/or BetaCoV VLP vaccine. In some embodiments, the effective amount is a dose equivalent to 2-1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, wherein the anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a live attenuated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, an inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV VLP vaccine.

In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a virus-like particle (VLP) vaccine comprising structural proteins of hMPV, PIV3, RSV, MeV and/or BetaCoV.

In some embodiments, the RNA (e.g., mRNA) vaccine is formulated in an effective amount to produce an antigen specific immune response in a subject.

In some embodiments, the effective amount is a total dose of 25 µg to 1000 µg, or 50 µg to 1000 µg. In some embodiments, the effective amount is a total dose of $100 \,\mu g$. In some embodiments, the effective amount is a dose of 25 µg administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 100 µg administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 400 µg administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 500 µg administered to the subject a total of two times.

In some embodiments, the efficacy (or effectiveness) of a RNA (e.g., mRNA) vaccine is greater than 60%. In some embodiments, the RNA (e.g., mRNA) polynucleotide of the vaccine at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides.

Vaccine efficacy may be assessed using standard analyses (see, e.g., Weinberg et al., J Infect Dis. 2010 Jun. 1; 201(11):1607-10). For example, vaccine efficacy may be measured by double-blind, randomized, clinical controlled trials. Vaccine efficacy may be expressed as a proportionate reduction in disease attack rate (AR) between the unvaccinated (ARU) and vaccinated (ARV) study cohorts and can be calculated from the relative risk (RR) of disease among the vaccinated group with use of the following formulas:

Likewise, vaccine effectiveness may be assessed using standard analyses (see, e.g., Weinberg et al., J Infect Dis. 2010 Jun. 1; 201(11):1607-10). Vaccine effectiveness is an

Efficacy=(ARU-ARV)/ARU×100; and

Efficacy=(1-RR)×100.

assessment of how a vaccine (which may have already proven to have high vaccine efficacy) reduces disease in a population. This measure can assess the net balance of benefits and adverse effects of a vaccination program, not just the vaccine itself, under natural field conditions rather than in a controlled clinical trial. Vaccine effectiveness is proportional to vaccine efficacy (potency) but is also affected by how well target groups in the population are immunized, as well as by other non-vaccine-related factors that influence the 'real-world' outcomes of hospitalizations, ambulatory visits, or costs. For example, a retrospective case control analysis may be used, in which the rates of vaccination among a set of infected cases and appropriate controls are compared. Vaccine effectiveness may be expressed as a 15 rate difference, with use of the odds ratio (OR) for developing infection despite vaccination:

Effectiveness=(1-OR)×100.

In some embodiments, the efficacy (or effectiveness) of a 20 RNA (e.g., mRNA) vaccine is at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, or at least 90%.

In some embodiments, the vaccine immunizes the subject against hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses for up to 2 years. In some embodiments, the vaccine immunizes the subject against hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses for more than 2 years, more than 3 years, more than 4 years, or for 5-10 years. 35

In some embodiments, the subject is about 5 years old or younger. For example, the subject may be between the ages of about 1 year and about 5 years (e.g., about 1, 2, 3, 5 or 5 years), or between the ages of about 6 months and about 1 year (e.g., about 6, 7, 8, 9, 10, 11 or 12 months). In some 40 embodiments, the subject is about 12 months or younger (e.g., 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2 months or 1 month). In some embodiments, the subject is about 6 months or younger.

In some embodiments, the subject was born full term 45 (e.g., about 37-42 weeks). In some embodiments, the subject was born prematurely, for example, at about 36 weeks of gestation or earlier (e.g., about 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26 or 25 weeks). For example, the subject may have been born at about 32 weeks of gestation or earlier. In some 50 embodiments, the subject was born prematurely between about 32 weeks and about 36 weeks of gestation. In such subjects, a RNA (e.g., mRNA) vaccine may be administered later in life, for example, at the age of about 6 months to about 5 years, or older. 55

In some embodiments, the subject is pregnant (e.g., in the first, second or third trimester) when administered an RNA (e.g., mRNA) vaccine. Viruses such as hMPV, PIV3 and RSV causes infections of the lower respiratory tract, mainly in infants and young children. One-third of RSV related 60 deaths, for example, occur in the first year of life, with 99 percent of these deaths occurring in low-resource countries. It's so widespread in the United States that nearly all children become infected with the virus before their second birthdays. Thus, the present disclosure provides RNA (e.g., 65 mRNA) vaccines for maternal immunization to improve mother-to-child transmission of protection against the virus.

In some embodiments, the subject is a young adult between the ages of about 20 years and about 50 years (e.g., about 20, 25, 30, 35, 40, 45 or 50 years old).

In some embodiments, the subject is an elderly subject about 60 years old, about 70 years old, or older (e.g., about 60, 65, 70, 75, 80, 85 or 90 years old).

In some embodiments, the subject is has a chronic pulmonary disease (e.g., chronic obstructive pulmonary disease (COPD) or asthma). Two forms of COPD include chronic bronchitis, which involves a long-term cough with mucus, and emphysema, which involves damage to the lungs over time. Thus, a subject administered a RNA (e.g., mRNA) vaccine may have chronic bronchitis or emphysema.

In some embodiments, the subject has been exposed to hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses; the subject is infected with hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses; or subject is at risk of infection by hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-NL63, HCoV-NL, HCoV-NL63, HCoV-229E, HCoV-NL63, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses.

In some embodiments, the subject is immunocompromised (has an impaired immune system, e.g., has an immune disorder or autoimmune disorder).

In some embodiments the nucleic acid vaccines described herein are chemically modified. In other embodiments the nucleic acid vaccines are unmodified.

Yet other aspects provide compositions for and methods of vaccinating a subject comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first respiratory virus antigenic polypeptide, wherein the RNA polynucleotide does not include a stabilization ele-40 ment, and wherein an adjuvant is not coformulated or co-administered with the vaccine.

In other aspects the invention is a composition for or method of vaccinating a subject comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide wherein a dosage of between 10 µg/kg and 400 µg/kg of the nucleic acid vaccine is administered to the subject. In some embodiments the dosage of the RNA polynucleotide is 1-5 µg, 5-10 µg, 10-15 $\mu g,\,15\text{-}20\,\mu g,\,10\text{-}25\,\mu g,\,20\text{-}25\,\mu g,\,20\text{-}50\,\mu g,\,30\text{-}50\,\mu g,\,40\text{-}50$ $\mu g,\,40\text{-}60~\mu g,\,60\text{-}80~\mu g,\,60\text{-}100~\mu g,\,50\text{-}100~\mu g,\,80\text{-}120~\mu g,$ 40-120 µg, 40-150 µg, 50-150 µg, 50-200 µg, 80-200 µg, 100-200 µg, 120-250 µg, 150-250 µg, 180-280 µg, 200-300 μg, 50-300 μg, 80-300 μg, 100-300 μg, 40-300 μg, 50-350 55 µg, 100-350 µg, 200-350 µg, 300-350 µg, 320-400 µg, 40-380 µg, 40-100 µg, 100-400 µg, 200-400 µg, or 300-400 µg per dose. In some embodiments, the nucleic acid vaccine is administered to the subject by intradermal or intramuscular injection. In some embodiments, the nucleic acid vaccine is administered to the subject on day zero. In some embodiments, a second dose of the nucleic acid vaccine is administered to the subject on day twenty one.

In some embodiments, a dosage of 25 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 100 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some

embodiments, a dosage of 50 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 75 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some 5 embodiments, a dosage of 150 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 400 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some 10 embodiments, a dosage of 200 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, the RNA polynucleotide accumulates at a 100 fold higher level in the local lymph node in comparison with the distal lymph node. 15 In other embodiments the nucleic acid vaccine is chemically modified and in other embodiments the nucleic acid vaccine is not chemically modified.

Aspects of the invention provide a nucleic acid vaccine comprising one or more RNA polynucleotides having an 20 open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide does not include a stabilization element, and a pharmaceutically acceptable carrier or excipient, wherein an adjuvant is not included in the vaccine. In some embodiments, the stabilization element is 25 a histone stem-loop. In some embodiments, the stabilization element is a nucleic acid sequence having increased GC content relative to wild type sequence.

Aspects of the invention provide nucleic acid vaccines comprising one or more RNA polynucleotides having an 30 open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide is present in the formulation for in vivo administration to a host, which confers an antibody titer superior to the criterion for seroprotection for the first antigen for an acceptable percentage of human 35 subjects. In some embodiments, the antibody titer produced by the mRNA vaccines of the invention is a neutralizing antibody titer. In some embodiments the neutralizing antibody titer is greater than a protein vaccine. In other embodiments the neutralizing antibody titer produced by the mRNA 40 vaccines of the invention is greater than an adjuvanted protein vaccine. In yet other embodiments the neutralizing antibody titer produced by the mRNA vaccines of the invention is 1,000-10,000, 1,200-10,000, 1,400-10,000, 1,500-10,000, 1,000-5,000, 1,000-4,000, 1,800-10,000, 45 2000-10,000, 2,000-5,000, 2,000-3,000, 2,000-4,000, 3,000-5.000, 3.000-4.000, or 2.000-2.500. A neutralization titer is typically expressed as the highest serum dilution required to achieve a 50% reduction in the number of plaques.

Also provided are nucleic acid vaccines comprising one 50 or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide is present in a formulation for in vivo administration to a host for eliciting a longer lasting high antibody titer than an antibody titer elicited by an mRNA vaccine 55 having a stabilizing element or formulated with an adjuvant and encoding the first antigenic polypeptide. In some embodiments, the RNA polynucleotide is formulated to produce a neutralizing antibodies within one week of a single administration. In some embodiments, the adjuvant is 60 selected from a cationic peptide and an immunostimulatory nucleic acid. In some embodiments, the cationic peptide is protamine.

Aspects provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame 65 comprising at least one chemical modification or optionally no nucleotide modification, the open reading frame encod-

ing a first antigenic polypeptide, wherein the RNA polynucleotide is present in the formulation for in vivo administration to a host such that the level of antigen expression in the host significantly exceeds a level of antigen expression produced by an mRNA vaccine having a stabilizing element or formulated with an adjuvant and encoding the first antigenic polypeptide.

Other aspects provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification or optionally no nucleotide modification, the open reading frame encoding a first antigenic polypeptide, wherein the vaccine has at least 10 fold less RNA polynucleotide than is required for an unmodified mRNA vaccine to produce an equivalent antibody titer. In some embodiments, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

Aspects of the invention also provide a unit of use vaccine, comprising between 10 ug and 400 ug of one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification or optionally no nucleotide modification, the open reading frame encoding a first antigenic polypeptide, and a pharmaceutically acceptable carrier or excipient, formulated for delivery to a human subject. In some embodiments, the vaccine further comprises a cationic lipid nanoparticle.

Aspects of the invention provide methods of creating, maintaining or restoring antigenic memory to a respiratory virus strain in an individual or population of individuals comprising administering to said individual or population an antigenic memory booster nucleic acid vaccine comprising (a) at least one RNA polynucleotide, said polynucleotide comprising at least one chemical modification or optionally no nucleotide modification and two or more codon-optimized open reading frames, said open reading frames encoding a set of reference antigenic polypeptides, and (b) optionally a pharmaceutically acceptable carrier or excipient. In some embodiments, the vaccine is administered to the individual via a route selected from the group consisting of intramuscular administration, intradermal administration and subcutaneous administration. In some embodiments, the administering step comprises contacting a muscle tissue of the subject with a device suitable for injection of the composition. In some embodiments, the administering step comprises contacting a muscle tissue of the subject with a device suitable for injection of the composition in combination with electroporation.

Aspects of the invention provide methods of vaccinating a subject comprising administering to the subject a single dosage of between 25 ug/kg and 400 ug/kg of a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide in an effective amount to vaccinate the subject.

Other aspects provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification, the open reading frame encoding a first antigenic polypeptide, wherein the vaccine has at least 10 fold less RNA polynucleotide than is required for an unmodified mRNA vaccine to produce an equivalent antibody titer. In some embodiments, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

Other aspects provide nucleic acid vaccines comprising an LNP formulated RNA polynucleotide having an open reading frame comprising no nucleotide modifications (unmodified), the open reading frame encoding a first antigenic polypeptide, wherein the vaccine has at least 10 fold less RNA polynucleotide than is required for an unmodified

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mRNA vaccine not formulated in a LNP to produce an equivalent antibody titer. In some embodiments, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

The data presented in the Examples demonstrate significant enhanced immune responses using the formulations of 5 the invention. Both chemically modified and unmodified RNA vaccines are useful according to the invention. Surprisingly, in contrast to prior art reports that it was preferable to use chemically unmodified mRNA formulated in a carrier for the production of vaccines, it is described herein that 10 chemically modified mRNA-LNP vaccines required a much lower effective mRNA dose than unmodified mRNA, i.e., tenfold less than unmodified mRNA when formulated in carriers other than LNP. Both the chemically modified and unmodified RNA vaccines of the invention produce better 15 immune responses than mRNA vaccines formulated in a different lipid carrier.

In other aspects the invention encompasses a method of treating an elderly subject age 60 years or older comprising administering to the subject a nucleic acid vaccine compris- 20 ing one or more RNA polynucleotides having an open reading frame encoding a respiratory virus antigenic polypeptide in an effective amount to vaccinate the subject.

In other aspects the invention encompasses a method of treating a young subject age 17 years or younger comprising 25 administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a respiratory virus antigenic polypeptide in an effective amount to vaccinate the subject.

In other aspects the invention encompasses a method of 30 treating an adult subject comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a respiratory virus antigenic polypeptide in an effective amount to vaccinate the subject.

In some aspects the invention is a method of vaccinating a subject with a combination vaccine including at least two nucleic acid sequences encoding respiratory antigens wherein the dosage for the vaccine is a combined therapeutic dosage wherein the dosage of each individual nucleic acid 40 encoding an antigen is a sub therapeutic dosage. In some embodiments, the combined dosage is 25 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 100 micrograms of the RNA polynucleotide in the 45 nucleic acid vaccine administered to the subject. In some embodiments the combined dosage is 50 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 75 micrograms of the RNA polynucleotide in the 50 nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 150 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 400 micrograms of the RNA polynucleotide in the 55 nucleic acid vaccine administered to the subject. In some embodiments, the sub therapeutic dosage of each individual nucleic acid encoding an antigen is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 micrograms. In other embodiments the nucleic acid vaccine is chemically 60 modified and in other embodiments the nucleic acid vaccine is not chemically modified.

The RNA polynucleotide is one of SEQ ID NO: 1-4, 9-12, 20-23, 35-46, 57-61, and 64-80 and includes at least one chemical modification. In other embodiments the RNA 65 polynucleotide is one of SEQ ID NO: 1-4, 9-12, 20-23, 35-46, 57-61, and 64-80 and does not include any nucleotide

modifications, or is unmodified. In yet other embodiments the at least one RNA polynucleotide encodes an antigenic protein of any of SEQ ID NO: 5-8, 12-13, 24-34, and 47-50 and includes at least one chemical modification. In other embodiments the RNA polynucleotide encodes an antigenic protein of any of SEQ ID NO: 5-8, 12-13, 24-34, and 47-50 and does not include any nucleotide modifications, or is unmodified.

In preferred aspects, vaccines of the invention (e.g., LNP-encapsulated mRNA vaccines) produce prophylactically- and/or therapeutically-efficacious levels, concentrations and/or titers of antigen-specific antibodies in the blood or serum of a vaccinated subject. As defined herein, the term antibody titer refers to the amount of antigen-specific antibody produces in s subject, e.g., a human subject. In exemplary embodiments, antibody titer is expressed as the inverse of the greatest dilution (in a serial dilution) that still gives a positive result. In exemplary embodiments, antibody titer is determined or measured by enzyme-linked immunosorbent assay (ELISA). In exemplary embodiments, antibody titer is determined or measured by neutralization assay, e.g., by microneutralization assay. In certain aspects, antibody titer measurement is expressed as a ratio, such as 1:40, 1:100, etc. In exemplary embodiments of the invention, an efficacious vaccine produces an antibody titer of greater than 1:40, greater that 1:100, greater than 1:400, greater than 1:1000, greater than 1:2000, greater than 1:3000, greater than 1:4000, greater than 1:500, greater than 1:6000, greater than 1:7500, greater than 1:10000. In exemplary embodiments, the antibody titer is produced or reached by 10 days following vaccination, by 20 days following vaccination, by 30 days following vaccination, by 40 days following vaccination, or by 50 or more days following vaccination. In exemplary embodiments, the titer is produced or reached following a single dose of vaccine administered to the subject. In other embodiments, the titer is produced or reached following multiple doses, e.g., following a first and a second dose (e.g., a booster dose.) In exemplary aspects of the invention, antigen-specific antibodies are measured in units of µg/ml or are measured in units of IU/L (International Units per liter) or mIU/ml (milli International Units per ml). In exemplary embodiments of the invention, an efficacious vaccine produces >0.5 µg/ml, >0.1 µg/ml, >0.2 µg/ml, >0.35 $\mu g/ml$, >0.5 $\mu g/ml$, >1 $\mu g/ml$, >2 $\mu g/ml$, >5 $\mu g/ml$ or >10 µg/ml. In exemplary embodiments of the invention, an efficacious vaccine produces >10 mIU/ml, >20 mIU/ml, >50 mIU/ml, >100 mIU/ml, >200 mIU/ml, >500 mIU/ml or >1000 mIU/ml. In exemplary embodiments, the antibody level or concentration is produced or reached by 10 days following vaccination, by 20 days following vaccination, by 30 days following vaccination, by 40 days following vaccination, or by 50 or more days following vaccination. In exemplary embodiments, the level or concentration is produced or reached following a single dose of vaccine administered to the subject. In other embodiments, the level or concentration is produced or reached following multiple doses, e.g., following a first and a second dose (e.g., a booster dose.) In exemplary embodiments, antibody level or concentration is determined or measured by enzyme-linked immunosorbent assay (ELISA). In exemplary embodiments, antibody level or concentration is determined or measured by neutralization assay, e.g., by microneutralization assay.

The details of various embodiments of the disclosure are set forth in the description below. Other features, objects, 15

and advantages of the disclosure will be apparent from the description and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing and other objects, features and advantages will be apparent from the following description of particular embodiments of the disclosure, as illustrated in the accompanying drawings in which like reference characters refer to 10the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating the principles of various embodiments of the disclosure.

FIG. 1 shows a schematic of one example of a RNA (e.g. mRNA) vaccine construct of the present disclosure. The construct depicts a human metapneumovirus and human respiratory syncytial virus full length fusion protein obtained from wild-type strains (The Journal of General Virology. 2008; 89(Pt 12):3113-3118, incorporated herein by refer- 20 ence).

FIGS. 2A-2C are graphs showing the levels of anti-hMPV fusion protein-specific antibodies in the serum of mice immunized with hMPV mRNA vaccines on day 0 (FIG. 2A), day 14 (FIG. 2B) and day 35 (FIG. 2C) post immunization. 25 The mice were immunized with a single dose $(2 \mu g \text{ or } 10 \mu g)$ on day 0 and were given a boost dose (2 µg or 10 µg) on day 21. hMPV fusion protein-specific antibodies were detected at up to 1:10000 dilution of serum on day 35 for both doses.

FIGS. 3A-3C are graphs showing the result of IgG 30 isotyping in the serum of mice immunized with hMPV mRNA vaccines. The levels of hMPV fusion protein-specific IgG2a (FIG. 3A) and IgG1 (FIG. 3B) antibodies in the serum are measured by ELISA. FIG. 3C shows that hMPV fusion protein mRNA vaccine induced a mixed Th1/Th2 cytokine 35 response with a Th1 bias.

FIG. 4 is a graph showing in vitro neutralization of a hMPV B2 strain (TN/91-316) using the sera of mice immunized with a mRNA vaccine encoding hMPV fusion protein. Mouse serum obtained from mice receiving a 10 µg or a 2 40 titers in cotton rats that received different dosages of PIV µg dose contained hMPV-neutralizing antibodies.

FIGS. 5A-5C are graphs showing a Th1 cytokine response induced by a hMPV fusion peptide pool (15-mers-50 (overlap)) in splenocytes isolated from mice immunized with the hMPV mRNA vaccines. Virus-free media was used as a 45 negative control and Concanavalin A (ConA, a positive control for splenocyte stimulation) was included. The cytokines tested included IFN-y (FIG. 5A), IL-2 (FIG. 5B) and IL12 (FIG. 5C).

FIGS. 6A-6E are graphs showing the Th2 cytokine 50 response induced by a hMPV fusion peptide pool (15-mers-50) in splenocytes isolated from mice immunized with the hMPV mRNA vaccines. Virus-free media was used as a negative control and Concanavalin A was also included. The cytokines tested included IL-10 (FIG. 6A), TNF-a (FIG. 55 immunization. 6B), IL4 (FIG. 6C), IL-5 (FIG. 6D) and IL-6 (FIG. 6E).

FIGS. 7A-7C are graphs showing the Th1 response induced by inactivated hMPV virus in splenocytes isolated from mice immunized with hMPV mRNA vaccines. Virusfree media was used as a negative control and Concanavalin 60 A was included. The cytokines tested included IFN-y (FIG. 7A), IL-2 (FIG. 7B) and IL12 (FIG. 7C).

FIGS. 8A-8E are graphs showing the Th2 response induced by inactivated hMPV virus in splenocytes isolated from mice immunized with the hMPV mRNA vaccines. 65 Virus-free media was used as a negative control and Concanavalin A was included. The cytokines tested include

IL-10 (FIG. 8A), TNF-a (FIG. 8B), IL4 (FIG. 8C), IL-5 (FIG. 8D) and IL-6 (FIG. 8E).

FIGS. 9A-9B are graphs showing the results of cotton rat challenge experiments. Two different doses of the hMPV mRNA vaccines were used (2 µg or 10 µg doses) to immunize the cotton rats before challenge. The hMPV mRNA vaccines reduced the viral titer in the lung and nose of the cotton rat, with the 10 µg dose being more effective in reducing viral titer. Use of a 10 µg dose resulted in 100% protection in the lung and a ~2 log reduction in nose viral titer. Use of a 2 µg dose resulted in a 1 log reduction in lung vital titer and no reduction in nose viral titer. The vaccine was administered on Day 0, and a boost was administered on Day 21.

FIG. 10 is a graph showing the lung histopathology of cotton rats that received hMPV mRNA vaccines. Pathology associated with vaccine-enhanced disease was not observed in immunized groups.

FIG. 11 is a graph showing hMPV neutralization antibody titers in cotton rats that received hMPV mRNA vaccines (2 µg or 10 µg doses) on days 35 and 42 post immunization.

FIG. 12 is a graph showing the lung and nose viral load in cotton rats challenged with a hMPV/A2 strain after immunization with the indicated mRNA vaccines (hMPV mRNA vaccine or hMPV/PIV mRNA combination vaccine). Vaccinated cotton rats showed reduced lung and nose viral loads after challenge, compared to control.

FIG. 13 is a graph showing the lung and nose viral load in cotton rats challenged with PIV3 strain after immunization with indicated mRNA vaccines (PIV mRNA vaccine or hMPV/PIV combination vaccine). Vaccinated cotton rats showed reduced lung and nose viral loads after challenge, compared to control.

FIG. 14 is a graph showing hMPV neutralizing antibody titers in cotton rats that received different dosages of hMPV mRNA vaccines or hMPV/PIV combination mRNA vaccines on day 42 post immunization. The dosages of the vaccine are indicated in Table 9.

FIG. 15 is a graph showing PIV3 neutralizing antibody mRNA vaccines or hMPV/PIV combination mRNA vaccines on day 42 post immunization. The dosages of the vaccine are indicated in Table 9.

FIG. 16 is a graph showing the lung histopathology score of cotton rats immunized with hMPV mRNA vaccines, PIV mRNA vaccines or hMPV/PIV combination mRNA vaccines as indicated in Table 9. Low occurrence of alevolitis and interstitial pneumonia was observed, indicating no antibody-dependent enhancement (ADE) of hMPV associated diseases.

FIG. 17 is a graph showing the reciprocal MERS-CoV neutralizing antibody titers in mice immunized with betacoronavirus mRNA vaccine encoding the MERS-CoV fulllength Spike protein, on days 0, 21, 42, and 56 post

FIG. 18 is a graph showing the reciprocal MERS-CoV neutralizing antibody titers in mice immunized with betacoronavirus mRNA vaccine encoding either the MERS-CoV full-length Spike protein, or the S2 subunit of the Spike protein. The full length spike protein induced a stronger immune response compared to the S2 subunit alone.

FIGS. 19A-19C are graphs showing the viral load in the nose and throat, the bronchoalveolar lavage (BAL), or the lungs of New Zealand white rabbits 4 days post challenge with MERS-CoV. The New Zealand white rabbits were immunized with one 20 µg-dose (on day 0) or two 20 µg-doses (on day 0 and 21) of MERS-CoV mRNA vaccine encoding the full-length Spike protein before challenge. FIG. **19**A shows that two doses of MERS-CoV mRNA vaccine resulted in a 3 log reduction of viral load in the nose and led to complete protection in the throat of the New Zealand white rabbits. FIG. **19**B shows that two doses of ⁵ MERS-CoV mRNA vaccine resulted in a 4 log reduction of viral load in the BAL of the New Zealand white rabbits. FIG. **19**C show one dose of MERS-CoV mRNA vaccine resulted in a 2 log reduction of viral load, while two doses of MERS-CoV mRNA vaccine resulted in an over 4 log ¹⁰ reduction of viral load in the lungs of the New Zealand white rabbits.

FIGS. 20A-20B are images and graphs showing viral load or replicating virus detected by PCR in the lungs of New 15 Zealand white rabbits 4 days post challenge with MERS-CoV. The New Zealand white rabbits were immunized with a single 20 µg dose (on day 0, Group 1a) of MERS-CoV mRNA vaccine encoding the full-length Spike protein, two 20 µg doses (on day 0 and 21, Group 1b) of MERS-CoV 20 mRNA vaccine encoding the full-length Spike protein, or placebo (Group 2) before challenge. FIG. 20A shows that two doses of 20 µg a MERS-CoV mRNA vaccine reduced over 99% (2 log) of viruses in the lungs of New Zealand white rabbits. FIG. 20B shows that the group of New 25 Zealand white rabbits that received 2 doses of 20 µg MERS-CoV mRNA vaccine did not have any detectable replicating MERS-CoV virus in their lungs.

FIG. **21** is a graph showing the MERS-CoV neutralizing antibody titers in New Zealand white rabbits immunized ³⁰ with MERS-CoV mRNA vaccine encoding the full-length Spike protein. Immunization of the in New Zealand white rabbits were carried out as described in FIGS. **21A-21C**. The results show that two doses of 20 μ g MERS-CoV mRNA vaccine induced a significant amount of neutralizing antibodies against MERS-CoV (EC₅₀ between 500-1000). The MERS-CoV mRNA vaccine induced antibody titer is 3-5 fold better than any other vaccines tested in the same model.

DETAILED DESCRIPTION

The present disclosure provides, in some embodiments, vaccines that comprise RNA (e.g., mRNA) polynucleotides encoding a human metapneumovirus (hMPV) antigenic 45 polypeptide, a parainfluenza virus type 3 (PIV3) antigenic polypeptide, a respiratory syncytial virus (RSV) antigenic polypeptide, a measles virus (MeV) antigenic polypeptide, or a betacoronavirus antigenic polypeptide (e.g., Middle East respiratory syndrome coronavirus (MERS-CoV), 50 SARS-CoV, human coronavirus (HCoV)-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH (New Haven) and HCoV-HKU1) (see, e.g., Esper F. et al. Emerging Infectious Diseases, 12(5), 2006; and Pyrc K. et al. Journal of Virology, 81(7):3051-57, 2007, the contents of each of 55 which is here incorporated by reference in their entirety). The present disclosure also provides, in some embodiments, combination vaccines that comprise at least one RNA (e.g., mRNA) polynucleotide encoding at least two antigenic polypeptides selected from hMPV antigenic polypeptides, 60 PIV3 antigenic polypeptides, RSV antigenic polypeptides, MeV antigenic polypeptides and BetaCoV antigenic polypeptides. Also provided herein are methods of administering the RNA (e.g., mRNA) vaccines, methods of producing the RNA (e.g., mRNA) vaccines, compositions (e.g., pharma- 65 ceutical compositions) comprising the RNA (e.g., mRNA) vaccines, and nucleic acids (e.g., DNA) encoding the RNA

(e.g., mRNA) vaccines. In some embodiments, a RNA (e.g., mRNA) vaccine comprises an adjuvant, such as a flagellin adjuvant, as provided herein.

The RNA (e.g., mRNA) vaccines (e.g., hMPV, PIV3, RSV, MeV, BetaCoV RNA vaccines and combinations thereof), in some embodiments, may be used to induce a balanced immune response, comprising both cellular and humoral immunity, without many of the risks associated with DNA vaccination.

The entire contents of International Application No. PCT/ US2015/02740 is incorporated herein by reference.

Human Metapneumovirus (hMPV)

hMPV shares substantial homology with respiratory syncytial virus (RSV) in its surface glycoproteins. hMPV fusion protein (F) is related to other paramyxovirus fusion proteins and appears to have homologous regions that may have similar functions. The hMPV fusion protein amino acid sequence contains features characteristic of other paramyxovirus F proteins, including a putative cleavage site and potential N-linked glycosylation sites. Paramyxovirus fusion proteins are synthesized as inactive precursors (F0) that are cleaved by host cell proteases into the biologically fusion-active F1 and F2 domains (see, e.g., Cseke G. et al. Journal of Virology 2007; 81(2):698-707, incorporated herein by reference). hMPV has one putative cleavage site, in contrast to the two sites established for RSV F, and only shares 34% amino acid sequence identity with RSV F. F2 is extracellular and disulfide linked to F1. Fusion proteins are type I glycoproteins existing as trimers, with two 4-3 heptad repeat domains at the N- and C-terminal regions of the protein (HR1 and HR2), which form coiled-coil alphahelices. These coiled coils become apposed in an antiparallel fashion when the protein undergoes a conformational change into the fusogenic state. There is a hydrophobic fusion peptide N proximal to the N-terminal heptad repeat, which is thought to insert into the target cell membrane, while the association of the heptad repeats brings the trans-40 membrane domain into close proximity, inducing membrane fusion (see, e.g., Baker, K A et al. Mol. Cell 1999; 3:309-319). This mechanism has been proposed for a number of different viruses, including RSV, influenza virus, and human immunodeficiency virus. Fusion proteins are major antigenic determinants for all known paramyxoviruses and for other viruses that possess similar fusion proteins such as human immunodeficiency virus, influenza virus, and Ebola virus.

In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV fusion protein (F). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding a F1 or F2 subunit of a hMPV F protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV glycoprotein (G). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV matrix protein (M). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV phosphoprotein (P). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV nucleoprotein (N). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV SH protein (SH).

In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein, M protein, P protein, N protein and SH protein.

In some embodiments, a hMPV vaccine of the present 5 disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and G protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M protein. In some embodiments, a hMPV vaccine of the 10 present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein.

In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and N protein. In some embodiments, a 15 hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and SH protein.

In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide 20 encoding G protein and M protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and P protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) poly- 25 nucleotide encoding G protein and N protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and SH protein.

In some embodiments, a hMPV vaccine of the present 30 disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and M protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and P protein. In some embodiments, a 35 hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and P protein. In some embodiments, a 35 hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and N protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and SH pro- 40 tein.

A hMPV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV antigenic polypeptide identified by any one of SEQ ID NO: 5-8 (Table 3; see also 45 amino acid sequences of Table 4).

A hMPV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 1-4 (Table 2).

The present disclosure is not limited by a particular strain of hMPV. The strain of hMPV used in a vaccine may be any strain of hMPV. Non-limiting examples of strains of hMPV for use as provide herein include the CAN98-75 (CAN75) and the CAN97-83 (CAN83) hMPV strains (Skiadopoulos 55 M H et al. *J Virol.* 20014; 78(13)6927-37, incorporated herein by reference), a hMPV A1, A2, B1 or B2 strain (see, e.g., de Graaf M et al. *The Journal of General Virology* 2008; 89:975-83; Peret T C T et al. *The Journal of Infectious Disease* 2002; 185:1660-63, incorporated herein by reference), a hMPV isolate TN/92-4 (e.g., SEQ ID NO: 1 and 5), a hMPV isolate NL/1/99 (e.g., SEQ ID NO: 2 and 6), or a hMPV isolate PER/CFI0497/2010/B (e.g., SEQ ID NO: 3 and 7).

In some embodiments, at least one hMPV antigenic 65 polypeptide is obtained from a hMPV A1, A2, B1 or B2 strain (see, e.g., de Graaf M et al. *The Journal of General*

Virology 2008; 89:975-83; Peret T C T et al. *The Journal of Infectious Disease* 2002; 185:1660-63, incorporated herein by reference). In some embodiments, at least one antigenic polypeptide is obtained from the CAN98-75 (CAN75) hMPV strain. In some embodiments, at least one antigenic polypeptide is obtained from the CAN97-83 (CAN83) hMPV strain. In some embodiments, at least one antigenic polypeptide is obtained from hMPV isolate TN/92-4 (e.g., SEQ ID NO: 1 and 5). In some embodiments, at least one antigenic polypeptide is obtained from hMPV isolate NL/1/ 99 (e.g., SEQ ID NO: 2 and 6). In some embodiments, at least one antigenic polypeptide is obtained from hMPV isolate NL/1/ 91 (e.g., SEQ ID NO: 2 and 6). In some embodiments, at least one antigenic polypeptide is obtained from hMPV isolate PER/CFI0497/2010/B (e.g., SEQ ID NO: 3 and 7). In some embodiments, hMPV vaccines comprise RNA

(e.g., mRNA) polynucleotides encoding a hMPV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with hMPV F protein and having F protein activity.

A protein is considered to have F protein activity if, for example, the protein acts to fuse the viral envelope and host cell plasma membrane, mediates viral entry into a host cell via an interaction with arginine-glycine-aspartate RGDbinding integrins, or a combination thereof (see, e.g., Cox R G et al. *J Virol.* 2012; 88(22):12148-60, incorporated herein by reference).

In some embodiments, hMPV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding hMPV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with hMPV G protein and having G protein activity.

A protein is considered to have G protein activity if, for example, the protein acts to modulate (e.g., inhibit) hMPVinduced cellular (immune) responses (see, e.g., Bao X et al. *PLoS Pathog.* 2008; 4(5):e1000077, incorporated herein by reference).

Human Parainfluenza Virus Type 3 (PIV3)

Parainfluenza viruses belong to the family Paramyxoviridae. These are enveloped viruses with a negative-sense single-stranded RNA genome. Parainfluenza viruses belong to the subfamily Paramyxoviridae, which is subdivided into three genera: Respirovirus (PIV-1, PIV-3, and Sendai virus (SeV)), Rubulavirus (PIV-2, PIV-4 and mumps virus) and Morbillivirus (measles virus, rinderpest virus and canine distemper virus (CDV)). Their genome, a ~15 500 nucleotide-long negative-sense RNA molecule, encodes two envelope glycoproteins, the hemagglutinin-neuraminidase (HN), the fusion protein (F or F0), which is cleaved into F1 and F2 subunits, a matrix protein (M), a nucleocapsid protein (N) and several nonstructural proteins including the viral replicase (L). All parainfluenza viruses, except for PIV-1, express a non-structural V protein that blocks IFN signaling in the infected cell and acts therefore as a virulence factor (see, e.g., Nishio M et al. J Virol. 2008; 82(13):6130-38).

PIV3 hemagglutinin-neuraminidase (HN), a structural protein, is found on the viral envelope, where it is necessary for attachment and cell entry. It recognizes and binds to sialic acid-containing receptors on the host cell's surface. As a neuroaminidase, HN removes sialic acid from virus particles, preventing self-aggregation of the virus, and promoting the efficient spread of the virus. Furthermore, HN promotes the activity of the fusion (F or F0) protein, contributing to the penetration of the host cell's surface.

PIV3 fusion protein (PIV3 F) is located on the viral envelope, where it facilitates the viral fusion and cell entry. The F protein is initially inactive, but proteolytic cleavage leads to its active forms, F1 and F2, which are linked by disulfide bonds. This occurs when the HN protein binds its

receptor on the host cell's surface. During early phases of infection, the F glycoprotein mediates penetration of the host cell by fusion of the viral envelope to the plasma membrane. In later stages of the infection, the F protein facilitates the fusion of the infected cells with neighboring uninfected cells, which leads to the formation of a syncytium and spread of the infection.

PIV3 matrix protein (M) is found within the viral envelope and assists with viral assembly. It interacts with the nucleocapsid and envelope glycoproteins, where it facilitates the budding of progeny viruses through its interactions with specific sites on the cytoplasmic tail of the viral glycoproteins and nucleocapsid. It also plays a role in transporting viral components to the budding site.

PIV3 phosphoprotein (P) and PIV3 large polymerase protein (L) are found in the nucleocapsid where they form part of the RNA polymerase complex. The L protein, a viral RNA-dependent RNA polymerase, facilitates genomic transcription, while the host cell's ribosomes translate the viral 20 mRNA into viral proteins.

PIV3 V is a non-structural protein that blocks IFN signaling in the infected cell, therefore acting as a virulence factor.

PIV3 nucleoprotein (N) encapsidates the genome in a 25 ratio of 1 N per 6 ribonucleotides, protecting it from nucleases. The nucleocapsid (NC) has a helical structure.

The encapsidated genomic RNA is termed the NC and serves as template for transcription and replication. During replication, encapsidation by PIV3 N is coupled to RNA 30 synthesis and all replicative products are resistant to nucleases. PIV3 N homo-multimerizes to form the nucleocapsid and binds to viral genomic RNA. PIV3 N binds the P protein and thereby positions the polymerase on the template.

In some embodiments, a PIV3 vaccine of the present 35 disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 fusion protein (F). In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding a F1 or F2 subunit of a PIV3 F protein. In some embodiments, a PIV3 vaccine of 40 the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 hemagglutinin-neuraminidase (HN) (see, e.g., van Wyke Coelingh K L et al. J Virol. 1987; 61(5):1473-77, incorporated herein by reference). In some embodiments, a PIV3 vaccine of the present disclosure 45 comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 matrix protein (M). In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 phosphoprotein (P). In some embodiments, a PIV3 vaccine of the present dis- 50 closure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 nucleoprotein (N).

In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein, M protein, P protein, and N 55 protein.

In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and HN protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA 60 (e.g., mRNA) polynucleotide encoding F protein and M protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a PIV3 vaccine of the present disclosure 65 comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and N protein.

In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HN protein and M protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HN protein and P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HN protein and N protein.

In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein and M protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein and P protein. In some embodiments, a 15 PIV3 vaccine of the present disclosure comprises a RNA

(e.g., mRNA) polynucleotide encoding F protein, HN protein and N protein.

A PIV3 vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one PIV3 antigenic polypeptide identified by any one of SEQ ID NO: 12-13 (Table 6; see also amino acid sequences of Table 7).

A PIV3 vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 9-12 (Table 5; see also nucleic acid sequences of Table 7).

The present disclosure is not limited by a particular strain of PIV3. The strain of PIV3 used in a vaccine may be any strain of PIV3. A non-limiting example of a strain of PIV3 for use as provide herein includes HPIV3/Homo sapiens/ PER/FLA4815/2008.

In some embodiments, PIV3 vaccines comprise RNA (e.g., mRNA) polynucleotides encoding a PIV3 antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with PIV3 F protein and having F protein activity.

In some embodiments, PIV3 vaccines comprise RNA (e.g., mRNA) polynucleotides encoding PIV3 antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with PIV3 hemagglutinin-neuraminidase (HN) and having hemagglutininneuraminidase activity.

A protein is considered to have hemagglutinin-neuraminidase activity if, for example, it is capable of both receptor binding and receptor cleaving. Such proteins are major surface glycoproteins that have functional sites for cell attachment and for neuraminidase activity. They are able to cause red blood cells to agglutinate and to cleave the glycosidic linkages of neuraminic acids, so they have the potential to both bind a potential host cell and then release the cell if necessary, for example, to prevent self-aggregation of the virus.

In some embodiments, PIV3 vaccines comprise RNA (e.g., mRNA) polynucleotides encoding PIV3 antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with PIV3 HN, F (e.g., F, F1 or F2), M, N, L or V and having HN, F (e.g., F, F1 or F2), M, N, L or V activity, respectively. Respiratory Syncytial Virus (RSV)

RSV is a negative-sense, single-stranded RNA virus of the genus Pneumovirinae. The virus is present in at least two antigenic subgroups, known as Group A and Group B, primarily resulting from differences in the surface G glycoproteins. Two RSV surface glycoproteins—G and F—mediate attachment with and attachment to cells of the respiratory epithelium. F surface glycoproteins mediate coalescence of neighboring cells. This results in the forma-

tion of syncytial cells. RSV is the most common cause of bronchiolitis. Most infected adults develop mild cold-like symptoms such as congestion, low-grade fever, and wheezing. Infants and small children may suffer more severe symptoms such as bronchiolitis and pneumonia. The disease 5 may be transmitted among humans via contact with respiratory secretions.

The genome of RSV encodes at least three surface glycoproteins, including F, G, and SH, four nucleocapsid proteins, including L, P, N, and M2, and one matrix protein, M. 10 Glycoprotein F directs viral penetration by fusion between the virion and the host membrane. Glycoprotein G is a type II transmembrane glycoprotein and is the major attachment protein. SH is a short integral membrane protein. Matrix protein M is found in the inner layer of the lipid bilayer and 15 assists virion formation. Nucleocapsid proteins L, P, N, and M2 modulate replication and transcription of the RSV genome. It is thought that glycoprotein G tethers and stabilizes the virus particle at the surface of bronchial epithelial cells, while glycoprotein F interacts with cellular gly- 20 cosaminoglycans to mediate fusion and delivery of the RSV virion contents into the host cell (Krzyzaniak M A et al. PLoS Pathog 2013; 9(4)).

In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide 25 encoding F protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding L protein. In some 30 embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding N protein. In some embodiments, a 35 PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding M2 protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding M protein.

In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein, L protein, P protein, N protein, M2 protein and M protein.

In some embodiments, a RSV vaccine of the present 45 disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and G protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and L protein. In some embodiments, a RSV vaccine of the present 50 disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and N protein. In some embodiments, a RSV vaccine of the present 55 disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M2 protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M protein.

In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and L protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and P 65 protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide

encoding G protein and N protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and M2 protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and M protein.

In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and L protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and P protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and N protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and N protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and M2 protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and M protein.

The present disclosure is not limited by a particular strain of RSV. The strain of RSV used in a vaccine may be any strain of RSV.

In some embodiments, RSV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding a RSV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with RSV F protein and having F protein activity.

In some embodiments, RSV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding RSV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with RSV G protein and having G protein activity.

A protein is considered to have G protein activity if, for example, the protein acts to modulate (e.g., inhibit) hMPVinduced cellular (immune) responses (see, e.g., Bao X et al. *PLoS Pathog.* 2008; 4(5):e1000077, incorporated herein by reference).

40 Measles Virus (MeV) Molecular epidemiologic investigations and virologic surveillance contribute notably to the control and prevention of measles. Nearly half of measlesrelated deaths worldwide occur in India, yet virologic surveillance data are incomplete for many regions of the 45 country. Previous studies have documented the presence of measles virus genotypes D4, D7, and D8 in India, and genotypes D5, D9, D11, H1, and G3 have been detected in neighboring countries. Recently, MeV genotype B3 was detected in India (Kuttiatt V S et al. *Emerg Infect Dis.* 2014; 50 20(10): 1764-66).

The glycoprotein complex of paramyxoviruses mediates receptor binding and membrane fusion. In particular, the MeV fusion (F) protein executes membrane fusion, after receptor binding by the hemagglutinin (HA) protein (Muhlebach M D et al. Journal of Virology 2008; 82(22):11437-45). The MeV P gene codes for three proteins: P, an essential polymerase cofactor, and V and C, which have multiple functions but are not strictly required for viral propagation in cultured cells. V shares the amino-terminal domain with 60 P but has a zinc-binding carboxyl-terminal domain, whereas C is translated from an overlapping reading frame. The MeV C protein is an infectivity factor. During replication, the P protein binds incoming monomeric nucleocapsid (N) proteins with its amino-terminal domain and positions them for assembly into the nascent ribonucleocapsid. The P protein amino-terminal domain is natively unfolded (Deveaux P et al. Journal of Virology 2004; 78(21): 11632-40).

In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein. In some embodiments, a ⁵ MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding P protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein.

In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide 15 encoding HA protein, F protein, P protein, V protein and C protein.

In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and F protein. In some embodiments, ²⁰ a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and P protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and V protein. In some embodiments, ²⁵ a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and V protein. In some embodiments, ²⁵ a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and C protein.

some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encod- 30 ing F protein and P protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F 35 protein and C protein.

In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein and P protein. In some embodiments, a MeV vaccine of the present disclosure 40 comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein and V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein and C protein. 45

In some embodiments, MeV vaccines comprise RNA (e.g., mRNA) encoding a MeV antigenic polypeptide having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with MeV HA protein and having MeV HA protein activity.

In some embodiments, MeV vaccines comprise RNA (e.g., mRNA) encoding a MeV antigenic polypeptide having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with MeV F protein and having MeV F protein activity.

A protein is considered to have HA protein activity if the protein mediates receptor binding and/or membrane fusion. MeV F protein executes membrane fusion, after receptor binding by the MeV HA protein.

A MeV vaccine may comprise, for example, at least one 60 RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one MeV antigenic polypeptide identified by any one of SEQ ID NO: 47-50 (Table 14; see also amino acid sequences of Table 15).

A MeV vaccine may comprise, for example, at least one 65 RNA (e.g., mRNA) polynucleotide identified by any one of SEQ ID NO: 37, 40, 43, 46 (Table 13).

A MeV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 35, 36, 38, 39, 41, 42, 44 and 45 (Table 13).

The present disclosure is not limited by a particular strain of MeV. The strain of MeV used in a vaccine may be any strain of MeV. Non-limiting examples of strains of MeV for use as provide herein include B3/B3.1, C2, D4, D6, D7, D8, G3, H1, Moraten, Rubeovax, MVi/New Jersey.USA/45.05,

MVi/Texas.USA/4.07, AIK-C, MVi/New York.USA/26.09/ 3, MVi/California.USA/16.03, MVi/Virginia.USA/15.09, MVi/California.USA/8.04, and MVi/Pennsylvania.USA/ 20.09.

MeV proteins may be from MeV genotype D4, D5, D7, D8, D9, D11, H1, G3 or B3. In some embodiments, a MeV HA protein or a MeV F protein is from MeV genotype D8. In some embodiments, a MeV HA protein or a MeV F protein is from MeV genotype B3.

Betacoronaviruses (BetaCoV)

MERS-CoV. MERS-CoV is a positive-sense, singlestranded RNA virus of the genus Betacoronavirus. The genomes are phylogenetically classified into two clades, clade A and clade B. It has a strong tropism for non-ciliated bronchial epithelial cells, evades the innate immune response and antagonizes interferon (IFN) production in infected cells. Dipeptyl peptidase 4 (DDP4, also known as CD26) has been identified as a functional cellular receptor for MERS-CoV. Its enzymatic activity is not required for infection, although its amino acid sequence is highly conserved across species and is expressed in the human bronchial epithelium and kidneys. Most infected individuals develop severe acute respiratory illnesses, including fever, cough, and shortness of breath, and the virus can be fatal. The disease may be transmitted among humans, generally among those in close contact.

The genome of MERS-CoV encodes at least four unique accessory proteins, such as 3, 4a, 4b and 5, two replicase proteins (open reading frame 1a and 1b), and four major structural proteins, including spike (S), envelope (E), nucleocapsid (N), and membrane (M) proteins (Almazan F et al. MBio 2013; 4(5):e00650-13). The accessory proteins play nonessential roles in MERS-CoV replication, but they are likely structural proteins or interferon antagonists, modulating in vivo replication efficiency and/or pathogenesis, as in the case of SARS-CoV (Almazan F et al. MBio 2013; 4(5):e00650-13; Totura A L et al. Curr Opin Virol 2012; 2(3):264-75; Scobey T et al. Proc Natl Acad Sci USA 2013; 110(40):16157-62). The other proteins of MERS-CoV maintain different functions in virus replication. The E protein, for example, involves in virulence, and deleting the E-coding gene results in replication-competent and propagation-defective viruses or attenuated viruses (Almazan F et al. MBio 2013; 4(5):e00650-13). The S protein is particularly essential in mediating virus binding to cells expressing 55 receptor dipeptidyl peptidase-4 (DPP4) through receptorbinding domain (RBD) in the S1 subunit, whereas the S2 subunit subsequently mediates virus entry via fusion of the virus and target cell membranes (Li F. J Virol 2015; 89(4): 1954-64; Raj V S et al. Nature 2013; 495(7440):251-4).

In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding the S1 subunit of the S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding the S2 subunit of the S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding E protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding N protein. In 5 some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding M protein.

In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) poly- 10 nucleotide encoding S protein (S, S1 and/or S2), E protein, N protein and M protein.

In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and E 15 protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) poly- 20 nucleotide encoding S protein (S, S1 and/or S2) and M protein.

In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein 25 and M protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a 30 RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), M protein and N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding E protein, M protein and N protein.

A MERS-CoV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one MERS-CoV antigenic polypeptide identified by any one of SEQ ID NO: 24-38 or 33 (Table 11; see also amino acid sequences of Table 12). 40

A MERS-CoV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 20-23 (Table 10).

The present disclosure is not limited by a particular strain 45 of MERS-CoV. The strain of MERS-CoV used in a vaccine may be any strain of MERS-CoV. Non-limiting examples of strains of MERS-CoV for use as provide herein include Riyadh_14_2013, and 2cEMC/2012, Hasa_1_2013.

SARS-CoV. The genome of SARS-CoV includes of a 50 single, positive-strand RNA that is approximately 29,700 nucleotides long. The overall genome organization of SARS-CoV is similar to that of other coronaviruses. The reference genome includes 13 genes, which encode at least 14 proteins. Two large overlapping reading frames (ORFs) 55 encompass 71% of the genome. The remainder has 12 potential ORFs, including genes for structural proteins S (spike), E (small envelope), M (membrane), and N (nucleocapsid). Other potential ORFs code for unique putative SARS-CoV-specific polypeptides that lack obvious 60 sequence similarity to known proteins. A detailed analysis of the SARS-CoV genome has been published in J Mol Biol 2003; 331: 991-1004.

In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) poly- 65 nucleotide encoding S protein (S, S1 and/or S2), E protein, N protein and M protein.

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In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and E protein. In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and N protein. In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and M protein.

In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and M protein. In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and N protein. In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), M protein and N protein. In some embodiments, a SARS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding E protein, M protein and N protein.

A SARS-CoV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one SARS-CoV antigenic polypeptide identified by any one of SEQ ID NO: 29, 32 or 34 (Table 11; see also amino acid sequences of Table 12).

The present disclosure is not limited by a particular strain of SARS-CoV. The strain of SARS-CoV used in a vaccine may be any strain of SARS-CoV.

HCoV-OC43.

Human coronavirus OC43 is an enveloped, positivesense, single-stranded RNA virus in the species Betacoro-35 navirus-1 (genus Betacoronavirus, subfamily Coronavirinae, family Coronaviridae, order Nidovirales). Four HCoV-OC43 genotypes (A to D), have been identified with genotype D most likely arising from recombination. The complete genome sequencing of two genotype C and D strains and bootscan analysis shows recombination events between genotypes B and C in the generation of genotype D. Of 29 strains identified, none belong to the more ancient genotype A. Along with HCoV-229E, a species in the Alphacoronavirus genus, HCoV-OC43 are among the known viruses that cause the common cold. Both viruses can cause severe lower respiratory tract infections, including pneumonia in infants, the elderly, and immunocompromised individuals such as those undergoing chemotherapy and those with HIV-AIDS.

HCoV-HKU1.

Human coronavirus HKU1 (HCoV-H KU 1) is a positivesense, single-stranded RNA virus with the HE gene, which distinguishes it as a group 2, or betacoronavirus. It was discovered in January 2005 in two patients in Hong Kong. The genome of HCoV-HKU1 is a 29,926-nucleotide, polyadenylated RNA. The GC content is 32%, the lowest among all known coronaviruses. The genome organization is the same as that of other group II coronaviruses, with the characteristic gene order 1a, 1b, HE, S, E, M, and N. Furthermore, accessory protein genes are present between the S and E genes (ORF4) and at the position of the N gene (ORF8). The TRS is presumably located within the AAUC-UAAAC sequence, which precedes each ORF except E. As in sialodacryoadenitis virus and mouse hepatitis virus (MHV), translation of the E protein possibly occurs via an internal ribosomal entry site. The 3' untranslated region contains a predicted stem-loop structure immediately down-

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stream of the N ORF (nucleotide position 29647 to 29711). Further downstream, a pseudoknot structure is present at nucleotide position 29708 to 29760. Both RNA structures are conserved in group II coronaviruses and are critical for virus replication.

HCoV-NL63.

The RNA genome of human coronavirus NL63 (HCoV-NL63) is 27,553 nucleotides, with a poly(A) tail (FIG. 1). With a GC content of 34%, HCoV-NL63 has one of the lowest GC contents of the coronaviruses, for which GC 10 content ranges from 32 to 42%. Untranslated regions of 286 and 287 nucleotides are present at the 5' and 3' termini, respectively. Genes predicted to encode the S, E, M, and N proteins are found in the 3' part of the HCoV-NL63 genome. The HE gene, which is present in some group II coronavi- 15 ruses, is absent, and there is only a single, monocistronic accessory protein ORF (ORF3) located between the S and E genes. Subgenomic mRNAs are generated for all ORFs (S, ORF3, E, M, and N), and the core sequence of the TRS of HCoV-NL63 is defined as AACUAAA. This sequence is 20 situated upstream of every ORF except for the E ORF, which contains the suboptimal core sequence AACUAUA. Interestingly, a 13-nucleotide sequence with perfect homology to the leader sequence is situated upstream of the suboptimal E TRS. Annealing of this 13-nucleotide sequence to the leader 25 sequence may act as a compensatory mechanism for the disturbed leader-TRS/body-TRS interaction.

HCoV-229E.

Human coronavirus 229E (HCoV-229E) is a singlestranded, positive-sense, RNA virus species in the Alpha- 30 coronavirus genus of the subfamily Coronavirinae, in the family Coronaviridae, of the order Nidovirales. Along with Human coronavirus OC43, it is responsible for the common cold. HCoV-NL63 and HCoV-229E are two of the four human coronaviruses that circulate worldwide. These two 35 viruses are unique in their relationship towards each other. Phylogenetically, the viruses are more closely related to each other than to any other human coronavirus, yet they only share 65% sequence identity. Moreover, the viruses use different receptors to enter their target cell. HCoV-NL63 is 40 vaccine comprises a RNA (e.g., mRNA) polynucleotide associated with croup in children, whereas all signs suggest that the virus probably causes the common cold in healthy adults. HCoV-229E is a proven common cold virus in healthy adults, so it is probable that both viruses induce comparable symptoms in adults, even though their mode of 45 infection differs (HCoV-NL63 and HCoV-229E are two of the four human coronaviruses that circulate worldwide. These two viruses are unique in their relationship towards each other. Phylogenetically, the viruses are more closely related to each other than to any other human coronavirus, 50 yet they only share 65% sequence identity. Moreover, the viruses use different receptors to enter their target cell. HCoV-NL63 is associated with croup in children, whereas all signs suggest that the virus probably causes the common cold in healthy adults. HCoV-229E is a proven common cold 55 virus in healthy adults, so it is probable that both viruses induce comparable symptoms in adults, even though their mode of infection differs (Dijkman R. et al. J Formos Med Assoc. 2009 April; 108(4):270-9, the contents of which is incorporated herein by reference in their entirety). Combination Vaccines

Embodiments of the present disclosure also provide combination RNA (e.g., mRNA) vaccines. A "combination RNA (e.g., mRNA) vaccine" of the present disclosure refers to a vaccine comprising at least one (e.g., at least 2, 3, 4, or 5) 65 RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a combination of any two or more (or all of)

antigenic polypeptides selected from hMPV antigenic polypeptides, PIV3 antigenic polypeptides, RSV antigenic polypeptides, MeV antigenic polypeptides, and BetaCoV antigenic polypeptides (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a RSV antigenic polypeptide, a MeV antigenic polypeptide, and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a PIV3 antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a RSV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a MeV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a BetaCoV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide and a RSV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide and a MeV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) encoding a PIV3 antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a RSV antigenic polypeptide and a MeV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, 60 HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a MeV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, 10 SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1). encoding a RS polypeptide and a BetaCoV 10 HCoV-HKU1). encoding a RS polypeptide and a BetaCoV 10 HCoV-NL63, 10 HCoV-NL (HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a RSV antigenic 15 polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) 20 vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide, a RSV antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, 25 HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide and a RSV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide and a MeV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) 35 vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and 40 HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a RSV antigenic polypeptide and a MeV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, 50 HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a MeV antigenic 55 polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) 60 vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a MeV antigenic polypeptide.

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide 65 encoding a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g.,

selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a RSV antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

Other combination respiratory virus RNA (e.g., mRNA) vaccines are encompassed by the present disclosure.

It has been discovered that the mRNA vaccines described herein are superior to current vaccines in several ways. First, the lipid nanoparticle (LNP) delivery is superior to other formulations including a protamine base approach described in the literature and no additional adjuvants are to be necessary. The use of LNPs enables the effective delivery of chemically modified or unmodified mRNA vaccines. Additionally it has been demonstrated herein that both modified and unmodified LNP formulated mRNA vaccines were superior to conventional vaccines by a significant degree. In some embodiments the mRNA vaccines of the invention are superior to conventional vaccines by a factor of at least 10 fold, 20 fold, 40 fold, 50 fold, 100 fold, 500 fold or 1,000 fold.

Although attempts have been made to produce functional RNA vaccines, including mRNA vaccines and self-replicating RNA vaccines, the therapeutic efficacy of these RNA vaccines have not yet been fully established. Quite surprisingly, the inventors have discovered, according to aspects of the invention a class of formulations for delivering mRNA vaccines in vivo that results in significantly enhanced, and in many respects synergistic, immune responses including enhanced antigen generation and functional antibody production with neutralization capability. These results can be achieved even when significantly lower doses of the mRNA are administered in comparison with mRNA doses used in other classes of lipid based formulations. The formulations of the invention have demonstrated significant unexpected in vivo immune responses sufficient to establish the efficacy of functional mRNA vaccines as prophylactic and therapeutic agents. Additionally, self-replicating RNA vaccines rely on viral replication pathways to deliver enough RNA to a cell to produce an immunogenic response. The formulations of the invention do not require viral replication to produce enough protein to result in a strong immune response. Thus, the mRNA of the invention are not self-replicating RNA and do not include components necessary for viral replication.

The invention involves, in some aspects, the surprising finding that lipid nanoparticle (LNP) formulations significantly enhance the effectiveness of mRNA vaccines, including chemically modified and unmodified mRNA vaccines. The efficacy of mRNA vaccines formulated in LNP was examined in vivo using several distinct antigens. The results presented herein demonstrate the unexpected superior efficacy of the mRNA vaccines formulated in LNP over other commercially available vaccines.

In addition to providing an enhanced immune response, the formulations of the invention generate a more rapid immune response with fewer doses of antigen than other vaccines tested. The mRNA-LNP formulations of the invention also produce quantitatively and qualitatively better immune responses than vaccines formulated in a different carriers.

The data described herein demonstrate that the formulations of the invention produced significant unexpected

improvements over existing antigen vaccines. Additionally, the mRNA-LNP formulations of the invention are superior to other vaccines even when the dose of mRNA is lower than other vaccines. Mice immunized with either 10 μ g or 2 μ g doses of an hMPV fusion protein mRNA LNP vaccine or a 5 PIV3 mRNA LNP vaccine produced neutralizing antibodies which for instance, successfully neutralized the hMPV B2 virus. A 10 µg dose of mRNA vaccine protected 100% of mice from lethal challenge and drastically reduced the viral titer after challenge (~2 log reduction). 10

Two 20 µg doses of MERS-CoV mRNA LNP vaccine significantly reduced viral load and induced significant amount of neutralizing antibodies against MERS-CoV (ECso between 500-1000). The MERS-CoV mRNA vaccine induced antibody titer was 3-5 fold better than any other 15 vaccines tested in the same model.

The LNP used in the studies described herein has been used previously to deliver siRNA in various animal models as well as in humans. In view of the observations made in association with the siRNA delivery of LNP formulations. 20 the fact that LNP is useful in vaccines is quite surprising. It has been observed that therapeutic delivery of siRNA formulated in LNP causes an undesirable inflammatory response associated with a transient IgM response, typically leading to a reduction in antigen production and a compro- 25 1-100, 2-50 or 2-100 antigenic polypeptides. mised immune response. In contrast to the findings observed with siRNA, the LNP-mRNA formulations of the invention are demonstrated herein to generate enhanced IgG levels, sufficient for prophylactic and therapeutic methods rather than transient IgM responses.

Nucleic Acids/Polynucleotides

Respiratory virus vaccines, as provided herein, comprise at least one (one or more) ribonucleic acid (RNA) (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide selected from 35 hMPV, PIV3, RSV, MeV and BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) antigenic polypeptides. The term "nucleic acid" includes any compound and/or substance that comprises a polymer of 40 nucleotides (nucleotide monomer). These polymers are referred to as polynucleotides. Thus, the terms "nucleic acid" and "polynucleotide" are used interchangeably.

Nucleic acids may be or may include, for example, ribonucleic acids (RNAs), deoxyribonucleic acids (DNAs), 45 threose nucleic acids (TNAs), glycol nucleic acids (GNAs), peptide nucleic acids (PNAs), locked nucleic acids (LNAs, including LNA having a β -D-ribo configuration, α -LNA having an α -L-ribo configuration (a diastereomer of LNA), 2'-amino-LNA having a 2'-amino functionalization, and 50 2'-amino- α -LNA having a 2'-amino functionalization), ethylene nucleic acids (ENA), cyclohexenyl nucleic acids (CeNA) or chimeras or combinations thereof.

In some embodiments, polynucleotides of the present disclosure function as messenger RNA (mRNA). "Messen- 55 rally-occurring or wild-type mRNA sequence encoding a ger RNA" (mRNA) refers to any polynucleotide that encodes a (at least one) polypeptide (a naturally-occurring, non-naturally-occurring, or modified polymer of amino acids) and can be translated to produce the encoded polypeptide in vitro, in vivo, in situ or ex vivo. The skilled artisan 60 will appreciate that, except where otherwise noted, polynucleotide sequences set forth in the instant application will recite "T"s in a representative DNA sequence but where the sequence represents RNA (e.g., mRNA), the "T"s would be substituted for "U"s. Thus, any of the RNA polynucleotides 65 encoded by a DNA identified by a particular sequence identification number may also comprise the corresponding

RNA (e.g., mRNA) sequence encoded by the DNA, where each "T" of the DNA sequence is substituted with "U."

The basic components of an mRNA molecule typically include at least one coding region, a 5' untranslated region (UTR), a 3' UTR, a 5' cap and a poly-A tail. Polynucleotides of the present disclosure may function as mRNA but can be distinguished from wild-type mRNA in their functional and/or structural design features, which serve to overcome existing problems of effective polypeptide expression using nucleic-acid based therapeutics.

In some embodiments, a RNA polynucleotide of an RNA (e.g., mRNA) vaccine encodes 2-10, 2-9, 2-8, 2-7, 2-6, 2-5, 2-4, 2-3, 3-10, 3-9, 3-8, 3-7, 3-6, 3-5, 3-4, 4-10, 4-9, 4-8, 4-7, 4-6, 4-5, 5-10, 5-9, 5-8, 5-7, 5-6, 6-10, 6-9, 6-8, 6-7, 7-10, 7-9, 7-8, 8-10, 8-9 or 9-10 antigenic polypeptides. In some embodiments, a RNA (e.g., mRNA) polynucleotide of a respiratory virus vaccine encodes at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 antigenic polypeptides. In some embodiments, a RNA (e.g., mRNA) polynucleotide of a respiratory virus vaccine encodes at least 100 or at least 200 antigenic polypeptides. In some embodiments, a RNA polynucleotide of an respiratory virus vaccine encodes 1-10, 5-15, 10-20, 15-25, 20-30, 25-35, 30-40, 35-45, 40-50, 1-50,

Polynucleotides of the present disclosure, in some embodiments, are codon optimized. Codon optimization methods are known in the art and may be used as provided herein. Codon optimization, in some embodiments, may be used to match codon frequencies in target and host organisms to ensure proper folding; bias GC content to increase mRNA stability or reduce secondary structures; minimize tandem repeat codons or base runs that may impair gene construction or expression; customize transcriptional and translational control regions; insert or remove protein trafficking sequences; remove/add post translation modification sites in encoded protein (e.g. glycosylation sites); add, remove or shuffle protein domains; insert or delete restriction sites; modify ribosome binding sites and mRNA degradation sites; adjust translational rates to allow the various domains of the protein to fold properly; or to reduce or eliminate problem secondary structures within the polynucleotide. Codon optimization tools, algorithms and services are known in the art-non-limiting examples include services from GeneArt (Life Technologies), DNA2.0 (Menlo Park Calif.) and/or proprietary methods. In some embodiments, the open reading frame (ORF) sequence is optimized using optimization algorithms.

In some embodiments, a codon optimized sequence shares less than 95% sequence identity, less than 90% sequence identity, less than 85% sequence identity, less than 80% sequence identity, or less than 75% sequence identity to a naturally-occurring or wild-type sequence (e.g., a natupolypeptide or protein of interest (e.g., an antigenic protein or antigenic polypeptide)).

In some embodiments, a codon-optimized sequence shares between 65% and 85% (e.g., between about 67% and about 85%, or between about 67% and about 80%) sequence identity to a naturally-occurring sequence or a wild-type sequence (e.g., a naturally-occurring or wild-type mRNA sequence encoding a polypeptide or protein of interest (e.g., an antigenic protein or polypeptide)). In some embodiments, a codon-optimized sequence shares between 65% and 75%, or about 80% sequence identity to a naturally-occurring sequence or wild-type sequence (e.g., a naturally-occurring

or wild-type mRNA sequence encoding a polypeptide or protein of interest (e.g., an antigenic protein or polypeptide)).

In some embodiments a codon-optimized RNA (e.g., mRNA) may, for instance, be one in which the levels of G/C are enhanced. The G/C-content of nucleic acid molecules may influence the stability of the RNA. RNA having an increased amount of guanine (G) and/or cytosine (C) residues may be functionally more stable than nucleic acids containing a large amount of adenine (A) and thymine (T) or 10 uracil (U) nucleotides. WO02/098443 discloses a pharmaceutical composition containing an mRNA stabilized by sequence modifications in the translated region. Due to the degeneracy of the genetic code, the modifications work by substituting existing codons for those that promote greater 15 RNA stability without changing the resulting amino acid. The approach is limited to coding regions of the RNA. Antigens/Antigenic Polypeptides

In some embodiments, an antigenic polypeptide (e.g., a hMPV, PIV3, RSV, MeV or BetaCoV antigenic polypeptide) 20 is longer than 25 amino acids and shorter than 50 amino acids. Polypeptides include gene products, naturally occurring polypeptides, synthetic polypeptides, homologs, orthologs, paralogs, fragments and other equivalents, variants, and analogs of the foregoing. A polypeptide may be a 25 single molecule or may be a multi-molecular complex such as a dimer, trimer or tetramer. Polypeptides may also comprise single chain polypeptides or multichain polypeptides, such as antibodies or insulin, and may be associated or linked to each other. Most commonly, disulfide linkages are 30 found in multichain polypeptides. The term "polypeptide" may also apply to amino acid polymers in which at least one amino acid residue is an artificial chemical analogue of a corresponding naturally-occurring amino acid.

A "polypeptide variant" is a molecule that differs in its 35 amino acid sequence relative to a native sequence or a reference sequence. Amino acid sequence variants may possess substitutions, deletions, insertions, or a combination of any two or three of the foregoing, at certain positions within the amino acid sequence, as compared to a native 40 sequence or a reference sequence. Ordinarily, variants possess at least 50% identity to a native sequence or a reference sequence. In some embodiments, variants share at least 80% identity or at least 90% identity with a native sequence or a reference sequence.

In some embodiments "variant mimics" are provided. A "variant mimic" contains at least one amino acid that would mimic an activated sequence. For example, glutamate may serve as a mimic for phosphoro-threonine and/or phosphoroserine. Alternatively, variant mimics may result in deacti- 50 vation or in an inactivated product containing the mimic. For example, phenylalanine may act as an inactivating substitution for tyrosine, or alanine may act as an inactivating substitution for serine.

evolved from a common ancestral gene by speciation. Normally, orthologs retain the same function in the course of evolution. Identification of orthologs is important for reliable prediction of gene function in newly sequenced genomes.

"Analogs" is meant to include polypeptide variants that differ by one or more amino acid alterations, for example, substitutions, additions or deletions of amino acid residues that still maintain one or more of the properties of the parent or starting polypeptide.

The present disclosure provides several types of compositions that are polynucleotide or polypeptide based, includ-

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ing variants and derivatives. These include, for example, substitutional, insertional, deletion and covalent variants and derivatives. The term "derivative" is synonymous with the term "variant" and generally refers to a molecule that has been modified and/or changed in any way relative to a reference molecule or a starting molecule.

As such, polynucleotides encoding peptides or polypeptides containing substitutions, insertions and/or additions, deletions and covalent modifications with respect to reference sequences, in particular the polypeptide sequences disclosed herein, are included within the scope of this disclosure. For example, sequence tags or amino acids, such as one or more lysines, can be added to peptide sequences (e.g., at the N-terminal or C-terminal ends). Sequence tags can be used for peptide detection, purification or localization. Lysines can be used to increase peptide solubility or to allow for biotinylation. Alternatively, amino acid residues located at the carboxy and amino terminal regions of the amino acid sequence of a peptide or protein may optionally be deleted providing for truncated sequences. Certain amino acids (e.g., C-terminal residues or N-terminal residues) alternatively may be deleted depending on the use of the sequence, as for example, expression of the sequence as part of a larger sequence that is soluble, or linked to a solid support.

"Substitutional variants" when referring to polypeptides are those that have at least one amino acid residue in a native or starting sequence removed and a different amino acid inserted in its place at the same position. Substitutions may be single, where only one amino acid in the molecule has been substituted, or they may be multiple, where two or more (e.g., 3, 4 or 5) amino acids have been substituted in the same molecule.

As used herein the term "conservative amino acid substitution" refers to the substitution of an amino acid that is normally present in the sequence with a different amino acid of similar size, charge, or polarity. Examples of conservative substitutions include the substitution of a non-polar (hydrophobic) residue such as isoleucine, valine and leucine for another non-polar residue. Likewise, examples of conservative substitutions include the substitution of one polar (hydrophilic) residue for another such as between arginine and lysine, between glutamine and asparagine, and between glycine and serine. Additionally, the substitution of a basic residue such as lysine, arginine or histidine for another, or the substitution of one acidic residue such as aspartic acid or glutamic acid for another acidic residue are additional examples of conservative substitutions. Examples of nonconservative substitutions include the substitution of a nonpolar (hydrophobic) amino acid residue such as isoleucine, valine, leucine, alanine, methionine for a polar (hydrophilic) residue such as cysteine, glutamine, glutamic acid or lysine and/or a polar residue for a non-polar residue.

"Features" when referring to polypeptide or polynucle-"Orthologs" refers to genes in different species that 55 otide are defined as distinct amino acid sequence-based or nucleotide-based components of a molecule respectively. Features of the polypeptides encoded by the polynucleotides include surface manifestations, local conformational shape, folds, loops, half-loops, domains, half-domains, sites, ter-60 mini and any combination(s) thereof.

As used herein when referring to polypeptides the term "domain" refers to a motif of a polypeptide having one or more identifiable structural or functional characteristics or properties (e.g., binding capacity, serving as a site for protein-protein interactions).

As used herein when referring to polypeptides the terms "site" as it pertains to amino acid based embodiments is used

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synonymously with "amino acid residue" and "amino acid side chain." As used herein when referring to polynucleotides the terms "site" as it pertains to nucleotide based embodiments is used synonymously with "nucleotide." A site represents a position within a peptide or polypeptide or 5 polynucleotide that may be modified, manipulated, altered, derivatized or varied within the polypeptide-based or polynucleotide-based molecules.

As used herein the terms "termini" or "terminus" when referring to polypeptides or polynucleotides refers to an 10 extremity of a polypeptide or polynucleotide respectively. Such extremity is not limited only to the first or final site of the polypeptide or polynucleotide but may include additional amino acids or nucleotides in the terminal regions. Polypeptide-based molecules may be characterized as hav- 15 ing both an N-terminus (terminated by an amino acid with a free amino group (NH2)) and a C-terminus (terminated by an amino acid with a free carboxyl group (COOH)). Proteins are in some cases made up of multiple polypeptide chains brought together by disulfide bonds or by non-covalent 20 forces (multimers, oligomers). These proteins have multiple N- and C-termini. Alternatively, the termini of the polypeptides may be modified such that they begin or end, as the case may be, with a non-polypeptide based moiety such as an organic conjugate.

As recognized by those skilled in the art, protein fragments, functional protein domains, and homologous proteins are also considered to be within the scope of polypeptides of interest. For example, provided herein is any protein fragment (meaning a polypeptide sequence at least one amino 30 acid residue shorter than a reference polypeptide sequence but otherwise identical) of a reference protein having a length of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or longer than 100 amino acids. In another example, any protein that includes a stretch of 20, 30, 40, 50, or 100 (contiguous) 35 amino acids that are 40%, 50%, 60%, 70%, 80%, 90%, 95%, or 100% identical to any of the sequences described herein can be utilized in accordance with the disclosure. In some embodiments, a polypeptide includes 2, 3, 4, 5, 6, 7, 8, 9, 10, or more mutations as shown in any of the sequences pro- 40 vided herein or referenced herein. In another example, any protein that includes a stretch of 20, 30, 40, 50, or 100 amino acids that are greater than 80%, 90%, 95%, or 100% identical to any of the sequences described herein, wherein the protein has a stretch of 5, 10, 15, 20, 25, or 30 amino 45 acids that are less than 80%, 75%, 70%, 65% to 60% identical to any of the sequences described herein can be utilized in accordance with the disclosure.

Polypeptide or polynucleotide molecules of the present disclosure may share a certain degree of sequence similarity 50 or identity with the reference molecules (e.g., reference polypeptides or reference polynucleotides), for example, with art-described molecules (e.g., engineered or designed molecules or wild-type molecules). The term "identity," as known in the art, refers to a relationship between the 55 sequences of two or more polypeptides or polynucleotides, as determined by comparing the sequences. In the art, identity also means the degree of sequence relatedness between two sequences as determined by the number of matches between strings of two or more amino acid residues 60 or nucleic acid residues. Identity measures the percent of identical matches between the smaller of two or more sequences with gap alignments (if any) addressed by a particular mathematical model or computer program (e.g., "algorithms"). Identity of related peptides can be readily 65 calculated by known methods. "% identity" as it applies to polypeptide or polynucleotide sequences is defined as the

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percentage of residues (amino acid residues or nucleic acid residues) in the candidate amino acid or nucleic acid sequence that are identical with the residues in the amino acid sequence or nucleic acid sequence of a second sequence after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent identity. Methods and computer programs for the alignment are well known in the art. Identity depends on a calculation of percent identity but may differ in value due to gaps and penalties introduced in the calculation. Generally, variants of a particular polynucleotide or polypeptide have at least 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% but less than 100% sequence identity to that particular reference polynucleotide or polypeptide as determined by sequence alignment programs and parameters described herein and known to those skilled in the art. Such tools for alignment include those of the BLAST suite (Stephen F. Altschul, et al. (1997)." Gapped BLAST and PSI-BLAST: a new generation of protein database search programs," Nucleic Acids Res. 25:3389-3402). Another popular local alignment technique is based on the Smith-Waterman algorithm (Smith, T. F. & Waterman, M. S. (1981) "Identification of common molecular subsequences." J. Mol. Biol. 147:195-197). A general global alignment technique based on dynamic programming is the Needleman-Wunsch algorithm (Needleman, S. B. & Wunsch, C. D. (1970) "A general method applicable to the search for similarities in the amino acid sequences of two proteins." J. Mol. Biol. 48:443-453). More recently, a Fast Optimal Global Sequence Alignment Algorithm (FOGSAA) was developed that purportedly produces global alignment of nucleotide and protein sequences faster than other optimal global alignment methods, including the Needleman-Wunsch algorithm. Other tools are described herein, specifically in the definition of "identity" below.

As used herein, the term "homology" refers to the overall relatedness between polymeric molecules, e.g. between nucleic acid molecules (e.g. DNA molecules and/or RNA molecules) and/or between polypeptide molecules. Polymeric molecules (e.g. nucleic acid molecules (e.g. DNA molecules and/or RNA molecules) and/or polypeptide molecules) that share a threshold level of similarity or identity determined by alignment of matching residues are termed homologous. Homology is a qualitative term that describes a relationship between molecules and can be based upon the quantitative similarity or identity. Similarity or identity is a quantitative term that defines the degree of sequence match between two compared sequences. In some embodiments, polymeric molecules are considered to be "homologous" to one another if their sequences are at least 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% identical or similar. The term "homologous" necessarily refers to a comparison between at least two sequences (polynucleotide or polypeptide sequences). Two polynucleotide sequences are considered homologous if the polypeptides they encode are at least 50%, 60%, 70%, 80%, 90%, 95%, or even 99% for at least one stretch of at least 20 amino acids. In some embodiments, homologous polynucleotide sequences are characterized by the ability to encode a stretch of at least 4-5 uniquely specified amino acids. For polynucleotide sequences less than 60 nucleotides in length, homology is determined by the ability to encode a stretch of at least 4-5 uniquely specified amino acids. Two protein sequences are considered homologous if the proteins are at least 50%, 60%, 70%, 80%, or 90% identical for at least one stretch of at least 20 amino acids.

Homology implies that the compared sequences diverged in evolution from a common origin. The term "homolog" refers to a first amino acid sequence or nucleic acid sequence (e.g., gene (DNA or RNA) or protein sequence) that is related to a second amino acid sequence or nucleic acid 5 sequence by descent from a common ancestral sequence. The term "homolog" may apply to the relationship between genes and/or proteins separated by the event of speciation or to the relationship between genes and/or proteins separated by the event of genetic duplication. "Orthologs" are genes 10 (or proteins) in different species that evolved from a common ancestral gene (or protein) by speciation. Typically, orthologs retain the same function in the course of evolution. "Paralogs" are genes (or proteins) related by duplication within a genome. Orthologs retain the same function in the 15 course of evolution, whereas paralogs evolve new functions, even if these are related to the original one.

The term "identity" refers to the overall relatedness between polymeric molecules, for example, between polynucleotide molecules (e.g. DNA molecules and/or RNA 20 molecules) and/or between polypeptide molecules. Calculation of the percent identity of two polynucleic acid sequences, for example, can be performed by aligning the two sequences for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second 25 nucleic acid sequences for optimal alignment and nonidentical sequences can be disregarded for comparison purposes). In certain embodiments, the length of a sequence aligned for comparison purposes is at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, 30 at least 90%, at least 95%, or 100% of the length of the reference sequence. The nucleotides at corresponding nucleotide positions are then compared. When a position in the first sequence is occupied by the same nucleotide as the corresponding position in the second sequence, then the 35 molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which needs to be introduced for optimal alignment of the 40 two sequences. The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. For example, the percent identity between two nucleic acid sequences can be determined using methods such as those described in 45 Computational Molecular Biology, Lesk, A. M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D. W., ed., Academic Press, New York, 1993; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; Computer Analysis 50 of Sequence Data, Part I, Griffin, A. M., and Griffin, H. G., eds., Humana Press, New Jersey, 1994; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991; each of which is incorporated herein by reference. For example, the percent identity 55 between two nucleic acid sequences can be determined using the algorithm of Meyers and Miller (CABIOS, 1989, 4:11-17), which has been incorporated into the ALIGN program (version 2.0) using a PAM 120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. The 60 percent identity between two nucleic acid sequences can, alternatively, be determined using the GAP program in the GCG software package using an NWSgapdna.CMP matrix. Methods commonly employed to determine percent identity between sequences include, but are not limited to those 65 disclosed in Carillo, H., and Lipman, D., SIAM J Applied Math., 48:1073 (1988); incorporated herein by reference.

Techniques for determining identity are codified in publicly available computer programs. Exemplary computer software to determine homology between two sequences include, but are not limited to, GCG program package, Devereux, J., et al., *Nucleic Acids Research*, 12(1), 387 (1984)), BLASTP, BLASTN, and FASTA Altschul, S. F. et al., *J. Molec. Biol.*, 215, 403 (1990)).

Multiprotein and Multicomponent Vaccines

The present disclosure encompasses respiratory virus vaccines comprising multiple RNA (e.g., mRNA) polynucleotides, each encoding a single antigenic polypeptide, as well as respiratory virus vaccines comprising a single RNA polynucleotide encoding more than one antigenic polypeptide (e.g., as a fusion polypeptide). Thus, a vaccine composition comprising a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a first antigenic polypeptide and a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a second antigenic polypeptide encompasses (a) vaccines that comprise a first RNA polynucleotide encoding a first antigenic polypeptide and a second RNA polynucleotide encoding a second antigenic polypeptide, and (b) vaccines that comprise a single RNA polynucleotide encoding a first and second antigenic polypeptide (e.g., as a fusion polypeptide). RNA (e.g., mRNA) vaccines of the present disclosure, in some embodiments, comprise 2-10 (e.g., 2, 3, 4, 5, 6, 7, 8, 9 or 10), or more, RNA polynucleotides having an open reading frame, each of which encodes a different antigenic polypeptide (or a single RNA polynucleotide encoding 2-10, or more, different antigenic polypeptides). The antigenic polypeptides may be selected from hMPV, PIV3, RSV, MEV and BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) antigenic polypeptides.

In some embodiments, a respiratory virus vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral capsid protein, a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral premembrane/membrane protein, and a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral envelope protein. In some embodiments, a respiratory virus vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral fusion (F) protein and a RNA polynucleotide having an open reading frame encoding a viral major surface glycoprotein (G protein). In some embodiments, a vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral F protein. In some embodiments, a vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral G protein. In some embodiments, a vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a HN protein.

In some embodiments, a multicomponent vaccine comprises at least one RNA (e.g., mRNA) polynucleotide encoding at least one antigenic polypeptide fused to a signal peptide (e.g., any one of SEQ ID NO: 15-19). The signal peptide may be fused at the N-terminus or the C-terminus of an antigenic polypeptide. An antigenic polypeptide fused to a signal peptide may be selected from hMPV, PIV3, RSV, MEV and BetaCoV (e.g., selected from MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) antigenic polypeptides. Signal Peptides

In some embodiments, antigenic polypeptides encoded by respiratory virus RNA (e.g., mRNA) polynucleotides comprise a signal peptide. Signal peptides, comprising the

N-terminal 15-60 amino acids of proteins, are typically needed for the translocation across the membrane on the secretory pathway and, thus, universally control the entry of most proteins both in eukaryotes and prokaryotes to the secretory pathway. Signal peptides generally include three 5 regions: an N-terminal region of differing length, which usually comprises positively charged amino acids; a hydrophobic region; and a short carboxy-terminal peptide region. In eukaryotes, the signal peptide of a nascent precursor protein (pre-protein) directs the ribosome to the rough 10 endoplasmic reticulum (ER) membrane and initiates the transport of the growing peptide chain across it for processing. ER processing produces mature proteins, wherein the signal peptide is cleaved from precursor proteins, typically by a ER-resident signal peptidase of the host cell, or they 15 remain uncleaved and function as a membrane anchor. A signal peptide may also facilitate the targeting of the protein to the cell membrane. The signal peptide, however, is not responsible for the final destination of the mature protein. Secretory proteins devoid of additional address tags in their 20 sequence are by default secreted to the external environment. During recent years, a more advanced view of signal peptides has evolved, showing that the functions and immunodominance of certain signal peptides are much more versatile than previously anticipated.

Respiratory virus vaccines of the present disclosure may comprise, for example, RNA (e.g., mRNA) polynucleotides encoding an artificial signal peptide, wherein the signal peptide coding sequence is operably linked to and is in frame with the coding sequence of the antigenic polypeptide. Thus, 30 respiratory virus vaccines of the present disclosure, in some embodiments, produce an antigenic polypeptide comprising an antigenic polypeptide (e.g., hMPV, PIV3, RSV, MeV or BetaCoV) fused to a signal peptide. In some embodiments, a signal peptide is fused to the N-terminus of the antigenic 35 polypeptide. In some embodiments, a signal peptide is fused to the C-terminus of the antigenic polypeptide.

In some embodiments, the signal peptide fused to the antigenic polypeptide is an artificial signal peptide. In some embodiments, an artificial signal peptide fused to the anti- 40 genic polypeptide encoded by the RNA (e.g., mRNA) vaccine is obtained from an immunoglobulin protein, e.g., an IgE signal peptide or an IgG signal peptide. In some embodiments, a signal peptide fused to the antigenic polypeptide encoded by a RNA (e.g., mRNA) vaccine is an Ig 45 heavy chain epsilon-1 signal peptide (IgE HC SP) having the sequence of: MDWTWILFLVAAATRVHS (SEQ ID NO: 16). In some embodiments, a signal peptide fused to the antigenic polypeptide encoded by the (e.g., mRNA) RNA (e.g., mRNA) vaccine is an IgGk chain V-III region HAH 50 signal peptide (IgGk SP) having the sequence of MET-PAQLLFLLLWLPDTTG (SEQ ID NO: 15). In some embodiments, the signal peptide is selected from: Japanese encephalitis PRM signal sequence (MLGSNSGQRV-VFTILLLLVAPAYS; SEQ ID NO: 17), VSVg protein signal 55 sequence (MKCLLYLAFLFIGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWLVS-LAIVTACAGA; SEQ ID NO: 19).

In some embodiments, the antigenic polypeptide encoded by a RNA (e.g., mRNA) vaccine comprises an amino acid 60 sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, 47-50 or 54-56 (Tables 3, 6, 11, 14 or 17; see also amino acid sequences of Tables 4, 7, 12 or 15) fused to a signal peptide identified by any one of SEQ ID NO: 15-19 (Table 8). The examples disclosed herein are not meant to be 65 limiting and any signal peptide that is known in the art to facilitate targeting of a protein to ER for processing and/or

targeting of a protein to the cell membrane may be used in accordance with the present disclosure.

A signal peptide may have a length of 15-60 amino acids. For example, a signal peptide may have a length of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, or 60 amino acids. In some embodiments, a signal peptide has a length of 20-60, 25-60, 30-60, 35-60, 40-60, 45-60, 50-60, 55-60, 15-55, 20-55, 25-55, 30-55, 35-55, 40-55, 45-55, 50-55, 15-50, 20-50, 25-50, 30-50, 35-50, 40-50, 45-50, 15-45, 20-45, 25-45, 30-45, 35-45, 40-45, 15-40, 20-40, 25-40, 30-40, 35-40, 15-35, 20-35, 25-35, 30-35, 15-30, 20-30, 25-30, 15-25, 20-25, or 15-20 amino acids.

A signal peptide is typically cleaved from the nascent polypeptide at the cleavage junction during ER processing. The mature antigenic polypeptide produce by a respiratory virus RNA (e.g., mRNA) vaccine of the present disclosure typically does not comprise a signal peptide.

Chemical Modifications

Respiratory virus vaccines of the present disclosure, in some embodiments, comprise at least RNA (e.g. mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide that comprises at least one 25 chemical modification.

The terms "chemical modification" and "chemically modified" refer to modification with respect to adenosine (A), guanosine (G), uridine (U), thymidine (T) or cytidine (C) ribonucleosides or deoxyribnucleosides in at least one of their position, pattern, percent or population. Generally, these terms do not refer to the ribonucleotide modifications in naturally occurring 5'-terminal mRNA cap moieties. With respect to a polypeptide, the term "modification" refers to a modification relative to the canonical set 20 amino acids. Polypeptides, as provided herein, are also considered "modified" of they contain amino acid substitutions, insertions or a combination of substitutions and insertions.

Polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides), in some embodiments, comprise various (more than one) different modifications. In some embodiments, a particular region of a polynucleotide contains one, two or more (optionally different) nucleoside or nucleotide modifications. In some embodiments, a modified RNA polynucleotide (e.g., a modified mRNA polynucleotide), introduced to a cell or organism, exhibits reduced degradation in the cell or organism, respectively, relative to an unmodified polynucleotide (e.g., a modified mRNA polynucleotide), introduced into a cell or organism, may exhibit reduced immunogenicity in the cell or organism, respectively (e.g., a reduced innate response).

Modifications of polynucleotides include, without limitation, those described herein. Polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) may comprise modifications that are naturally-occurring, non-naturally-occurring or the polynucleotide may comprise a combination of naturally-occurring and non-naturally-occurring modifications. Polynucleotides may include any useful modification, for example, of a sugar, a nucleobase, or an internucleoside linkage (e.g., to a linking phosphate, to a phosphodiester linkage or to the phosphodiester backbone).

Polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides), in some embodiments, comprise non-natural modified nucleotides that are introduced during synthesis or post-synthesis of the polynucleotides to achieve desired functions or properties. The modifications may be present on an internucleotide linkages, purine or pyrimidine

bases, or sugars. The modification may be introduced with chemical synthesis or with a polymerase enzyme at the terminal of a chain or anywhere else in the chain. Any of the regions of a polynucleotide may be chemically modified.

The present disclosure provides for modified nucleosides 5 and nucleotides of a polynucleotide (e.g., RNA polynucleotides, such as mRNA polynucleotides). A "nucleoside" refers to a compound containing a sugar molecule (e.g., a pentose or ribose) or a derivative thereof in combination with an organic base (e.g., a purine or pyrimidine) or a 10 derivative thereof (also referred to herein as "nucleobase"). A nucleotide" refers to a nucleoside, including a phosphate group. Modified nucleotides may by synthesized by any useful method, such as, for example, chemically, enzymatically, or recombinantly, to include one or more modified or 15 non-natural nucleosides. Polynucleotides may comprise a region or regions of linked nucleosides. Such regions may have variable backbone linkages. The linkages may be standard phosphdioester linkages, in which case the polynucleotides would comprise regions of nucleotides. 20

Modified nucleotide base pairing encompasses not only the standard adenosine-thymine, adenosine-uracil, or guanosine-cytosine base pairs, but also base pairs formed between nucleotides and/or modified nucleotides comprising non-standard or modified bases, wherein the arrange-25 ment of hydrogen bond donors and hydrogen bond acceptors permits hydrogen bonding between a non-standard base and a standard base or between two complementary non-standard base structures. One example of such non-standard base pairing is the base pairing between the modified nucleotide 30 inosine and adenine, cytosine or uracil. Any combination of base/sugar or linker may be incorporated into polynucleotides of the present disclosure.

Modifications of polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) that are useful in the 35 vaccines of the present disclosure include, but are not limited to the following: 2-methylthio-N6-(cis-hydroxyisopentenyl)adenosine; 2-methylthio-N6-methyladenosine; 2-methylthio-N6-threonyl carbamoyladenosine; N6-glycinylcarbamoyladenosine; N6-isopentenyladenosine; 40 N6-methyladenosine; N6-threonylcarbamoyladenosine; 1,2'-O-dimethyladenosine; 1-methyladenosine; 2'-O-methyladenosine; 2'-O-ribosyladenosine (phosphate); 2-methyladenosine; 2-methylthio-N6 isopentenyladenosine; 2-methylthio-N6-hydroxynorvalyl carbamoyladenosine; 2'-O- 45 methyladenosine; 2'-O-ribosyladenosine (phosphate); Isopentenyladenosine; N6-(cis-hydroxyisopentenyl)adenosine; N6,2'-O-dimethyladenosine; N6,2'-O-dimethyladenosine; N6,N6,2'-O-trimethyladenosine; N6,N6-dimethyladenosine; N6-acetyladenosine; 50 N6-hydroxynorvalylcarbamoyladenosine; N6-methyl-N6threonylcarbamoyladenosine; 2-methyladenosine; 2-methylthio-N6-isopentenyladenosine; 7-deaza-adenosine; N1-methyl-adenosine; N6, N6 (dimethyl)adenine; N6-cishydroxy-isopentenyl-adenosine; α -thio-adenosine; 2 55 (amino)adenine; 2 (aminopropyl)adenine; 2 (methylthio) N6 (isopentenyl)adenine; 2-(alkyl)adenine; 2-(aminoalkyl)adenine; 2-(aminopropyl)adenine; 2-(halo)adenine; 2-(halo) adenine; 2-(propyl)adenine; 2'-Amino-2'-deoxy-ATP; 2'-Azido-2'-deoxy-ATP; 2'-Deoxy-2'-a-aminoadenosine TP; 60 2'-Deoxy-2'-a-azidoadenosine TP; 6 (alkyl)adenine; 6 (methyl)adenine; 6-(alkyl)adenine; 6-(methyl)adenine; (deaza)adenine; 8 (alkenyl)adenine; 8 (alkynyl)adenine; 8 (amino)adenine; 8 (thioalkyl)adenine; 8-(alkenyl)adenine; 8-(alkyl)adenine; 8-(alkynyl)adenine; 8-(amino)adenine; 65 8-(halo)adenine; 8-(hydroxyl)adenine; 8-(thioalkyl)adenine; 8-(thiol)adenine; 8-azido-adenosine; aza adenine; deaza

adenine; N6 (methyl)adenine; N6-(isopentyl)adenine; 7-deaza-8-aza-adenosine; 7-methyladenine; 1-Deazaadenosine TP; 2'Fluoro-N6-Bz-deoxyadenosine TP; 2'-OMe-2-Amino-ATP; 2'O-methyl-N6-Bz-deoxyadenosine TP; 2'-a-Ethynyladenosine TP; 2-aminoadenine; 2-Aminoadenosine TP; 2-Amino-ATP; 2'-a-Trifluoromethyladenosine TP; 2-Azidoadenosine TP; 2'-b-Ethynyladenosine TP; 2-Bromoadenosine TP; 2'-b-Trifluoromethyladenosine TP: 2-Chloroadenosine TP; 2'-Deoxy-2', 2'-difluoroadenosine TP; 2'-Deoxy-2'-a-mercaptoadenosine TP; 2'-Deoxy-2'-athiomethoxyadenosine TP; 2'-Deoxy-2'-b-aminoadenosine TP; 2'-Deoxy-2'-b-azidoadenosine TP; 2'-Deoxy-2'-b-bromoadenosine TP; 2'-Deoxy-2'-b-chloroadenosine TP; 2'-Deoxy-2'-b-fluoroadenosine TP; 2'-Deoxy-2'-b-iodoadenosine TP; 2'-Deoxy-2'-b-mercaptoadenosine TP; 2'-Deoxy-2'-bthiomethoxyadenosine TP; 2-Fluoroadenosine TP; 2-lodoadenosine TP; 2-Mercaptoadenosine TP; 2-methoxy-adenine; 2-methylthio-adenine; 2-Trifluoromethyladenosine TP; 3-Deaza-3-bromoadenosine TP; 3-Deaza-3-chloroadenosine TP: 3-Deaza-3-fluoroadenosine TP: 3-Deaza-3-iodoadenosine TP; 3-Deazaadenosine TP; 4'-Azidoadenosine TP; 4'-Carbocyclic adenosine TP; 4'-Ethynyladenosine TP; 5'-Homo-adenosine TP; 8-Aza-ATP; 8-bromo-adenosine TP; 8-Trifluoromethyladenosine TP; 9-Deazaadenosine TP; 2-aminopurine; 7-deaza-2,6-diaminopurine; 7-deaza-8-aza-2,6-diaminopurine; 7-deaza-8-aza-2-aminopurine; 2,6-diaminopurine; 7-deaza-8-aza-adenine, 7-deaza-2-aminopurine; 2-thiocytidine; 3-methylcytidine; 5-formylcytidine; 5-hydroxymethylcytidine; 5-methylcytidine; N4-acetylcytidine; 2'-O-methylcytidine; 2'-O-methylcytidine; 5,2'-O-dimethylcytidine; 5-formyl-2'-O-methylcytidine; Lysidine; N4,2'-O-dimethylcytidine; N4-acetyl-2'-O-methylcytidine; N4-methylcytidine; N4,N4-Dimethyl-2'-OMe-Cytidine TP; 4-methylcytidine; 5-aza-cytidine; Pseudo-iso-cytidine; pyrrolo-cytidine; α-thio-cytidine; 2-(thio)cytosine; 2'-Amino-2'-deoxy-CTP; 2'-Azido-2'-deoxy-CTP; 2'-Deoxy-2'-aaminocytidine TP; 2'-Deoxy-2'-a-azidocytidine TP; 3 (deaza) 5 (aza)cytosine; 3 (methyl)cytosine; 3-(alkyl)cytosine; 3-(deaza) 5 (aza)cytosine; 3-(methyl)cytidine; 4,2'-Odimethylcytidine; 5 (halo)cytosine; 5 (methyl)cytosine; 5 (propynyl)cytosine; 5 (trifluoromethyl)cytosine; 5-(alkyl) cytosine; 5-(alkynyl)cytosine; 5-(halo)cytosine; 5-(propynyl)cytosine; 5-(trifluoromethyl)cytosine; 5-bromo-cytidine; 5-iodo-cytidine; 5-propynyl cytosine; 6-(azo)cytosine; 6-aza-cytidine; aza cytosine; deaza cytosine; N4 (acetyl) cytosine; 1-methyl-1-deaza-pseudoisocytidine; 1-methylpseudoisocvtidine; 2-methoxy-5-methyl-cytidine: 2-methoxy-cytidine; 2-thio-5-methyl-cytidine; 4-methoxy-1-methyl-pseudoisocytidine; 4-methoxy-pseudoisocytidine; 4-thio-1-methyl-1-deaza-pseudoisocytidine; 4-thio-1methyl-pseudoisocytidine; 4-thio-pseudoisocytidine; 5-azazebularine; 5-methyl-zebularine; pyrrolo-pseudoisocytidine; Zebularine; (E)-5-(2-Bromo-vinyl)cytidine TP; 2,2'-anhydro-cytidine TP hydrochloride; 2'Fluor-N4-Bz-cytidine TP; 2'Fluoro-N4-Acetyl-cytidine TP; 2'-O-Methyl-N4-Acetyl-cytidine TP; 2'O-methyl-N4-Bz-cytidine TP; 2'-a-Ethynylcytidine TP; 2'-a-Trifluoromethylcytidine TP; 2'-b-Ethynylcytidine TP; 2'-b-Trifluoromethylcytidine TP; 2'-Deoxy-2', 2'-difluorocytidine TP; 2'-Deoxy-2'-a-mercaptocytidine TP; 2'-Deoxy-2'-a-thiomethoxycytidine TP; 2'-Deoxy-2'-b-aminocytidine TP; 2'-Deoxy-2'-b-azidocytidine TP; 2'-Deoxy-2'-b-bromocytidine TP; 2'-Deoxy-2'-bchlorocytidine TP; 2'-Deoxy-2'-b-fluorocytidine TP; 2'-Deoxy-2'-b-iodocytidine TP; 2'-Deoxy-2'-b-mercaptocytidine TP; 2'-Deoxy-2'-b-thiomethoxycytidine TP; 2'-O-Methyl-5-(1-propynyl)cytidine TP; 3'-Ethynylcytidine TP; 4'-Azidocytidine TP; 4'-Carbocyclic cytidine TP; 4'-Ethynylcytidine

methyluridine;

TP; 5-(1-Propynyl)ara-cytidine TP; 5-(2-Chloro-phenyl)-2thiocytidine TP; 5-(4-Amino-phenyl)-2-thiocytidine TP; 5-Aminoallyl-CTP; 5-Cyanocytidine TP; 5-Ethynylara-cytidine TP; 5-Ethynylcytidine TP; 5'-Homo-cytidine TP; 5-Methoxycytidine TP; 5-Trifluoromethyl-Cytidine TP; 5 N4-Amino-cytidine TP; N4-Benzoyl-cytidine TP; Pseudoisocytidine; 7-methylguanosine; N2,2'-O-dimethylguanosine; N2-methylguanosine; Wyosine; 1,2'-O-dimethylguanosine; 1-methylguanosine; 2'-O-methylguanosine; 2'-O-ribosylguanosine (phosphate); 2'-O-methylguanosine; 10 2'-O-ribosylguanosine (phosphate); 7-aminomethyl-7deazaguanosine; 7-cyano-7-deazaguanosine; Archaeosine; Methylwyosine; N2,7-dimethylguanosine; N2,N2,2'-Otrimethylguanosine; N2,N2,7-trimethylguanosine; N2,N2dimethylguanosine; N2,7,2'-O-trimethylguanosine; 6-thio- 15 7-deaza-guanosine; 8-oxo-guanosine; guanosine; N1-methyl-guanosine; α -thio-guanosine; 2 (propyl)guanine; 2-(alkyl)guanine; 2'-Amino-2'-deoxy-GTP; 2'-Azido-2'-deoxy-GTP; 2'-Deoxy-2'-a-aminoguanosine TP; 2'-Deoxy-2'a-azidoguanosine TP; 6 (methyl)guanine; 6-(alkyl)guanine; 20 6-(methyl)guanine; 6-methyl-guanosine; 7 (alkyl)guanine; 7 (deaza)guanine; 7 (methyl)guanine; 7-(alkyl)guanine; 7-(deaza)guanine; 7-(methyl)guanine; 8 (alkyl)guanine; 8 (alkynyl)guanine; 8 (halo)guanine; 8 (thioalkyl)guanine; 8-(alkenyl)guanine; 8-(alkyl)guanine; 8-(alkynyl)guanine; 25 8-(amino)guanine; 8-(halo)guanine; 8-(hydroxyl)guanine; 8-(thioalkyl)guanine; 8-(thiol)guanine; aza guanine; deaza guanine; N (methyl)guanine; N-(methyl)guanine; 1-methyl-6-thio-guanosine; 6-methoxy-guanosine; 6-thio-7-deaza-8aza-guanosine; 6-thio-7-deaza-guanosine; 6-thio-7-methyl- 30 7-deaza-8-aza-guanosine; guanosine; 7-methyl-8-oxoguanosine; N2,N2-dimethyl-6-thio-guanosine; N2-methyl-6-thio-guanosine; 1-Me-GTP: 2'Fluoro-N2-isobutylguanosine TP; 2'O-methyl-N2-isobutyl-guanosine TP; 2'-a-Ethynylguanosine TP; 2'-a-Trifluoromethylguanosine TP; 35 2'-b-Ethynylguanosine TP; 2'-b-Trifluoromethylguanosine TP; 2'-Deoxy-2', 2'-difluoroguanosine TP; 2'-Deoxy-2'-amercaptoguanosine TP; 2'-Deoxy-2'-a-thiomethoxyguanosine TP; 2'-Deoxy-2'-b-aminoguanosine TP; 2'-Deoxy-2'-bazidoguanosine TP; 2'-Deoxy-2'-b-bromoguanosine TP; 40 2'-Deoxy-2'-b-chloroguanosine TP; 2'-Deoxy-2'-b-fluoroguanosine TP; 2'-Deoxy-2'-b-iodoguanosine TP; 2'-Deoxy-2'-b-mercaptoguanosine TP; 2'-Deoxy-2'-b-thiomethoxyguanosine TP; 4'-Azidoguanosine TP; 4'-Carbocyclic guanosine TP; 4'-Ethynylguanosine TP; 45 5'-Homo-guanosine TP; 8-bromo-guanosine TP; 9-Deazaguanosine TP: N2-isobutyl-guanosine TP: 1-methylinosine; 1,2'-O-dimethylinosine; 2'-O-methylinosine; Inosine: 7-methylinosine; 2'-O-methylinosine; Epoxyqueuosine; galactosyl-queuosine; Mannosylqueuosine; Queuosine; 50 allyamino-thymidine; aza thymidine; deaza thymidine; deoxy-thymidine; 2'-O-methyluridine; 2-thiouridine; 3-methyluridine; 5-carboxymethyluridine; 5-hydroxyuridine; 5-methyluridine; 5-taurinomethyl-2-thiouridine; 5-taurinomethyluridine; Dihydrouridine; Pseudouridine; (3-(3- 55 amino-3-carboxypropyl)uridine; 1-methyl-3-(3-amino-5carboxypropyl)pseudouridine; 1-methylpseduouridine; 1-methyl-pseudouridine; 2'-O-methyluridine; 2'-O-methylpseudouridine; 2'-O-methyluridine; 2-thio-2'-O-methyluridine; 3-(3-amino-3-carboxypropyl)uridine; 3,2'-O-dimethy- 60 luridine; 3-Methyl-pseudo-Uridine TP; 4-thiouridine; 5-(carboxyhydroxymethyl)uridine; 5-(carboxyhydroxymethyl)uridine methyl ester; 5,2'-O-dimethyluridine; 5,6-dihydro-uridine; 5-aminomethyl-2-thiouridine; 5-carbamoylmethyl-2'-O-methyluridine; 5-carbamoylmethyluridine; 65 5-carboxyhydroxymethyluridine; 5-carboxyhydroxymethyluridine methyl ester; 5-carboxymethylaminomethyl-2'-O-

5-carboxymethylaminomethyl-2-thiouri-

5-carboxymethylaminomethyl-2-thiouridine; dine; 5-carboxymethylaminomethyluridine; 5-carboxymethylaminomethyluridine; 5-Carbamoylmethyluridine TP: 5-methoxycarbonylmethyl-2'-O-methyluridine; 5-methoxycarbonylmethyl-2-thiouridine; 5-methoxycarbonylmethyluridine; 5-methoxyuridine; 5-methyl-2-thiouridine; 5-methylaminomethyl-2-selenouridine; 5-methylaminomethyl-2thiouridine; 5-methylaminomethyluridine; 5-Methyldihydrouridine; 5-Oxyacetic acid-Uridine TP; 5-Oxyacetic acid-methyl ester-Uridine TP; N1-methylpseudo-uridine; uridine 5-oxyacetic acid; uridine 5-oxyacetic acid methyl ester; 3-(3-Amino-3-carboxypropyl)-Uridine TP; 5-(iso-Pentenylaminomethyl)-2-thiouridine TP; 5-(iso-Pentenylaminomethyl)-2'-O-methyluridine TP; 5-(iso-Pentenylaminomethyl)uridine TP; 5-propynyl uracil; α -thio-uridine; 1 (aminoalkylamino-carbonylethylenyl)-2 (thio)-pseudouracil; 1 (aminoalkylaminocarbonylethylenyl)-2,4-(dithio)pseudouracil; 1 (aminoalkylaminocarbo-(thio)pseudouracil: nvlethvlenvl)-4 1 (aminoalkylaminocarbonylethylenyl)-pseudouracil; 1 (aminocarbonylethylenyl)-2(thio)-pseudouracil; 1 (aminocarbonylethylenyl)-2,4-(dithio)pseudouracil; 1 (aminocarbonylethylenyl)-4 (thio)pseudouracil; 1 (aminocarbonylethvlenvl)-pseudouracil; 1 substituted 2(thio)-pseudouracil; 1 substituted 2,4-(dithio)pseudouracil; 1 substituted 4 (thio) pseudouracil; 1 substituted pseudouracil; 1-(aminoalkylamino-carbonylethylenyl)-2-(thio)-pseudouracil; 1-Methyl-3-(3-amino-3-carboxypropyl) pseudouridine TP; 1-Methyl-3-(3-amino-3-carboxypropyl)pseudo-UTP; 1-Methyl-pseudo-UTP; 2 (thio)pseudouracil; 2' deoxy uridine; 2' fluorouridine; 2-(thio)uracil; 2,4-(dithio)psuedouracil; 2' methyl, 2'amino, 2' azido, 2'fluro-guanosine; 2'-Amino-2'-deoxy-UTP; 2'-Azido-2'-deoxy-UTP; 2'-Azido-deoxyuridine TP; 2'-O-methylpseudouridine; 2' deoxy uridine; 2' fluorouridine; 2'-Deoxy-2'-a-aminouridine TP; 2'-Deoxy-2'-a-azidouridine TP; 2-methylpseudouridine; 3 (3 amino-3 carboxypropyl)uracil; 4 (thio)pseudouracil; 4-(thio)pseudouracil; 4-(thio)uracil; 4-thiouracil; 5 (1,3-diazole-1-alkyl)uracil; 5 (2-aminopropyl)uracil; 5 (aminoalkyl)uracil; 5 (dimethylaminoalkyl)uracil; 5 (guanidiniumalkyl)uracil; 5 (methoxycarbonylmethyl)-2-(thio)uracil; 5 (methoxycarbonyl-methyl)uracil; 5 (methyl) 2 (thio)uracil; 5 (methyl) 2,4 (dithio)uracil; 5 (methyl) 4 (thio)uracil; 5 (methylaminomethyl)-2 (thio)uracil; 5 (methylaminomethyl)-2,4 (dithio)uracil; 5 (methylaminomethyl)-4 (thio) uracil; 5 (propynyl)uracil; 5 (trifluoromethyl)uracil; 5-(2aminopropyl)uracil; 5-(alkyl)-2-(thio)pseudouracil; (dithio)pseudouracil; 5-(alkyl)-4 5-(alkyl)-2,4 (thio) pseudouracil; 5-(alkyl)pseudouracil; 5-(alkyl)uracil; 5-(alkynyl)uracil; 5-(allylamino)uracil; 5-(cyanoalkyl)uracil; 5-(dialkylaminoalkyl)uracil; 5-(dimethylaminoalkyl) uracil; 5-(guanidiniumalkyl)uracil; 5-(halo)uracil; 5-(1,3-diazole-1-alkyl)uracil; 5-(methoxy)uracil; 5-(methoxycarbonylmethyl)-2-(thio)uracil; 5-(methoxycarbonyl-methyl)uracil; 5-(methyl) 2(thio)uracil; 5-(methyl) 2,4 (dithio)uracil; 5-(methyl) 4 (thio)uracil; 5-(methyl)-2-(thio)pseudouracil; 5-(methyl)-2,4 (dithio)pseudouracil; 5-(methyl)-4 (thio)pseudouracil; 5-(methyl)pseudouracil; 5-(methylaminomethyl)-2 (thio)uracil; 5-(methylaminomethyl)-2,4(dithio)uracil; 5-(methylaminomethyl)-4-(thio) uracil: 5-(propynyl)uracil; 5-(trifluoromethyl)uracil; 5-aminoallyl-uridine; 5-bromo-uridine; 5-iodo-uridine;

5-uracil; 6 (azo)uracil; 6-(azo)uracil; 6-aza-uridine; allyamino-uracil; aza uracil; deaza uracil; N3 (methyl)uracil; Pseudo-UTP-1-2-ethanoic acid; Pseudouracil; 4-Thiopseudo-UTP; 1-carboxymethyl-pseudouridine; 1-methyl-1deaza-pseudouridine; 1-propynyl-uridine; 1-taurinomethyl-1-methyl-uridine; 1-taurinomethyl-4-thio-uridine; 1-taurinomethyl-pseudouridine; 2-methoxy-4-thio-pseudouridine; 2-thio-1-methyl-1-deaza-pseudouridine; 2-thio-1methyl-pseudouridine; 2-thio-5-aza-uridine; 2-thio-dihy- 5 dropseudouridine; 2-thio-dihydrouridine; 2-thio-4-methoxy-2-thio-pseudouridine; pseudouridine; 4-methoxy-pseudouridine; 4-thio-1-methyl-pseudouridine; 4-thio-pseudouridine; 5-aza-uridine; Dihydropseudouridine; (±) 1-(2-Hydroxypropyl)pseudouridine TP; (2R)-1-(2-Hy- 10 droxypropyl)pseudouridine TP; (2S)-1-(2-Hydroxypropyl) pseudouridine TP; (E)-5-(2-Bromo-vinyl)ara-uridine TP; (E)-5-(2-Bromo-vinyl)uridine TP; (Z)-5-(2-Bromo-vinyl) ara-uridine TP; (Z)-5-(2-Bromo-vinyl)uridine TP; 1-(2,2,2-Trifluoroethyl)-pseudo-UTP; 1-(2,2,3,3,3-Pentafluoropro- 15 pyl)pseudouridine TP; 1-(2,2-Diethoxyethyl)pseudouridine TP; 1-(2,4,6-Trimethylbenzyl)pseudouridine TP; 1-(2,4,6-Trimethyl-benzyl)pseudo-UTP; 1-(2,4,6-Trimethyl-phenyl) pseudo-UTP; 1-(2-Amino-2-carboxyethyl)pseudo-UTP; 1-(2-Amino-ethyl)pseudo-UTP; 1-(2-Hvdroxvethvl) 20 pseudouridine TP; 1-(2-Methoxyethyl)pseudouridine TP; 1-(3,4-Bis-trifluoromethoxybenzyl)pseudouridine TP; 1-(3, 4-Dimethoxybenzyl)pseudouridine TP; 1-(3-Amino-3-carboxypropyl)pseudo-UTP; 1-(3-Amino-propyl)pseudo-UTP; 1-(3-Cyclopropyl-prop-2-ynyl)pseudouridine TP; 1-(4- 25 Amino-4-carboxybutyl)pseudo-UTP; 1-(4-Amino-benzyl) pseudo-UTP; 1-(4-Amino-butyl)pseudo-UTP; 1-(4-Aminophenyl)pseudo-UTP; 1-(4-Azidobenzyl)pseudouridine TP; 1-(4-Bromobenzyl)pseudouridine TP; 1-(4-Chlorobenzyl) pseudouridine TP; 1-(4-Fluorobenzyl)pseudouridine TP; 30 1-(4-Iodobenzyl)pseudouridine TP; 1-(4-Methanesulfonylbenzyl)pseudouridine TP; 1-(4-Methoxybenzyl)pseudouridine TP; 1-(4-Methoxy-benzyl)pseudo-UTP; 1-(4-Methoxyphenyl)pseudo-UTP; 1-(4-Methylbenzyl)pseudouridine TP; 1-(4-Methyl-benzyl)pseudo-UTP; 1-(4-Nitrobenzyl) 35 pseudouridine TP; 1-(4-Nitro-benzyl)pseudo-UTP; 1(4-Nitro-phenyl)pseudo-UTP; 1-(4-Thiomethoxybenzyl) pseudouridine TP; 1-(4-Trifluoromethoxybenzyl) pseudouridine TP: 1-(4-Trifluoromethylbenzyl) pseudouridine TP; 1-(5-Amino-pentyl)pseudo-UTP; 1-(6- 40 Amino-hexyl)pseudo-UTP; 1,6-Dimethyl-pseudo-UTP; 1-[3-(2-{2-[2-(2-Aminoethoxy)-ethoxy]-ethoxy}-ethoxy)propionyl]pseudouridine TP; 1-{3-[2-(2-Aminoethoxy)ethoxy]-propionyl}pseudouridine TP; 1-Acetylpseudouridine TP; 1-Alkyl-6-(1-propynyl)-pseudo-UTP; 1-Alkyl-6- 45 (2-propynyl)-pseudo-UTP; 1-Alkyl-6-allyl-pseudo-UTP; 1-Alkyl-6-ethynyl-pseudo-UTP; 1-Alkvl-6-homoallvlpseudo-UTP; 1-Alkyl-6-vinyl-pseudo-UTP; 1-Allylpseudouridine TP; 1-Aminomethyl-pseudo-UTP; 1-Benzoylpseudouridine TP; 1-Benzyloxymethylpseudouridine TP; 50 1-Benzyl-pseudo-UTP; 1-Biotinyl-PEG2-pseudouridine TP; 1-Biotinylpseudouridine TP; 1-Butyl-pseudo-UTP; 1-Cyanomethylpseudouridine TP; 1-Cyclobutylmethyl-pseudo-UTP; 1-Cyclobutyl-pseudo-UTP; 1-Cycloheptylmethylpseudo-UTP; 1-Cycloheptyl-pseudo-UTP; 55 1-Cyclohexylmethyl-pseudo-UTP; 1-Cyclohexyl-pseudo-UTP: 1-Cyclooctylmethyl-pseudo-UTP; 1-Cyclooctylpseudo-UTP; 1-Cyclopentylmethyl-pseudo-UTP; 1-Cyclopentyl-pseudo-UTP; 1-Cyclopropylmethyl-pseudo-UTP; 1-Cyclopropyl-pseudo-UTP; 1-Ethyl-pseudo-UTP; 60 1-Hexyl-pseudo-UTP; 1-Homoallylpseudouridine TP; 1-Hydroxymethylpseudouridine TP; 1-iso-propyl-pseudo-UTP; 1-Me-2-thio-pseudo-UTP; 1-Me-4-thio-pseudo-UTP; 1-Me-alpha-thio-pseudo-UTP; 1-Methanesulfonylmethylpseudouridine TP; 1-Methoxymethylpseudouridine TP; 65 1-Methyl-6-(2,2,2-Trifluoroethyl)pseudo-UTP; 1-Methyl-6-(4-morpholino)-pseudo-UTP; 1-Methyl-6-(4-thiomor56

pholino)-pseudo-UTP; 1-Methyl-6-(substituted phenyl) pseudo-UTP; 1-Methyl-6-amino-pseudo-UTP; 1-Methyl-6azido-pseudo-UTP; 1-Methyl-6-bromo-pseudo-UTP; 1-Methyl-6-butyl-pseudo-UTP; 1-Methyl-6-chloro-pseudo-UTP; 1-Methyl-6-cyano-pseudo-UTP; 1-Methyl-6-dimethylamino-pseudo-UTP; 1-Methyl-6-ethoxy-pseudo-UTP; 1-Methyl-6-ethylcarboxylate-pseudo-UTP; 1-Methyl-6-1-Methyl-6-fluoro-pseudo-UTP; ethyl-pseudo-UTP; 1-Methyl-6-formyl-pseudo-UTP; 1-Methyl-6-hydroxyamino-pseudo-UTP; 1-Methyl-6-hydroxy-pseudo-UTP; 1-Methyl-6-iodo-pseudo-UTP; 1-Methyl-6-iso-propyl-pseudo-UTP; 1-Methyl-6-methoxy-pseudo-UTP; 1-Methyl-6-methylamino-pseudo-UTP; 1-Methyl-6-phenylpseudo-UTP; 1-Methyl-6-propyl-pseudo-UTP; 1-Methyl-6tert-butyl-pseudo-UTP; 1-Methyl-6-trifluoromethoxypseudo-UTP; 1-Methyl-6-trifluoromethyl-pseudo-UTP; 1-Morpholinomethylpseudouridine TP; 1-Pentyl-pseudo-UTP; 1-Phenyl-pseudo-UTP; 1-Pivaloylpseudouridine TP; TP; 1-Propyl-pseudo-UTP; 1-Propargylpseudouridine 1-propynyl-pseudouridine; 1-p-tolyl-pseudo-UTP; 1-tert-Butyl-pseudo-UTP; 1-Thiomethoxymethylpseudouridine TP; 1-Thiomorpholinomethylpseudouridine TP; 1-Trifluoroacetylpseudouridine TP; 1-Trifluoromethyl-pseudo-UTP; 1-Vinylpseudouridine TP; 2,2'-anhydro-uridine TP: 2'-bromo-deoxyuridine TP; 2'-F-5-Methyl-2'-deoxy-UTP; 2'-OMe-5-Me-UTP; 2'-OMe-pseudo-UTP; 2'-a-Ethynyluridine TP; 2'-a-Trifluoromethyluridine TP; 2'-b-Ethynyluridine TP; 2'-b-Trifluoromethyluridine TP; 2'-Deoxy-2', 2'-difluorouridine TP; 2'-Deoxy-2'-a-mercaptouridine TP; 2'-Deoxy-2'-a-thiomethoxyuridine TP; 2'-Deoxy-2'-b-aminouridine TP; 2'-Deoxy-2'-b-azidouridine TP; 2'-Deoxy-2'-bbromouridine TP; 2'-Deoxy-2'-b-chlorouridine TP; 2'-Deoxy-2'-b-fluorouridine TP; 2'-Deoxy-2'-b-iodouridine TP; 2'-Deoxy-2'-b-mercaptouridine TP; 2'-Deoxy-2'-b-thiomethoxyuridine TP; 2-methoxy-4-thio-uridine; 2-methoxyuridine; 2'-O-Methyl-5-(1-propynyl)uridine TP; 3-Alkyl-pseudo-UTP; 4'-Azidouridine TP; 4'-Carbocyclic uridine TP; 4'-Ethynyluridine TP; 5-(1-Propynyl)ara-uridine TP; 5-(2-Furanyl)uridine TP; 5-Cyanouridine TP; 5-Dimethylaminouridine TP; 5'-Homo-uridine TP; 5-iodo-2'fluoro-deoxyuridine TP; 5-Phenylethynyluridine TP; 5-Trideuteromethyl-6-deuterouridine TP; 5-Trifluoromethyl-Uridine TP; 5-Vinylarauridine TP; 6-(2,2,2-Trifluoroethyl)pseudo-UTP; 6-(4-Morpholino)-pseudo-UTP; 6-(4-Thiomorpholino)-pseudo-UTP; 6-(Substituted-Phenyl)pseudo-UTP; 6-Amino-pseudo-UTP; 6-Azido-pseudo-UTP; 6-Bromo-pseudo-UTP; 6-Butyl-pseudo-UTP; 6-Chloropseudo-UTP; 6-Cyano-pseudo-UTP; 6-Dimethylaminopseudo-UTP; 6-Ethoxy-pseudo-UTP; 6-Ethylcarboxylatepseudo-UTP; 6-Ethyl-pseudo-UTP; 6-Fluoro-pseudo-UTP; 6-Formyl-pseudo-UTP; 6-Hydroxyamino-pseudo-UTP; 6-Hydroxy-pseudo-UTP; 6-Iodo-pseudo-UTP; 6-iso-Propyl-pseudo-UTP; 6-Methoxy-pseudo-UTP; 6-Methylamino-pseudo-UTP; 6-Methyl-pseudo-UTP; 6-Phenylpseudo-UTP; 6-Phenyl-pseudo-UTP; 6-Propyl-pseudo-UTP; 6-tert-Butyl-pseudo-UTP; 6-Trifluoromethoxypseudo-UTP; 6-Trifluoromethyl-pseudo-UTP; Alpha-thiopseudo-UTP; Pseudouridine 1-(4-methylbenzenesulfonic acid) TP; Pseudouridine 1-(4-methylbenzoic acid) TP; Pseudouridine TP 1-[3-(2-ethoxy)]propionic acid; Pseudou-1-[3-{2-(2-[2-(2-ethoxy)-ethoxy]-ethoxy)ridine ΤP ethoxy}]propionic acid; Pseudouridine TP 1-[3-{2-(2-[2-{2 (2-ethoxy)-ethoxy]-ethoxy]-ethoxy]propionic acid; Pseudouridine TP 1-[3-{2-(2-[2-ethoxy]-ethoxy)ethoxy}]propionic acid; Pseudouridine TP 1-[3-{2-(2ethoxy)-ethoxy}] propionic acid; Pseudouridine TP 1-methylphosphonic acid; Pseudouridine TP 1-methylphosphonic

acid diethyl ester; Pseudo-UTP-N1-3-propionic acid; Pseudo-UTP-N1-4-butanoic acid; Pseudo-UTP-N1-5-pentanoic acid; Pseudo-UTP-N1-6-hexanoic acid; Pseudo-UTP-N1-7-heptanoic acid; Pseudo-UTP-N1-methyl-p-benzoic acid; Pseudo-UTP-N1-p-benzoic acid; Wybutosine; 5 Hvdroxywybutosine: Isowyosine: Peroxywybutosine: undermodified hydroxywybutosine; 4-demethylwyosine; 2,6-(diamino)purine; 1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl: 1,3-(diaza)-2-(oxo)-phenthiazin-1-yl; 1,3-(diaza)-2-(oxo)-phenoxazin-1-yl; 1,3,5-(triaza)-2,6-(dioxa)-naphthalene;2 (amino)purine;2,4,5-(trimethyl)phenyl;2' methyl, 2'amino, 2'azido, 2'fluro-cytidine;2' methyl, 2' amino, 2'azido, 2'fluro-adenine;2'methyl, 2'amino, 2' azido, 2'flurouridine;2'-amino-2'-deoxyribose; 2-amino-6-Chloro-purine; 15 2-aza-inosinyl; 2'-azido-2'-deoxyribose; 2'fluoro-2'-deoxyribose; 2'-fluoro-modified bases; 2'-O-methyl-ribose; 2-oxo-7-aminopyridopyrimidin-3-yl; 2-oxo-pyridopyrimidine-3yl; 2-pyridinone; 3 nitropyrrole; 3-(methyl)-7-(propynyl) isocarbostyrilyl; 3-(methyl)isocarbostyrilyl; 4-(fluoro)-6- 20 4-(methyl)benzimidazole; (methyl)benzimidazole; 4-(methyl)indolyl; 4,6-(dimethyl)indolyl; 5 nitroindole; 5 substituted pyrimidines; 5-(methyl)isocarbostyrilyl; 5-nitroindole; 6-(aza)pyrimidine; 6-(azo)thymine; 6-(methyl)-7-(aza)indolyl; 6-chloro-purine; 6-phenyl-pyrrolo-pyrimidin- 25 2-on-3-yl; 7-(aminoalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)phenthiazin-1-yl; 7-(aminoalkylhydroxy)-1-(aza)-2-(thio)-7-(aminoalkylhydroxy)-1,3-3-(aza)-phenoxazin-1-yl; (diaza)-2-(oxo)-phenoxazin-1-yl; 7-(aminoalkylhydroxy)-1, 3-(diaza)-2-(oxo)-phenthiazin-1-yl;

7-(aminoalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenoxazin-1yl; 7-(aza)indolyl; 7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenoxazinl-yl; 7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenthiazin-1-yl;

7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phe- 35 noxazin-1-yl; 7-(guanidiniumalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenoxazin-1-yl; 7-(guanidiniumalkyl-hydroxy)-1,3-(diaza)-2-(oxo)-phenthiazin-1-yl;

7-(guanidiniumalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenoxazin-1-yl; 7-(propynyl)isocarbostyrilyl; 7-(propynyl)isocar- 40 bostyrilyl, propynyl-7-(aza)indolyl; 7-deaza-inosinyl; 7-substituted 1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl; 1,3-(diaza)-2-(oxo)-phenoxazin-1-yl; 7-substituted 9-(methyl)-imidizopyridinyl; Aminoindolyl; Anthracenyl; bis-ortho-(aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimi-45 din-2-on-3-yl; bis-ortho-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; Difluorotolyl; Hypoxanthine; Imidizopyridinyl; Inosinyl; Isocarbostyrilyl; Isoguanisine; N2-substituted purines; N6-methyl-2-amino-purine; N6-substituted purines; N-alkylated derivative; Napthale- 50 nyl; Nitrobenzimidazolyl; Nitroimidazolyl; Nitroindazolyl; Nitropyrazolyl; Nubularine; 06-substituted purines; O-alkylated derivative; ortho-(aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; ortho-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; Oxoformycin para- 55 TP: (aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimidin-2-on-3yl; para-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; Pentacenyl; Phenanthracenyl; Phenyl; propynyl-7-(aza)indolyl; Pyrenyl; pyridopyrimidin-3-yl; pyridopyrimidin-3-yl, 2-oxo-7-amino-pyridopyrimidin-3-yl; pyrrolo-pyrimidin-2- 60 on-3-yl; Pyrrolopyrimidinyl; Pyrrolopyrizinyl; Stilbenzyl; substituted 1,2,4-triazoles; Tetracenyl; Tubercidine; Xanthine; Xanthosine-5'-TP; 2-thio-zebularine; 5-aza-2-thio-zebularine; 7-deaza-2-amino-purine; pyridin-4-one ribonucleoside; 2-Amino-riboside-TP; Formycin A TP; 65 Formycin B TP; Pyrrolosine TP; 2'-OH-ara-adenosine TP; 2'-OH-ara-cytidine TP; 2'-OH-ara-uridine TP; 2'-OH-ara-

guanosine TP; 5-(2-carbomethoxyvinyl)uridine TP; and N6-(19-Amino-pentaoxanonadecyl)adenosine TP.

In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) include a combination of at least two (e.g., 2, 3, 4 or more) of the aforementioned modified nucleobases.

In some embodiments, modified nucleobases in polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) are selected from the group consisting of pseudouridine (ψ), N1-methylpseudouridine (m¹ ψ), N1-ethylpseudouridine, 2-thiouridine, 4'-thiouridine, 5-methylcyto sine. 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxypseudouridine, 4-thio-1-methyl-pseudouridine, 4-thiopseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyl uridine. In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) include a combination of at least two (e.g., 2, 3, 4 or more) of the aforementioned modified nucleobases.

In some embodiments, modified nucleobases in polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) are selected from the group consisting of 1-methyl-pseudouridine ($m^1\psi$), 5-methoxy-uridine (mo^5U), 5-methyl-cytidine (m^5C), pseudouridine (ψ), α -thio-guanosine and α -thio-adenosine. In some embodiments, polynucleotides includes a combination of at least two (e.g., 2, 3, 4 or more) of the aforementioned modified nucleobases.

In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise pseudouridine (v) and 5-methyl-cytidine (m⁵C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 1-methylpseudouridine $(m^1\psi)$. In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 1-methyl-pseudouridine $(m^{1}\psi)$ and 5-methyl-cytidine (m⁵C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2-thiouridine (s²U). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2-thiouridine and 5-methyl-cytidine (m⁵C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise methoxy-uridine (mo⁵U). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 5-methoxy-uridine (mo⁵U) and 5-methyl-cytidine (m⁵C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2'-O-methyl uridine. In some embodiments polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2'-Omethyl uridine and 5-methyl-cytidine (m⁵C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise N6-methyl-adenosine (m⁶A). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise N6-methyl-adenosine (m⁶A) and 5-methyl-cytidine (m⁵C).

In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) are uniformly modified (e.g., fully modified, modified throughout the entire sequence) for a particular modification. For example, a polynucleotide can be uniformly modified with 5-methyl-cytidine ($m^{s}C$), meaning that all cytosine residues in the mRNA sequence are replaced with 5-methyl-cytidine ($m^{s}C$).

Similarly, a polynucleotide can be uniformly modified for any type of nucleoside residue present in the sequence by replacement with a modified residue such as those set forth above.

Exemplary nucleobases and nucleosides having a modi-5 fied cytosine include N4-acetyl-cytidine (ac4C), 5-methylcytidine (m5C), 5-halo-cytidine (e.g., 5-iodo-cytidine), 5-hydroxymethyl-cytidine (hm5C), 1-methyl-pseudoisocytidine, 2-thio-cytidine (s2C), and 2-thio-5-methyl-cytidine.

In some embodiments, a modified nucleobase is a modified uridine. Exemplary nucleobases and In some embodiments, a modified nucleobase is a modified cytosine. nucleosides having a modified uridine include 5-cyano uridine, and 4'-thio uridine.

In some embodiments, a modified nucleobase is a modi-15 fied adenine. Exemplary nucleobases and nucleosides having a modified adenine include 7-deaza-adenine, 1-methyladenosine (m1A), 2-methyl-adenine (m2A), and N6-methyladenosine (m6A).

In some embodiments, a modified nucleobase is a modi- 20 fied guanine. Exemplary nucleobases and nucleosides having a modified guanine include inosine (I), 1-methyl-inosine (m1I), wyosine (imG), methylwyosine (mimG), 7-deazaguanosine, 7-cyano-7-deaza-guanosine (preQO), 7-aminomethyl-7-deaza-guanosine (preQ1), 7-methyl-guanosine 25 (m7G), 1-methyl-guanosine (mIG), 8-oxo-guanosine, 7-methyl-8-oxo-guanosine.

The polynucleotides of the present disclosure may be partially or fully modified along the entire length of the molecule. For example, one or more or all or a given type of 30 nucleotide (e.g., purine or pyrimidine, or any one or more or all of A, G, U, C) may be uniformly modified in a polynucleotide of the disclosure, or in a given predetermined sequence region thereof (e.g., in the mRNA including or excluding the polyA tail). In some embodiments, all nucleo-35 tides X in a polynucleotide of the present disclosure (or in a given sequence region thereof) are modified nucleotides, wherein X may any one of nucleotides A, G, U, C, or any one of the combinations A+G, A+U, A+C, G+U, G+C, U+C, A+G+U, A+G+C, G+U+C or A+G+C. 40

The polynucleotide may contain from about 1% to about 100% modified nucleotides (either in relation to overall nucleotide content, or in relation to one or more types of nucleotide, i.e., any one or more of A, G, U or C) or any intervening percentage (e.g., from 1% to 20%, from 1% to 45 25%, from 1% to 50%, from 1% to 60%, from 1% to 70%, from 1% to 80%, from 1% to 90%, from 1% to 95%, from 10% to 20%, from 10% to 25%, from 10% to 50%, from 10% to 60%, from 10% to 70%, from 10% to 80%, from 10% to 90%, from 10% to 95%, from 10% to 100%, from 50 20% to 25%, from 20% to 50%, from 20% to 60%, from 20% to 70%, from 20% to 80%, from 20% to 90%, from 20% to 95%, from 20% to 100%, from 50% to 60%, from 50% to 70%, from 50% to 80%, from 50% to 90%, from 50% to 95%, from 50% to 100%, from 70% to 80%, from 55 70% to 90%, from 70% to 95%, from 70% to 100%, from 80% to 90%, from 80% to 95%, from 80% to 100%, from 90% to 95%, from 90% to 100%, and from 95% to 100%). Any remaining percentage is accounted for by the presence of unmodified A, G, U, or C.

The polynucleotides may contain at a minimum 1% and at maximum 100% modified nucleotides, or any intervening percentage, such as at least 5% modified nucleotides, at least 10% modified nucleotides, at least 25% modified nucleotides, at least 50% modified nucleotides, at least 80% 65 modified nucleotides, or at least 90% modified nucleotides. For example, the polynucleotides may contain a modified

pyrimidine such as a modified uracil or cytosine. In some embodiments, at least 5%, at least 10%, at least 25%, at least 50%, at least 80%, at least 90% or 100% of the uracil in the polynucleotide is replaced with a modified uracil (e.g., a 5-substituted uracil). The modified uracil can be replaced by a compound having a single unique structure, or can be replaced by a plurality of compounds having different structures (e.g., 2, 3, 4 or more unique structures). n some embodiments, at least 5%, at least 10%, at least 25%, at least 50%, at least 80%, at least 90% or 100% of the cytosine in the polynucleotide is replaced with a modified cytosine (e.g., a 5-substituted cytosine). The modified cytosine can be replaced by a compound having a single unique structure, or can be replaced by a plurality of compounds having different structures (e.g., 2, 3, 4 or more unique structures).

Thus, in some embodiments, the RNA (e.g., mRNA) vaccines comprise a 5'UTR element, an optionally codon optimized open reading frame, and a 3'UTR element, a poly(A) sequence and/or a polyadenylation signal wherein the RNA is not chemically modified.

In some embodiments, the modified nucleobase is a modified uracil. Exemplary nucleobases and nucleosides having a modified uracil include pseudouridine (ψ), pyridin-4-one ribonucleoside, 5-aza-uridine, 6-aza-uridine, 2-thio-5-aza-uridine, 2-thio-uridine (s^2U), 4-thio-uridine (s^4U), 4-thio-pseudouridine, 2-thio-pseudouridine, 5-hydroxy-uridine (ho⁵U), 5-aminoallyl-uridine, 5-halo-uridine (e.g., 5-iodo-uridineor 5-bromo-uridine), 3-methyl-uridine (m³U), 5-methoxy-uridine (mo⁵U), uridine 5-oxyacetic acid (cmo^{5}U) , uridine 5-oxyacetic acid methyl ester (mcmo⁵U), 5-carboxymethyl-uridine $(cm^{2}U),$ 1-carboxymethylpseudouridine, 5-carboxyhydroxymethyl-uridine (chm⁵U), 5-carboxyhydroxymethyl-uridine methyl ester (mchm⁵U), 5-methoxycarbonylmethyl-uridine (mcm⁵U), 5-methoxycarbonylmethyl-2-thio-uridine (mcm⁵s²U), 5-aminomethyl-2-thio-uridine (nm^5s^2U) , 5-methylaminomethyl-uridine (mnm⁵U), 5-methylaminomethyl-2-thio-uridine $(mnm^5s^2U),$ 5-methylaminomethyl-2-seleno-uridine (mnm⁵se²U), 5-carbamoylmethyl-uridine (ncm⁵U), 5-carboxymethylaminomethyl-uridine (cmnm⁵U), 5-carboxymethylaminomethyl-2-thio-uridine (cmnm⁵s²U), 5-propynyluridine, 1-propynyl-pseudouridine, 5-taurinomethyl-uridine ($\tau m^5 U$), 1-taurinomethyl-pseudouridine, 5-taurinomethyl-2thio-uridine(m⁵s²U), 1-taurinomethyl-4-thio-pseudouridine, 5-methyl-uridine (m⁵U, i.e., having the nucleobase deoxythymine), 1-methyl-pseudouridine ($m^1\psi$), 5-methyl-2-thiouridine (m5s²U), 1-methyl-4-thio-pseudouridine (m¹s⁴ ψ), 4-thio-1-methyl-pseudouridine, 3-methyl-pseudouridine $(m^{3}\psi)$, 2-thio-1-methyl-pseudouridine, 1-methyl-1-deazapseudouridine, 2-thio-1-methyl-1-deaza-pseudouridine, dihydrouridine (D), dihydropseudouridine, 5,6-dihydrouridine, 5-methyl-dihydrouridine (m⁵D), 2-thio-dihydrouri-2-thio-dihydropseudouridine, 2-methoxy-uridine, dine. 2-methoxy-4-thio-uridine, 4-methoxy-pseudouridine, 4-methoxy-2-thio-pseudouridine, N1-methyl-pseudouridine. 3-(3-amino-3-carboxypropyl)uridine (acp³U), 1-methyl-3-(3-amino-3-carboxypropyl)pseudouridine (inm⁵U), $(acp^{3}\psi),$ 5-(isopentenylaminomethyl)uridine 5-(isopentenylaminomethyl)-2-thio-uridine $(inm^5s^2U),$ 60 α-thio-uridine, 2'-O-methyl-uridine (Um), 5,2'-O-dimethyluridine (msUm), 2'-O-methyl-pseudouridine (Wm), 2-thio-2'-O-methyl-uridine (s²Um), 5-methoxycarbonylmethyl-2'-O-methyl-uridine (mcm⁵Um), 5-carbamoylmethyl-2'-O-

D-methyl-uridine (mcm⁻Um), 5-carbamoyimethyl-2'-O-methyl-uridine (ncm⁵Um), 5-carboxymethylaminomethyl 2'-O-methyl-uridine (cmnm⁵Um), 3,2'-O-dimethyl-uridine (m³Um), and 5-(isopentenylaminomethyl)-2'-O-methyl-uridine (inm⁵Um), 1-thio-uridine, deoxythymidine, 2'-F-ara-

uridine, 2'-F-uridine, 2'-OH-ara-uridine, 5-(2-carbomethoxyvinyl) uridine, and 5-[3-(1-E-propenylamino)] uridine.

In some embodiments, the modified nucleobase is a modified cytosine. Exemplary nucleobases and nucleosides 5 having a modified cytosine include 5-aza-cytidine, 6-azacytidine, pseudoisocytidine, 3-methyl-cytidine $(m^{3}C),$ N4-acetyl-cytidine (ac^4C) , 5-formyl-cytidine (f⁵C), N4-methyl-cytidine (m⁴C), 5-methyl-cytidine $(m^{5}C),$ 5-halo-cytidine (e.g., 5-iodo-cytidine), 5-hydroxymethyl- 10 cytidine (hm⁵C), 1-methyl-pseudoisocytidine, pyrrolo-cytidine, pyrrolo-pseudoisocytidine, 2-thio-cytidine (s²C), 2-thio-5-methyl-cytidine, 4-thio-pseudoisocytidine, 4-thio-4-thio-1-methyl-1-deaza-1-methyl-pseudoisocytidine, pseudoisocytidine, 1-methyl-1-deaza-pseudoisocytidine, 15 zebularine, 5-aza-zebularine, 5-methyl-zebularine, 5-aza-2thio-zebularine, 2-thio-zebularine, 2-methoxy-cytidine, 2-methoxy-5-methyl-cytidine, 4-methoxy-pseudoisocytidine, 4-methoxy-1-methyl-pseudoisocytidine, lysidine (k₂C), α -thio-cytidine, 2'-O-methyl-cytidine (Cm), 5.2'-O- 20 dimethyl-cytidine (m⁵Cm), N4-acetyl-2'-O-methyl-cytidine (ac⁴Cm), N4,2'-O-dimethyl-cytidine (m⁴Cm), 5-formyl-2'-O-methyl-cytidine (f^sCm), N4,N4,2'-O-trimethyl-cytidine (m⁴2Cm), 1-thio-cytidine, 2'-F-ara-cytidine, 2'-F-cytidine, and 2'-OH-ara-cytidine. 25

In some embodiments, the modified nucleobase is a modified adenine. Exemplary nucleobases and nucleosides having a modified adenine include 2-amino-purine, 2, 6-diaminopurine, 2-amino-6-halo-purine (e.g., 2-amino-6chloro-purine), 6-halo-purine (e.g., 6-chloro-purine), 30 2-amino-6-methyl-purine, 8-azido-adenosine, 7-deaza-ad-7-deaza-8-aza-adenine, 7-deaza-2-amino-purine, enine, 7-deaza-8-aza-2-amino-purine, 7-deaza-2,6-diaminopurine, 7-deaza-8-aza-2,6-diaminopurine, 1-methyl-adenosine (m¹A), 2-methyl-adenine (m²A), N6-methyl-adenosine 35 2-methylthio-N6-methyl-adenosine (ms^2m^6A) , $(m^{6}A),$ N6-isopentenyl-adenosine (i⁶A), 2-methylthio-N6-isopentenyl-adenosine (ms²i⁶A), N6-(cis-hydroxyisopentenyl)adenosine (io⁶A), 2-methylthio-N6-(cis-hydroxyisopentenyl) adenosine (ms²io⁶A), N6-glycinylcarbamoyl-adenosine 40 (g⁶A), N6-threonylcarbamoyl-adenosine (t⁶A), N6-methyl-N6-threonylcarbamoyl-adenosine (m6t6A), 2-methylthio-N6-threonylcarbamoyl-adenosine (ms²g⁶A), N6,N6-dimethyl-adenosine (m⁶2A), N6-hydroxynorvalylcarbamoyl- $(hn^6A),$ 2-methylthio-N6- 45 adenosine $(ms^2hn^6A),$ hydroxynorvalylcarbamoyl-adenosine N6-acetyl-adenosine (ac⁶A), 7-methyl-adenine, 2-methylthio-adenine, 2-methoxy-adenine, α-thio-adenosine, 2'-O-N6,2'-O-dimethyl-adenosine methyl-adenosine (Am), (m⁶Am), N6,N6,2'-O-trimethyl-adenosine (m⁶2Am), 1,2'- 50 O-dimethyl-adenosine (m¹Am), 2'-O-ribosyladenosine (phosphate) (Ar(p)), 2-amino-N6-methyl-purine, 1-thio-adenosine, 8-azido-adenosine, 2'-F-ara-adenosine, 2'-F-adenosine, 2'-OH-ara-adenosine, and N6-(19-amino-pentaoxanonadecv1)-adenosine.

In some embodiments, the modified nucleobase is a modified guanine. Exemplary nucleobases and nucleosides having a modified guanine include inosine (I), 1-methylinosine (m¹I), wyosine (imG), methylwyosine (mimG), 4-demethyl-wyosine (imG-14), isowyosine (imG2), wybu- 60 tosine (yW), peroxywybutosine (o₂yW), hydroxywybutosine (OhyW), undermodified hydroxywybutosine (OhyW*), 7-deaza-guanosine, queuosine (Q), epoxyqueuosine (oQ), galactosyl-queuosine (galQ), mannosyl-queuosine (manQ), 7-cyano-7-deaza-guanosine (preQ₀), 7-aminomethyl-7- 65 deaza-guanosine (preQ₁), archaeosine (G⁺), 7-deaza-8-azaguanosine, 6-thio-guanosine, 6-thio-7-deaza-guanosine,

6-thio-7-deaza-8-aza-guanosine, 7-methyl-guanosine 6-thio-7-methyl-guanosine, $(m^{7}G),$ 7-methyl-inosine, 6-methoxy-guanosine, 1-methyl-guanosine (mG). N2-methyl-guanosine (m^2G) , N2,N2-dimethyl-guanosine (m²2G), N2,7-dimethyl-guanosine (m^{2,7}G), N2, N2,7-dimethyl-guanosine (m^{2,2,7}G), 8-oxo-guanosine, 7-methyl-8oxo-guanosine, 1-methyl-6-thio-guanosine, N2-methyl-6thio-guanosine, N2,N2-dimethyl-6-thio-guanosine, a-thioguanosine, 2'-O-methyl-guanosine (Gm), N2-methyl-2'-Omethyl-guanosine (m²Gm), N2,N2-dimethyl-2'-O-methylguanosine (m²2Gm), 1-methyl-2'-O-methyl-guanosine (mGm), N2,7-dimethyl-2'-O-methyl-guanosine (m²'7Gm), 2'-O-methyl-inosine (Im), 1,2'-O-dimethyl-inosine (m¹Im), 2'-O-ribosylguanosine (phosphate) (Gr(p)), 1-thio-guanosine, 06-methyl-guanosine, 2'-F-ara-guanosine, and 2'-Fguanosine.

N-Linked Glycosylation Site Mutants

N-linked glycans of viral proteins play important roles in modulating the immune response. Glycans can be important for maintaining the appropriate antigenic conformations, shielding potential neutralization epitopes, and may alter the proteolytic susceptibility of proteins. Some viruses have putative N-linked glycosylation sites. Deletion or modification of an N-linked glycosylation site may enhance the immune response. Thus, the present disclosure provides, in some embodiments, RNA (e.g., mRNA) vaccines comprising nucleic acids (e.g., mRNA) encoding antigenic polypeptides that comprise a deletion or modification at one or more N-linked glycosylation sites.

In Vitro Transcription of RNA (e.g., mRNA)

Respiratory virus vaccines of the present disclosure comprise at least one RNA polynucleotide, such as a mRNA (e.g., modified mRNA). mRNA, for example, is transcribed in vitro from template DNA, referred to as an "in vitro transcription template." In some embodiments, an in vitro transcription template encodes a 5' untranslated (UTR) region, contains an open reading frame, and encodes a 3' UTR and a polyA tail. The particular nucleic acid sequence composition and length of an in vitro transcription template will depend on the mRNA encoded by the template.

A "5' untranslated region" (5'UTR) refers to a region of an mRNA that is directly upstream (i.e., 5') from the start codon (i.e., the first codon of an mRNA transcript translated by a ribosome) that does not encode a polypeptide.

A "3' untranslated region" (3'UTR) refers to a region of an mRNA that is directly downstream (i.e., 3') from the stop codon (i.e., the codon of an mRNA transcript that signals a termination of translation) that does not encode a polypeptide.

An "open reading frame" is a continuous stretch of DNA beginning with a start codon (e.g., methionine (ATG)), and ending with a stop codon (e.g., TAA, TAG or TGA) and encodes a polypeptide.

A "polyA tail" is a region of mRNA that is downstream,
e.g., directly downstream (i.e., 3'), from the 3' UTR that contains multiple, consecutive adenosine monophosphates. A polyA tail may contain 10 to 300 adenosine monophosphates. For example, a polyA tail may contain 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290 or 300 adenosine monophosphates. In some embodiments, a polyA tail contains 50 to 250 adenosine monophosphates. In a relevant biological setting (e.g., in cells, in vivo) the poly(A) tail functions to protect mRNA from enzymatic 65 degradation, e.g., in the cytoplasm, and aids in transcription termination, export of the mRNA from the nucleus and translation.

In some embodiments, a polynucleotide includes 200 to 3,000 nucleotides. For example, a polynucleotide may include 200 to 500, 200 to 1000, 200 to 1500, 200 to 3000, 500 to 1000, 500 to 1500, 500 to 2000, 500 to 3000, 1000 to 1500, 1000 to 2000, 1000 to 3000, 1500 to 3000, or 2000 5 to 3000 nucleotides.

Flagellin Adjuvants

Flagellin is an approximately 500 amino acid monomeric protein that polymerizes to form the flagella associated with bacterial motion. Flagellin is expressed by a variety of 10 flagellated bacteria (Salmonella typhimurium for example) as well as non-flagellated bacteria (such as Escherichia coli). Sensing of flagellin by cells of the innate immune system (dendritic cells, macrophages, etc.) is mediated by the Tolllike receptor 5 (TLR5) as well as by Nod-like receptors 15 (NLRs) Ipaf and Naip5. TLRs and NLRs have been identified as playing a role in the activation of innate immune response and adaptive immune response. As such, flagellin provides an adjuvant effect in a vaccine.

The nucleotide and amino acid sequences encoding 20 known flagellin polypeptides are publicly available in the NCBI GenBank database. The flagellin sequences from S.

Typhimurium, H. Pylori, V. Cholera, S. marcesens, S. flexneri, T. Pallidum, L. pneumophila, B. burgdorferei, C. difficile, R. meliloti, A. tumefaciens, R. lupini, B. clar- 25 ridgeiae, P. Mirabilis, B. subtilus, L. monocytogenes, P. aeruginosa, and E. coli, among others are known.

A flagellin polypeptide, as used herein, refers to a full length flagellin protein, immunogenic fragments thereof, and peptides having at least 50% sequence identify to a 30 flagellin protein or immunogenic fragments thereof. Exemplary flagellin proteins include flagellin from Salmonella typhi (UniPro Entry number: Q56086), Salmonella typhimu-(A0A0C9DG09), rium Salmonella enteritidis (AOAOC9BAB7), and Salmonella choleraesuis (Q6V2X8), 35 includes at least two separate RNA polynucleotides, one and SEQ ID NO: 54-56 (Table 17). In some embodiments, the flagellin polypeptide has at least 60%, 70%, 75%, 80%, 90%, 95%, 97%, 98%, or 99% sequence identify to a flagellin protein or immunogenic fragments thereof.

In some embodiments, the flagellin polypeptide is an 40 immunogenic fragment. An immunogenic fragment is a portion of a flagellin protein that provokes an immune response. In some embodiments, the immune response is a TLR5 immune response. An example of an immunogenic fragment is a flagellin protein in which all or a portion of a hinge region has been deleted or replaced with other amino acids. For example, an antigenic polypeptide may be inserted in the hinge region. Hinge regions are the hypervariable regions of a flagellin. Hinge regions of a flagellin are also referred to as "D3 domain or region, "propeller 50 domain or region," "hypervariable domain or region" and "variable domain or region." "At least a portion of a hinge region," as used herein, refers to any part of the hinge region of the flagellin, or the entirety of the hinge region. In other embodiments an immunogenic fragment of flagellin is a 20, 55 25, 30, 35, or 40 amino acid C-terminal fragment of flagel-

The flagellin monomer is formed by domains D0 through D3. D0 and D1, which form the stem, are composed of tandem long alpha helices and are highly conserved among 60 different bacteria. The D1 domain includes several stretches of amino acids that are useful for TLR5 activation. The entire D1 domain or one or more of the active regions within the domain are immunogenic fragments of flagellin. Examples of immunogenic regions within the D1 domain 65 include residues 88-114 and residues 411-431 (in Salmonella typhimurium FliC flagellin. Within the 13 amino acids

in the 88-100 region, at least 6 substitutions are permitted between Salmonella flagellin and other flagellins that still preserve TLR5 activation. Thus, immunogenic fragments of flagellin include flagellin like sequences that activate TLR5 and contain a 13 amino acid motif that is 53% or more identical to the Salmonella sequence in 88-100 of FliC (LQRVRELAVQSAN; SEQ ID NO: 84).

In some embodiments, the RNA (e.g., mRNA) vaccine includes an RNA that encodes a fusion protein of flagellin and one or more antigenic polypeptides. A "fusion protein" as used herein, refers to a linking of two components of the construct. In some embodiments, a carboxy-terminus of the antigenic polypeptide is fused or linked to an amino terminus of the flagellin polypeptide. In other embodiments, an amino-terminus of the antigenic polypeptide is fused or linked to a carboxy-terminus of the flagellin polypeptide. The fusion protein may include, for example, one, two, three, four, five, six or more flagellin polypeptides linked to one, two, three, four, five, six or more antigenic polypeptides. When two or more flagellin polypeptides and/or two or more antigenic polypeptides are linked such a construct may be referred to as a "multimer."

Each of the components of a fusion protein may be directly linked to one another or they may be connected through a linker. For instance, the linker may be an amino acid linker. The amino acid linker encoded for by the RNA (e.g., mRNA) vaccine to link the components of the fusion protein may include, for instance, at least one member selected from the group consisting of a lysine residue, a glutamic acid residue, a serine residue and an arginine residue. In some embodiments the linker is 1-30, 1-25, 1-25, 5-10, 5, 15, or 5-20 amino acids in length.

In other embodiments the RNA (e.g., mRNA) vaccine encoding one or more antigenic polypeptides and the other encoding the flagellin polypeptide. The at least two RNA polynucleotides may be co-formulated in a carrier such as a lipid nanoparticle.

Broad Spectrum RNA (e.g., mRNA) Vaccines

There may be situations where persons are at risk for infection with more than one strain of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). RNA (e.g., mRNA) therapeutic vaccines are particularly amenable to combination vaccination approaches due to a number of factors including, but not limited to, speed of manufacture, ability to rapidly tailor vaccines to accommodate perceived geographical threat, and the like. Moreover, because the vaccines utilize the human body to produce the antigenic protein, the vaccines are amenable to the production of larger, more complex antigenic proteins, allowing for proper folding, surface expression, antigen presentation, etc. in the human subject. To protect against more than one strain of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1), a combination vaccine can be administered that includes RNA (e.g., mRNA) encoding at least one antigenic polypeptide protein (or antigenic portion thereof) of a first respiratory virus and further includes RNA encoding at least one antigenic polypeptide protein (or antigenic portion thereof) of a second respiratory virus. RNA (e.g., mRNA) can be co-formulated, for example, in a single lipid nanoparticle (LNP) or can be formulated in separate LNPs for co-administration.

Methods of Treatment

Provided herein are compositions (e.g., pharmaceutical compositions), methods, kits and reagents for prevention and/or treatment of respiratory diseases/infections in humans and other mammals. Respiratory virus RNA (e.g. 5 mRNA) vaccines can be used as therapeutic or prophylactic agents, alone or in combination with other vaccine(s). They may be used in medicine to prevent and/or treat respiratory disease/infection. In exemplary aspects, the RNA (e.g., mRNA) vaccines of the present disclosure are used to 10 provide prophylactic protection from hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). Prophylactic protection from hMPV, PIV3, RSV, MeV and/or BetaCoV (including 15 MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) can be achieved following administration of a RNA (e.g., mRNA) vaccine of the present disclosure. Respiratory virus RNA (e.g., mRNA) vaccines of the present disclosure may 20 be used to treat or prevent viral "co-infections" containing two or more respiratory infections. Vaccines can be administered once, twice, three times, four times or more, but it is likely sufficient to administer the vaccine once (optionally followed by a single booster). It is possible, although less 25 desirable, to administer the vaccine to an infected individual to achieve a therapeutic response. Dosing may need to be adjusted accordingly.

A method of eliciting an immune response in a subject against hMPV, PIV3, RSV, MeV and/or BetaCoV (including 30 MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) is provided in aspects of the present disclosure. The method involves administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine comprising at least one RNA 35 (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide thereof, thereby 40 inducing in the subject an immune response specific to hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, 45 wherein anti-antigenic polypeptide antibody titer in the subject is increased following vaccination relative to antiantigenic polypeptide antibody titer in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against hMPV, PIV3, RSV, MeV and/or BetaCoV 50 (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). An "anti-antigenic polypeptide antibody" is a serum antibody the binds specifically to the antigenic polypeptide.

In some embodiments, a RNA (e.g., mRNA) vaccine 55 (e.g., a hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1 RNA vaccine) capable of eliciting an immune response is administered intramuscularly via a composition including a 60 compound according to Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe) (e.g., Compound 3, 18, 20, 25, 26, 29, 30, 60, 108-112, or 122).

A prophylactically effective dose is a therapeutically effective dose that prevents infection with the virus at a 65 clinically acceptable level. In some embodiments the therapeutically effective dose is a dose listed in a package insert

for the vaccine. A traditional vaccine, as used herein, refers to a vaccine other than the RNA (e.g., mRNA) vaccines of the present disclosure. For instance, a traditional vaccine includes but is not limited to live/attenuated microorganism vaccines, killed/inactivated microorganism vaccines, subunit vaccines, protein antigen vaccines, DNA vaccines, VLP vaccines, etc. In exemplary embodiments, a traditional vaccine is a vaccine that has achieved regulatory approval and/or is registered by a national drug regulatory body, for example the Food and Drug Administration (FDA) in the United States or the European Medicines Agency (EMA).

In some embodiments the anti-antigenic polypeptide antibody titer in the subject is increased 1 log to 10 log following vaccination relative to anti-antigenic polypeptide antibody titer in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1).

In some embodiments the anti-antigenic polypeptide antibody titer in the subject is increased 1 log, 2 log, 3 log, 5 log or 10 log following vaccination relative to anti-antigenic polypeptide antibody titer in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1).

A method of eliciting an immune response in a subject against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) is provided in other aspects of the disclosure. The method involves administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine comprising at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, thereby inducing in the subject an immune response specific to hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, wherein the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine against the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) at 2 times to 100 times the dosage level relative to the RNA (e.g., mRNA) vaccine.

In some embodiments, the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine at 2, 3, 4, 5, 10, 50, 100 times the dosage level relative to the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) RNA (e.g., mRNA) vaccine.

In some embodiments the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine at 10-100 times, or 100-1000 times, the dosage level relative to the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, 5

HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) RNA (e.g., mRNA) vaccine.

In some embodiments the immune response is assessed by determining [protein] antibody titer in the subject.

Some aspects of the present disclosure provide a method of eliciting an immune response in a subject against a In some embodiments the immune response in the subject is equivalent to an immune response in a subject vaccinated 10with a traditional vaccine at 2, 3, 4, 5, 10, 50, 100 times the dosage level relative to the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) RNA (e.g., mRNA) vaccine by admin-15 istering to the subject a respiratory virus RNA (e.g., mRNA) vaccine comprising at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, 20 mRNA) vaccine is provided based, at least in part, on the HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide, thereby inducing in the subject an immune response specific to the antigenic polypeptide or an immunogenic fragment thereof, wherein the immune response in the subject is induced 2 days to 10 weeks earlier 25 relative to an immune response induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against the hMPV, PIV3, RSV, MeV and/or Beta-CoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or 30 HCoV-HKU1). In some embodiments, the immune response in the subject is induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine at 2 times to 100 times the dosage level relative to the RNA (e.g., mRNA) vaccine.

In some embodiments, the immune response in the subject is induced 2 days earlier, or 3 days earlier, relative to an immune response induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine.

In some embodiments the immune response in the subject 40 is induced 1 week, 2 weeks, 3 weeks, 5 weeks, or 10 weeks earlier relative to an immune response induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine.

Also provided herein is a method of eliciting an immune 45 response in a subject against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) by administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine having an open 50 reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide does not include a stabilization element, and wherein an adjuvant is not co-formulated or co-administered with the vaccine.

Therapeutic and Prophylactic Compositions

Provided herein are compositions (e.g., pharmaceutical compositions), methods, kits and reagents for prevention, treatment or diagnosis of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH 60 and/or HCoV-HKU1) in humans and other mammals, for example. Respiratory virus RNA (e.g. mRNA) vaccines can be used as therapeutic or prophylactic agents. They may be used in medicine to prevent and/or treat infectious disease. In some embodiments, the respiratory RNA (e.g., mRNA) 65 vaccines of the present disclosure are used fin the priming of immune effector cells, for example, to activate peripheral

blood mononuclear cells (PBMCs) ex vivo, which are then infused (re-infused) into a subject.

In some embodiments, respiratory virus vaccine containing RNA (e.g., mRNA) polynucleotides as described herein can be administered to a subject (e.g., a mammalian subject, such as a human subject), and the RNA (e.g., mRNA) polynucleotides are translated in vivo to produce an antigenic polypeptide.

The respiratory virus RNA (e.g., mRNA) vaccines may be induced for translation of a polypeptide (e.g., antigen or immunogen) in a cell, tissue or organism. In some embodiments, such translation occurs in vivo, although such translation may occur ex vivo, in culture or in vitro. In some embodiments, the cell, tissue or organism is contacted with an effective amount of a composition containing a respiratory virus RNA (e.g., mRNA) vaccine that contains a polynucleotide that has at least one a translatable region encoding an antigenic polypeptide.

An "effective amount" of an respiratory virus RNA (e.g. target tissue, target cell type, means of administration, physical characteristics of the polynucleotide (e.g., size, and extent of modified nucleosides) and other components of the vaccine, and other determinants. In general, an effective amount of the respiratory virus RNA (e.g., mRNA) vaccine composition provides an induced or boosted immune response as a function of antigen production in the cell, preferably more efficient than a composition containing a corresponding unmodified polynucleotide encoding the same antigen or a peptide antigen. Increased antigen production may be demonstrated by increased cell transfection (the percentage of cells transfected with the RNA, e.g., mRNA, vaccine), increased protein translation from the polynucleotide, decreased nucleic acid degradation (as dem-35 onstrated, for example, by increased duration of protein translation from a modified polynucleotide), or altered antigen specific immune response of the host cell.

In some embodiments, RNA (e.g. mRNA) vaccines (including polynucleotides their encoded polypeptides) in accordance with the present disclosure may be used for treatment of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1).

Respiratory RNA (e.g. mRNA) vaccines may be administered prophylactically or therapeutically as part of an active immunization scheme to healthy individuals or early in infection during the incubation phase or during active infection after onset of symptoms. In some embodiments, the amount of RNA (e.g., mRNA) vaccine of the present disclosure provided to a cell, a tissue or a subject may be an amount effective for immune prophylaxis.

Respiratory virus RNA (e.g. mRNA) vaccines may be administrated with other prophylactic or therapeutic com-55 pounds. As a non-limiting example, a prophylactic or therapeutic compound may be an adjuvant or a booster. As used herein, when referring to a prophylactic composition, such as a vaccine, the term "booster" refers to an extra administration of the prophylactic (vaccine) composition. A booster (or booster vaccine) may be given after an earlier administration of the prophylactic composition. The time of administration between the initial administration of the prophylactic composition and the booster may be, but is not limited to, 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 6 minutes, 7 minutes, 8 minutes, 9 minutes, 10 minutes, 15 minutes, 20 minutes 35 minutes, 40 minutes, 45 minutes, 50 minutes, 55 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5

hours, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, 12 hours, 13 hours, 14 hours, 15 hours, 16 hours, 17 hours, 18 hours, 19 hours, 20 hours, 21 hours, 22 hours, 23 hours, 1 day, 36 hours, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 10 days, 2 weeks, 3 weeks, 1 month, 2 months, 3 5 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 1 year, 18 months, 2 years, 3 years, 4 years, 5 years, 6 years, 7 years, 8 years, 9 years, 10 years, 11 years, 12 years, 13 years, 14 years, 15 years, 16 years, 17 years, 18 years, 19 years, 20 years, 25 years, 30 10 years, 35 years, 40 years, 45 years, 50 years, 55 years, 60 years, 65 years, 70 years, 75 years, 80 years, 85 years, 90 years, 95 years or more than 99 years. In some embodiments, the time of administration between the initial administration of the prophylactic composition and the booster 15 may be, but is not limited to, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, 3 months, 6 months or 1 year.

In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines may be administered intramuscularly or intradermally, similarly to the administration of inactivated 20 vaccines known in the art.

Respiratory virus RNA (e.g. mRNA) vaccines may be utilized in various settings depending on the prevalence of the infection or the degree or level of unmet medical need. As a non-limiting example, the RNA (e.g., mRNA) vaccines 25 may be utilized to treat and/or prevent a variety of respiratory infections. RNA (e.g., mRNA) vaccines have superior properties in that they produce much larger antibody titers and produce responses early than commercially available anti-viral agents/compositions. 30

Provided herein are pharmaceutical compositions including respiratory virus RNA (e.g. mRNA) vaccines and RNA (e.g. mRNA) vaccine compositions and/or complexes optionally in combination with one or more pharmaceutically acceptable excipients.

Respiratory virus RNA (e.g. mRNA) vaccines may be formulated or administered alone or in conjunction with one or more other components. For instance, hMPV/PIV3/RSV RNA (e.g., mRNA) vaccines (vaccine compositions) may comprise other components including, but not limited to, 40 adjuvants.

In some embodiments, respiratory virus (e.g. mRNA) vaccines do not include an adjuvant (they are adjuvant free).

Respiratory virus RNA (e.g. mRNA) vaccines may be formulated or administered in combination with one or more 45 pharmaceutically-acceptable excipients. In some embodiments, vaccine compositions comprise at least one additional active substances, such as, for example, a therapeutically-active substance, a prophylactically-active substance, or a combination of both. Vaccine compositions may be 50 sterile, pyrogen-free or both sterile and pyrogen-free. General considerations in the formulation and/or manufacture of pharmaceutical agents, such as vaccine compositions, may be found, for example, in Remington: The Science and Practice of Pharmacy 21st ed., Lippincott Williams & 55 Wilkins, 2005 (incorporated herein by reference in its entirety).

In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines are administered to humans, human patients or subjects. For the purposes of the present disclo- 60 sure, the phrase "active ingredient" generally refers to the RNA (e.g., mRNA) vaccines or the polynucleotides contained therein, for example, RNA polynucleotides (e.g., mRNA polynucleotides) encoding antigenic polypeptides.

Formulations of the respiratory virus vaccine composi-65 tions described herein may be prepared by any method known or hereafter developed in the art of pharmacology. In

general, such preparatory methods include the step of bringing the active ingredient (e.g., mRNA polynucleotide) into association with an excipient and/or one or more other accessory ingredients, and then, if necessary and/or desirable, dividing, shaping and/or packaging the product into a desired single- or multi-dose unit.

Relative amounts of the active ingredient, the pharmaceutically acceptable excipient, and/or any additional ingredients in a pharmaceutical composition in accordance with the disclosure will vary, depending upon the identity, size, and/or condition of the subject treated and further depending upon the route by which the composition is to be administered. By way of example, the composition may comprise between 0.1% and 100%, e.g., between 0.5 and 50%, between 1-30%, between 5-80%, at least 80% (w/w) active ingredient.

Respiratory virus RNA (e.g. mRNA) vaccines can be formulated using one or more excipients to: (1) increase stability; (2) increase cell transfection; (3) permit the sustained or delayed release (e.g., from a depot formulation); (4) alter the biodistribution (e.g., target to specific tissues or cell types); (5) increase the translation of encoded protein in vivo; and/or (6) alter the release profile of encoded protein (antigen) in vivo. In addition to traditional excipients such as any and all solvents, dispersion media, diluents, or other liquid vehicles, dispersion or suspension aids, surface active agents, isotonic agents, thickening or emulsifying agents, preservatives, excipients can include, without limitation, lipidoids, liposomes, lipid nanoparticles, polymers, lipoplexes, core-shell nanoparticles, peptides, proteins, cells transfected with respiratory virus RNA (e.g. mRNA)vaccines (e.g., for transplantation into a subject), hyaluronidase, nanoparticle mimics and combinations thereof.

35 Stabilizing Elements

Naturally-occurring eukaryotic mRNA molecules have been found to contain stabilizing elements, including, but not limited to untranslated regions (UTR) at their 5'-end (5'UTR) and/or at their 3'-end (3'UTR), in addition to other structural features, such as a 5'-cap structure or a 3'-poly(A) tail. Both the 5'UTR and the 3'UTR are typically transcribed from the genomic DNA and are elements of the premature mRNA. Characteristic structural features of mature mRNA, such as the 5'-cap and the 3'-poly(A) tail are usually added to the transcribed (premature) mRNA during mRNA processing. The 3'-poly(A) tail is typically a stretch of adenine nucleotides added to the 3'-end of the transcribed mRNA. It can comprise up to about 400 adenine nucleotides. In some embodiments the length of the 3'-poly(A) tail may be an essential element with respect to the stability of the individual mRNA.

In some embodiments the RNA (e.g., mRNA) vaccine may include one or more stabilizing elements. Stabilizing elements may include for instance a histone stem-loop. A stem-loop binding protein (SLBP), a 32 kDa protein has been identified. It is associated with the histone stem-loop at the 3'-end of the histone messages in both the nucleus and the cytoplasm. Its expression level is regulated by the cell cycle; it peaks during the S-phase, when histone mRNA levels are also elevated. The protein has been shown to be essential for efficient 3'-end processing of histone premRNA by the U7 snRNP. SLBP continues to be associated with the stem-loop after processing, and then stimulates the translation of mature histone mRNAs into histone proteins in the cytoplasm. The RNA binding domain of SLBP is conserved through metazoa and protozoa; its binding to the histone stem-loop depends on the structure of the loop. The minimum binding site includes at least three nucleotides 5' and two nucleotides 3' relative to the stem-loop.

In some embodiments, the RNA (e.g., mRNA) vaccines include a coding region, at least one histone stem-loop, and optionally, a poly(A) sequence or polyadenylation signal. 5 The poly(A) sequence or polyadenylation signal generally should enhance the expression level of the encoded protein. The encoded protein, in some embodiments, is not a histone protein, a reporter protein (e.g. Luciferase, GFP, EGFP, β -Galactosidase, EGFP), or a marker or selection protein 10 (e.g. alpha-Globin, Galactokinase and Xanthine:guanine phosphoribosyl transferase (GPT)).

In some embodiments, the combination of a poly(A) sequence or polyadenylation signal and at least one histone stem-loop, even though both represent alternative mecha- 15 nisms in nature, acts synergistically to increase the protein expression beyond the level observed with either of the individual elements. It has been found that the synergistic effect of the combination of poly(A) and at least one histone stem-loop does not depend on the order of the elements or 20 the length of the poly(A) sequence.

In some embodiments, the RNA (e.g., mRNA) vaccine does not comprise a histone downstream element (HDE). "Histone downstream element" (HDE) includes a purinerich polynucleotide stretch of approximately 15 to 20 25 nucleotides 3' of naturally occurring stem-loops, representing the binding site for the U7 snRNA, which is involved in processing of histone pre-mRNA into mature histone mRNA. Ideally, the inventive nucleic acid does not include an intron. 30

In some embodiments, the RNA (e.g., mRNA) vaccine may or may not contain a enhancer and/or promoter sequence, which may be modified or unmodified or which may be activated or inactivated. In some embodiments, the histone stem-loop is generally derived from histone genes, 35 and includes an intramolecular base pairing of two neighbored partially or entirely reverse complementary sequences separated by a spacer, including (e.g., consisting of) a short sequence, which forms the loop of the structure. The unpaired loop region is typically unable to base pair with 40 either of the stem loop elements. It occurs more often in RNA, as is a key component of many RNA secondary structures, but may be present in single-stranded DNA as well. Stability of the stem-loop structure generally depends on the length, number of mismatches or bulges, and base 45 composition of the paired region. In some embodiments, wobble base pairing (non-Watson-Crick base pairing) may result. In some embodiments, the at least one histone stemloop sequence comprises a length of 15 to 45 nucleotides.

In other embodiments the RNA (e.g., mRNA) vaccine 50 DLin-MC3-DMA, DLin-KC2-DMA, DODMA and amino alcohol lipids. 51 sequences, sometimes referred to as AURES are destabilizing sequences found in the 3'UTR. The AURES may be removed from the RNA (e.g., mRNA) vaccines. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections. Alternatively the AURES may remain in the RNA (e.g., mRNA) sections are alsoluted. Alternatively the AURES may remain in th

Nanoparticle Formulations

In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines are formulated in a nanoparticle. In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines 60 are formulated in a lipid nanoparticle. In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines are formulated in a lipid-polycation complex, referred to as a cationic lipid nanoparticle. As a non-limiting example, the polycation may include a cationic peptide or a polypeptide 65 such as, but not limited to, polylysine, polyornithine and/or polyarginine. In some embodiments, respiratory virus RNA

(e.g., mRNA) vaccines are formulated in a lipid nanoparticle that includes a non-cationic lipid such as, but not limited to, cholesterol or dioleoyl phosphatidylethanolamine (DOPE).

A lipid nanoparticle formulation may be influenced by, but not limited to, the selection of the cationic lipid component, the degree of cationic lipid saturation, the nature of the PEGylation, ratio of all components and biophysical parameters such as size. In one example by Semple et al. (*Nature Biotech.* 2010 28:172-176), the lipid nanoparticle formulation is composed of 57.1% cationic lipid, 7.1% dipalmitoylphosphatidylcholine, 34.3% cholesterol, and 1.4% PEG-c-DMA. As another example, changing the composition of the cationic lipid can more effectively deliver siRNA to various antigen presenting cells (Basha et al. *Mol Ther.* 2011 19:2186-2200).

In some embodiments, lipid nanoparticle formulations may comprise 35 to 45% cationic lipid, 40% to 50% cationic lipid, 50% to 60% cationic lipid and/or 55% to 65% cationic lipid. In some embodiments, the ratio of lipid to RNA (e.g., mRNA) in lipid nanoparticles may be 5:1 to 20:1, 10:1 to 25:1, 15:1 to 30:1 and/or at least 30:1.

In some embodiments, the ratio of PEG in the lipid nanoparticle formulations may be increased or decreased and/or the carbon chain length of the PEG lipid may be modified from C14 to C18 to alter the pharmacokinetics and/or biodistribution of the lipid nanoparticle formulations. As a non-limiting example, lipid nanoparticle formulations may contain 0.5% to 3.0%, 1.0% to 3.5%, 1.5% to 4.0%, 2.0% to 4.5%, 2.5% to 5.0% and/or 3.0% to 6.0% of the lipid molar ratio of PEG-c-DOMG (R-3-[(ω -methoxy-poly(ethvleneglycol)2000)carbamoyl)]-1,2-dimyristyloxypropyl-3amine) (also referred to herein as PEG-DOMG) as compared to the cationic lipid, DSPC and cholesterol. In some embodiments, the PEG-c-DOMG may be replaced with a PEG lipid such as, but not limited to, PEG-DSG (1,2-Distearoyl-snglycerol, methoxypolyethylene glycol), PEG-DMG (1,2-Dimyristoyl-sn-glycerol) and/or PEG-DPG (1,2-Dipalmitoyl-sn-glycerol, methoxypolyethylene glycol). The cationic lipid may be selected from any lipid known in the art such as, but not limited to, DLin-MC3-DMA, DLin-DMA, C12-200 and DLin-KC2-DMA.

In some embodiments, an respiratory virus RNA (e.g. mRNA) vaccine formulation is a nanoparticle that comprises at least one lipid. The lipid may be selected from, but is not limited to, DLin-DMA, DLin-K-DMA, 98N12-5, C12-200, DLin-MC3-DMA, DLin-KC2-DMA, DODMA, PLGA, PEG, PEG-DMG, PEGylated lipids and amino alcohol lipids. In some embodiments, the lipid may be a cationic lipid such as, but not limited to, DLin-DMA, DCIn-DMA, DLin-DMA, DLin-MC3-DMA, DLin-KC2-DMA, DODMA and amino alcohol lipids.

The amino alcohol cationic lipid may be the lipids described in and/or made by the methods described in U.S. Patent Publication No. US20130150625, herein incorpothe cationic lipid may be 2-amino-3-[(9Z,12Z)-octadeca-9, 12-dien-1-yloxy]-2-{[(9Z,2Z)-octadeca-9,12-dien-1-yloxy] methyl}propan-1-ol (Compound 1 in US20130150625); 2-amino-3-[(9Z)-octadec-9-en-1-yloxy]-2-{[(9Z)-octadec-9-en-1-yloxy]methyl}propan-1-ol (Compound 2 in US20130150625); 2-amino-3-[(9Z,12Z)-octadeca-9,12dien-1-yloxy]-2-[(octyloxy)methyl]propan-1-ol (Compound 3 in US20130150625); and 2-(dimethylamino)-3-[(9Z,12Z)octadeca-9,12-dien-1-yloxy]-2-{[(9Z, 12Z)-octadeca-9,12dien-1-yloxy]methyl}propan-1-ol (Compound 4 in US20130150625); or any pharmaceutically acceptable salt or stereoisomer thereof.

Lipid nanoparticle formulations typically comprise a lipid, in particular, an ionizable cationic lipid, for example, 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobu-

tyrate (DLin-MC3-DMA), or di((Z)-non-2-en-1-yl) 9-((4-5 (dimethylamino)butanoyl)oxy)heptadecanedioate (L319), and further comprise a neutral lipid, a sterol and a molecule capable of reducing particle aggregation, for example a PEG or PEG-modified lipid.

In some embodiments, a lipid nanoparticle formulation 10 consists essentially of (i) at least one lipid selected from the group consisting of 2,2-dilinoleyl-4-dimethylaminoethyl-[1, 3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2en-1-vl) 9-((4-(dimethylamino)butanoyl)oxy) 15 heptadecanedioate (L319); (ii) a neutral lipid selected from DSPC, DPPC, POPC, DOPE and SM; (iii) a sterol, e.g., cholesterol; and (iv) a PEG-lipid, e.g., PEG-DMG or PEGcDMA, in a molar ratio of 20-60% cationic lipid: 5-25% neutral lipid: 25-55% sterol; 0.5-15% PEG-lipid.

In some embodiments, a lipid nanoparticle formulation includes 25% to 75% on a molar basis of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1- 25 yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), e.g., 35 to 65%, 45 to 65%, 60%, 57.5%, 50% or 40% on a molar basis.

In some embodiments, a lipid nanoparticle formulation includes 0.5% to 15% on a molar basis of the neutral lipid, 30 e.g., 3 to 12%, 5 to 10% or 15%, 10%, or 7.5% on a molar basis. Examples of neutral lipids include, without limitation, DSPC, POPC, DPPC, DOPE and SM. In some embodiments, the formulation includes 5% to 50% on a molar basis of the sterol (e.g., 15 to 45%, 20 to 40%, 40%, 38.5%, 35%, 35 include 40% of a cationic lipid selected from 2,2-dilinoleylor 31% on a molar basis. A non-limiting example of a sterol is cholesterol. In some embodiments, a lipid nanoparticle formulation includes 0.5% to 20% on a molar basis of the PEG or PEG-modified lipid (e.g., 0.5 to 10%, 0.5 to 5%, 1.5%, 0.5%, 1.5%, 3.5%, or 5% on a molar basis. In some 40 embodiments, a PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of 2,000 Da. In some embodiments, a PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of less than 2,000, for example around 1,500 Da, around 1,000 45 Da, or around 500 Da. Non-limiting examples of PEGmodified lipids include PEG-distearoyl glycerol (PEG-DMG) (also referred herein as PEG-C14 or C14-PEG), PEG-cDMA (further discussed in Reyes et al. J. Controlled Release, 107, 276-287 (2005) the contents of which are 50 herein incorporated by reference in their entirety).

In some embodiments, lipid nanoparticle formulations include 25-75% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin- 55 MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 0.5-15% of the neutral lipid, 5-50% of the sterol, and 0.5-20% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, lipid nanoparticle formulations 60 include 35-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), 9-((4and di((Z)-non-2-en-1-yl) (L319), 65 (dimethylamino)butanoyl)oxy)heptadecanedioate 3-12% of the neutral lipid, 15-45% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

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In some embodiments, lipid nanoparticle formulations include 45-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl)9-((4-(L319), (dimethylamino)butanoyl)oxy)heptadecanedioate 5-10% of the neutral lipid, 25-40% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, lipid nanoparticle formulations include 60% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 7.5% of the neutral lipid, 31% of the sterol, and 1.5% of the PEG or PEGmodified lipid on a molar basis.

In some embodiments, lipid nanoparticle formulations include 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), 20 dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 10% of the neutral lipid, 38.5% of the sterol, and 1.5% of the PEG or PEGmodified lipid on a molar basis.

In some embodiments, lipid nanoparticle formulations include 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 10% of the neutral lipid, 35% of the sterol, 4.5% or 5% of the PEG or PEG-modified lipid, and 0.5% of the targeting lipid on a molar basis.

In some embodiments, lipid nanoparticle formulations 4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 15% of the neutral lipid, 40% of the sterol, and 5% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, lipid nanoparticle formulations include 57.2% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLindi((Z)-non-2-en-1-yl) 9-((4-MC3-DMA), and (dimethylamino)butanoyl)oxy)heptadecanedioate (L319). 7.1% of the neutral lipid, 34.3% of the sterol, and 1.4% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, lipid nanoparticle formulations include 57.5% of a cationic lipid selected from the PEG lipid is PEG-cDMA (PEG-cDMA is further discussed in Reves et al. (J. Controlled Release, 107, 276-287 (2005), the contents of which are herein incorporated by reference in their entirety), 7.5% of the neutral lipid, 31.5% of the sterol, and 3.5% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, lipid nanoparticle formulations consists essentially of a lipid mixture in molar ratios of 20-70% cationic lipid: 5-45% neutral lipid: 20-55% cholesterol: 0.5-15% PEG-modified lipid. In some embodiments, lipid nanoparticle formulations consists essentially of a lipid mixture in a molar ratio of 20-60% cationic lipid: 5-25% neutral lipid: 25-55% cholesterol: 0.5-15% PEG-modified lipid.

In some embodiments, the molar lipid ratio is 50/10/38.5/ 1.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/ PEG-modified lipid, e.g., PEG-DMG, PEG-DSG or PEG-

DPG), 57.2/7.1134.3/1.4 (mol % cationic lipid/neutral lipid, e.g., DPPC/Chol/PEG-modified lipid, e.g., PEG-cDMA), 40/15/40/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/ Chol/PEG-modified lipid, e.g., PEG-DMG), 50/10/35/4.5/ 0.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/ 5 PEG-modified lipid, e.g., PEG-DSG), 50/10/35/5 (cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG), 40/10/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA), 35/15/40/10 (mol % cationic lipid/neutral 10 lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA) or 52/13/30/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA).

Non-limiting examples of lipid nanoparticle compositions 15 and methods of making them are described, for example, in Semple et al. (2010) *Nat. Biotechnol.* 28:172-176; Jayarama et al. (2012), *Angew. Chem. Int. Ed.*, 51: 8529-8533; and Maier et al. (2013) *Molecular Therapy* 21, 1570-1578 (the contents of each of which are incorporated herein by refer- 20 ence in their entirety).

In some embodiments, lipid nanoparticle formulations may comprise a cationic lipid, a PEG lipid and a structural lipid and optionally comprise a non-cationic lipid. As a non-limiting example, a lipid nanoparticle may comprise 25 40-60% of cationic lipid, 5-15% of a non-cationic lipid, 1-2% of a PEG lipid and 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise 50% cationic lipid, 10% non-cationic lipid, 1.5% PEG lipid and 38.5% structural lipid. As yet another nonimiting example, a lipid nanoparticle may comprise 55% cationic lipid, 10% non-cationic lipid, 2.5% PEG lipid and 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and 35 L319.

In some embodiments, the lipid nanoparticle formulations described herein may be 4 component lipid nanoparticles. The lipid nanoparticle may comprise a cationic lipid, a non-cationic lipid, a PEG lipid and a structural lipid. As a 40 non-limiting example, the lipid nanoparticle may comprise 40-60% of cationic lipid, 5-15% of a non-cationic lipid, 1-2% of a PEG lipid and 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise 50% cationic lipid, 10% non-cationic lipid, 1.5% 45 PEG lipid and 38.5% structural lipid. As yet another nonlimiting example, the lipid nanoparticle may comprise 55% cationic lipid, 10% non-cationic lipid, 2.5% PEG lipid and 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but 50 not limited to, DLin-KC2-DMA, DLin-MC3-DMA and L319.

In some embodiments, the lipid nanoparticle formulations described herein may comprise a cationic lipid, a noncationic lipid, a PEG lipid and a structural lipid. As a 55 non-limiting example, the lipid nanoparticle comprise 50% of the cationic lipid DLin-KC2-DMA, 10% of the noncationic lipid DSPC, 1.5% of the PEG lipid PEG-DOMG and 38.5% of the structural lipid cholesterol. As a nonlimiting example, the lipid nanoparticle comprise 50% of the 60 cationic lipid DLin-MC3-DMA, 10% of the non-cationic lipid DSPC, 1.5% of the PEG lipid PEG-DOMG and 38.5% of the structural lipid cholesterol. As a non-limiting example, the lipid nanoparticle comprise 50% of the cationic lipid DSPC, 1.5% of the PEG lipid PEG-DOMG and 38.5% of the structural lipid cholesterol. As a non-limiting example, the lipid nanoparticle comprise 50% of the cationic lipid DLin-MC3-DMA, 10% of the non-cationic lipid 65 DSPC, 1.5% of the PEG lipid PEG-DMG and 38.5% of the structural lipid cholesterol. As yet another non-limiting

example, the lipid nanoparticle comprise 55% of the cationic lipid L319, 10% of the non-cationic lipid DSPC, 2.5% of the PEG lipid PEG-DMG and 32.5% of the structural lipid cholesterol.

Relative amounts of the active ingredient, the pharmaceutically acceptable excipient, and/or any additional ingredients in a vaccine composition may vary, depending upon the identity, size, and/or condition of the subject being treated and further depending upon the route by which the composition is to be administered. For example, the composition may comprise between 0.1% and 99% (w/w) of the active ingredient. By way of example, the composition may comprise between 0.1% and 100%, e.g., between 0.5 and 50%, between 1-30%, between 5-80%, at least 80% (w/w) active ingredient.

In some embodiments, the respiratory virus RNA (e.g. mRNA) vaccine composition may comprise the polynucleotide described herein, formulated in a lipid nanoparticle comprising MC3, Cholesterol, DSPC and PEG2000-DMG, the buffer trisodium citrate, sucrose and water for injection. As a non-limiting example, the composition comprises: 2.0 mg/mL of drug substance (e.g., polynucleotides encoding H10N8 hMPV), 21.8 mg/mL of MC3, 10.1 mg/mL of cholesterol, 5.4 mg/mL of DSPC, 2.7 mg/mL of PEG2000-DMG, 5.16 mg/mL of trisodium citrate, 71 mg/mL of sucrose and 1.0 mL of water for injection.

In some embodiments, a nanoparticle (e.g., a lipid nanoparticle) has a mean diameter of 10-500 nm, 20-400 nm, 30-300 nm, 40-200 nm. In some embodiments, a nanoparticle (e.g., a lipid nanoparticle) has a mean diameter of 50-150 nm, 50-200 nm, 80-100 nm or 80-200 nm.

Liposomes, Lipoplexes, and Lipid Nanoparticles

The RNA (e.g., mRNA) vaccines of the disclosure can be formulated using one or more liposomes, lipoplexes, or lipid nanoparticles. In some embodiments, pharmaceutical compositions of RNA (e.g., mRNA) vaccines include liposomes. Liposomes are artificially-prepared vesicles which may primarily be composed of a lipid bilayer and may be used as a delivery vehicle for the administration of nutrients and pharmaceutical formulations. Liposomes can be of different sizes such as, but not limited to, a multilamellar vesicle (MLV) which may be hundreds of nanometers in diameter and may contain a series of concentric bilayers separated by narrow aqueous compartments, a small unicellular vesicle (SUV) which may be smaller than 50 nm in diameter, and a large unilamellar vesicle (LUV) which may be between 50 and 500 nm in diameter. Liposome design may include, but is not limited to, opsonins or ligands in order to improve the attachment of liposomes to unhealthy tissue or to activate events such as, but not limited to, endocytosis. Liposomes may contain a low or a high pH in order to improve the delivery of the pharmaceutical formulations.

The formation of liposomes may depend on the physicochemical characteristics such as, but not limited to, the pharmaceutical formulation entrapped and the liposomal ingredients, the nature of the medium in which the lipid vesicles are dispersed, the effective concentration of the entrapped substance and its potential toxicity, any additional processes involved during the application and/or delivery of the vesicles, the optimization size, polydispersity and the shelf-life of the vesicles for the intended application, and the batch-to-batch reproducibility and possibility of large-scale production of safe and efficient liposomal products.

In some embodiments, pharmaceutical compositions described herein may include, without limitation, liposomes such as those formed from 1,2-dioleyloxy-N,N-dimethylam-inopropane (DODMA) liposomes, DiLa2 liposomes from

Marina Biotech (Bothell, Wash.), 1,2-dilinoleyloxy-3-dimethylaminopropane (DLin-DMA), 2,2-dilinoleyl-4-(2-dimethylaminoethyl)-[1,3]-dioxolane (DLin-KC2-DMA), and MC3 (US20100324120; herein incorporated by reference in its entirety) and liposomes which may deliver small molecule drugs such as, but not limited to, DOXIL® from Janssen Biotech, Inc. (Horsham, Pa.).

In some embodiments, pharmaceutical compositions described herein may include, without limitation, liposomes such as those formed from the synthesis of stabilized plasmid-lipid particles (SPLP) or stabilized nucleic acid lipid particle (SNALP) that have been previously described and shown to be suitable for oligonucleotide delivery in vitro and in vivo (see Wheeler et al. Gene Therapy. 1999 6:271-281; Zhang et al. Gene Therapy. 1999 6:1438-1447; Jeffs et al. Pharm Res. 2005 22:362-372; Morrissey et al., Nat Biotechnol. 2005 2:1002-1007; Zimmermann et al., Nature. 2006 441:111-114; Heyes et al. J Contr Rel. 2005 107:276-287; Semple et al. Nature Biotech. 2010 28:172-176; Judge 20 et al. J Clin Invest. 2009 119:661-673; deFougerolles Hum Gene Ther. 2008 19:125-132; U.S. Patent Publication No US20130122104; all of which are incorporated herein in their entireties). The original manufacture method by Wheeler et al. was a detergent dialysis method, which was 25 later improved by Jeffs et al. and is referred to as the spontaneous vesicle formation method. The liposome formulations are composed of 3 to 4 lipid components in addition to the polynucleotide. As an example a liposome can contain, but is not limited to, 55% cholesterol, 20% 30 disteroylphosphatidyl choline (DSPC), 10% PEG-S-DSG, 15% 1,2-dioleyloxy-N,N-dimethylaminopropane and (DODMA), as described by Jeffs et al. As another example, certain liposome formulations may contain, but are not limited to, 48% cholesterol, 20% DSPC, 2% PEG-c-DMA, 35 and 30% cationic lipid, where the cationic lipid can be 1,2-distearloxy-N,N-dimethylaminopropane (DSDMA). DODMA, DLin-DMA, or 1,2-dilinolenyloxy-3-dimethylaminopropane (DLenDMA), as described by Heyes et al.

In some embodiments, liposome formulations may com- 40 prise from about 25.0% cholesterol to about 40.0% cholesterol, from about 30.0% cholesterol to about 45.0% cholesterol, from about 35.0% cholesterol to about 50.0% cholesterol and/or from about 48.5% cholesterol to about 60% cholesterol. In some embodiments, formulations may 45 comprise a percentage of cholesterol selected from the group consisting of 28.5%, 31.5%, 33.5%, 36.5%, 37.0%, 38.5%, 39.0% and 43.5%. In some embodiments, formulations may comprise from about 5.0% to about 10.0% DSPC and/or from about 7.0% to about 15.0% DSPC. 50

In some embodiments, the RNA (e.g., mRNA) vaccine pharmaceutical compositions may be formulated in liposomes such as, but not limited to, DiLa2 liposomes (Marina Biotech, Bothell, Wash.), SMARTICLES® (Marina Biotech, Bothell, Wash.), neutral DOPC (1,2-dioleoyl-sn-55 glycero-3-phosphocholine) based liposomes (e.g., siRNA delivery for ovarian cancer (Landen et al. Cancer Biology & Therapy 2006 5(12)1708-1713); herein incorporated by reference in its entirety) and hyaluronan-coated liposomes (Quiet Therapeutics, Israel). 60

In some embodiments, the cationic lipid may be a low molecular weight cationic lipid such as those described in U.S. Patent Application No. 20130090372, the contents of which are herein incorporated by reference in their entirety.

In some embodiments, the RNA (e.g., mRNA) vaccines 65 may be formulated in a lipid vesicle, which may have crosslinks between functionalized lipid bilayers.

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In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid-polycation complex. The formation of the lipid-polycation complex may be accomplished by methods known in the art and/or as described in U.S. Pub. No. 20120178702, herein incorporated by reference in its entirety. As a non-limiting example, the polycation may include a cationic peptide or a polypeptide such as, but not limited to, polylysine, polyomithine and/or polyarginine. In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid-polycation complex, which may further include a non-cationic lipid such as, but not limited to, cholesterol or dioleoyl phosphatidylethanolamine (DOPE).

In some embodiments, the ratio of PEG in the lipid nanoparticle (LNP) formulations may be increased or decreased and/or the carbon chain length of the PEG lipid may be modified from C14 to C18 to alter the pharmacokinetics and/or biodistribution of the LNP formulations. As a non-limiting example, LNP formulations may contain from about 0.5% to about 3.0%, from about 1.0% to about 3.5%, from about 1.5% to about 4.0%, from about 2.0% to about 4.5%, from about 2.5% to about 5.0% and/or from about 3.0% to about 6.0% of the lipid molar ratio of PEG-c-DOMG (R-3-[(ω -methoxy-poly(ethyleneglycol)2000)carbamoyl)]-1,2-dimyristyloxypropyl-3-amine) (also referred to herein as PEG-DOMG) as compared to the cationic lipid, DSPC and cholesterol. In some embodiments, the PEG-c-DOMG may be replaced with a PEG lipid such as, but not limited to, PEG-DSG (1,2-Distearoyl-sn-glycerol, methoxypolyethylene glycol), PEG-DMG (1,2-Dimyristoyl-sn-glycerol) and/or PEG-DPG (1,2-Dipalmitoyl-sn-glycerol, methoxypolyethylene glycol). The cationic lipid may be selected from any lipid known in the art such as, but not limited to, DLin-MC3-DMA, DLin-DMA, C12-200 and DLin-KC2-DMA.

In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid nanoparticle.

In some embodiments, the RNA (e.g., mRNA) vaccine formulation comprising the polynucleotide is a nanoparticle which may comprise at least one lipid. The lipid may be selected from, but is not limited to, DLin-DMA, DLin-K-DMA, 98N12-5, C12-200, DLin-MC3-DMA, DLin-KC2-DMA, DODMA, PLGA, PEG, PEG-DMG, PEGylated lipids and amino alcohol lipids. In another aspect, the lipid may be a cationic lipid such as, but not limited to, DLin-DMA, DLin-D-DMA, DLin-MC3-DMA, DLin-KC2-DMA. DODMA and amino alcohol lipids. The amino alcohol cationic lipid may be the lipids described in and/or made by the methods described in U.S. Patent Publication No. US20130150625, herein incorporated by reference in its entirety. As a non-limiting example, the cationic lipid may be 2-amino-3-[(9Z, 12Z)-octadeca-9,12-dien-1-yloxy]-2-{ [(9Z,2Z)-octadeca-9,12-dien-1-yloxy]methyl}propan-1-ol (Compound 1 in US20130150625); 2-amino-3-[(9Z)-octadec-9-en-1-yloxy]-2-{[(9Z)-octadec-9-en-1-yloxy]

methyl}propan-1-ol (Compound 2 in US20130150625);
2-amino-3-[(9Z, 12Z)-octadeca-9,12-dien-1-yloxy]-2-[(oc-tyloxy)methyl]propan-1-ol (Compound 3 in US20130150625); and 2-(dimethylamino)-3-[(9Z, 12Z)-octadeca-9,12-dien-1-yloxy]methyl}propan-1-ol (Compound 4 in US20130150625); or any pharmaceutically acceptable salt or stereoisomer thereof.

Lipid nanoparticle formulations typically comprise a lipid, in particular, an ionizable cationic lipid, for example, 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobu-

tyrate (DLin-MC3-DMA), or di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), and further comprise a neutral lipid, a sterol and a molecule capable of reducing particle aggregation, for example a PEG or PEG-modified lipid.

In some embodiments, the lipid nanoparticle formulation consists essentially of (i) at least one lipid selected from the group consisting of 2,2-dilinoleyl-4-dimethylaminoethyl-[1, 3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2- 10 en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy) heptadecanedioate (L319); (ii) a neutral lipid selected from DSPC, DPPC, POPC, DOPE and SM; (iii) a sterol, e.g., cholesterol; and (iv) a PEG-lipid, e.g., PEG-DMG or PEGcDMA, in a molar ratio of about 20-60% cationic lipid: 15 5-25% neutral lipid: 25-55% sterol; 0.5-15% PEG-lipid.

In some embodiments, the formulation includes from about 25% to about 75% on a molar basis of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethyl- 20 aminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), e.g., from about 35 to about 65%, from about 45 to about 65%, about 60%, about 57.5%, about 50% or about 40% on a molar basis. 25

In some embodiments, the formulation includes from about 0.5% to about 15% on a molar basis of the neutral lipid e.g., from about 3 to about 12%, from about 5 to about 10% or about 15%, about 10%, or about 7.5% on a molar basis. Examples of neutral lipids include, but are not limited to, 30 DSPC, POPC, DPPC, DOPE and SM. In some embodiments, the formulation includes from about 5% to about 50% on a molar basis of the sterol (e.g., about 15 to about 45%, about 20 to about 40%, about 40%, about 38.5%, about 35%, or about 31% on a molar basis. An exemplary sterol is 35 cholesterol. In some embodiments, the formulation includes from about 0.5% to about 20% on a molar basis of the PEG or PEG-modified lipid (e.g., about 0.5 to about 10%, about 0.5 to about 5%, about 1.5%, about 0.5%, about 1.5%, about 3.5%, or about 5% on a molar basis. In some embodiments, 40 the PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of 2,000 Da. In other embodiments, the PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of less than 2,000, for example around 1,500 Da, around 1,000 Da, or 45 around 500 Da. Examples of PEG-modified lipids include, but are not limited to, PEG-distearoyl glycerol (PEG-DMG) (also referred herein as PEG-C14 or C14-PEG), PEGcDMA (further discussed in Reyes et al. J. Controlled Release, 107, 276-287 (2005) the contents of which are 50 herein incorporated by reference in their entirety)

In some embodiments, the formulations of the present disclosure include 25-75% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobu- 55 tyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 0.5-15% of the neutral lipid, 5-50% of the sterol, and 0.5-20% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, the formulations of the present 60 disclosure include 35-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobu-tyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 65 3-12% of the neutral lipid, 15-45% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

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In some embodiments, the formulations of the present disclosure include 45-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane

(DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 5-10% of the neutral lipid, 25-40% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, the formulations of the present disclosure include about 60% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobu-tyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), about 7.5% of the neutral lipid, about 31% of the sterol, and about 1.5% of the PEG or PEG-modified lipid on a molar

basis. In some embodiments, the formulations of the present disclosure include about 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), about 10% of the neutral lipid, about 38.5% of the sterol, and about 1.5% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, the formulations of the present disclosure include about 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), about 10% of the neutral lipid, about 35% of the sterol, about 4.5% or about 5% of the PEG or PEG-modified lipid, and about 0.5% of the targeting lipid on a molar basis.

In some embodiments, the formulations of the present disclosure include about 40% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobu-tyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), about 15% of the neutral lipid, about 40% of the sterol, and about 5% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, the formulations of the present disclosure include about 57.2% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobu-tyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), about 7.1% of the neutral lipid, about 34.3% of the sterol, and about 1.4% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, the formulations of the present disclosure include about 57.5% of a cationic lipid selected from the PEG lipid is PEG-cDMA (PEG-cDMA is further discussed in Reyes et al. (*J. Controlled Release*, 107, 276-287 (2005), the contents of which are herein incorporated by reference in their entirety), about 7.5% of the neutral lipid, about 31.5% of the sterol, and about 3.5% of the PEG or PEG-modified lipid on a molar basis.

In some embodiments, lipid nanoparticle formulation consists essentially of a lipid mixture in molar ratios of about 20-70% cationic lipid: 5-45% neutral lipid: 20-55% cholesterol: 0.5-15% PEG-modified lipid; more preferably in a molar ratio of about 20-60% cationic lipid: 5-25% neutral lipid: 25-55% cholesterol: 0.5-15% PEG-modified lipid.

In some embodiments, the molar lipid ratio is approximately 50/10/38.5/1.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG, PEG-DSG or PEG-DPG), 57.2/7.1134.3/1.4 (mol % cationic lipid/neutral lipid, e.g., DPPC/Chol/PEG-modified lipid, 5 e.g., PEG-cDMA), 40/15/40/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG), 50/10/35/4.5/0.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DSG), 50/10/35/5 (cationic lipid/neutral lipid, e.g., DSPC/Chol/ 10 PEG-modified lipid, e.g., PEG-DMG), 40/10/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA), 35/15/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA) or 52/13/30/5 (mol % 15 cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA).

Examples of lipid nanoparticle compositions and methods of making same are described, for example, in Semple et al. (2010) *Nat. Biotechnol.* 28:172-176; Jayarama et al. (2012), 20 *Angew. Chem. Int. Ed.*, 51: 8529-8533; and Maier et al. (2013) *Molecular Therapy* 21, 1570-1578 (the contents of each of which are incorporated herein by reference in their entirety).

In some embodiments, the lipid nanoparticle formulations 25 described herein may comprise a cationic lipid, a PEG lipid and a structural lipid and optionally comprise a non-cationic lipid. As a non-limiting example, the lipid nanoparticle may comprise about 40-60% of cationic lipid, about 5-15% of a non-cationic lipid, about 1-2% of a PEG lipid and about 30 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise about 50% cationic lipid, about 10% non-cationic lipid, about 1.5% PEG lipid and about 38.5% structural lipid. As yet another non-limiting example, the lipid nanoparticle may comprise 35 about 55% cationic lipid, about 10% non-cationic lipid, about 2.5% PEG lipid and about 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and L319.

In some embodiments, the lipid nanoparticle formulations described herein may be 4 component lipid nanoparticles. The lipid nanoparticle may comprise a cationic lipid, a non-cationic lipid, a PEG lipid and a structural lipid. As a non-limiting example, the lipid nanoparticle may comprise 45 about 40-60% of cationic lipid, about 5-15% of a noncationic lipid, about 1-2% of a PEG lipid and about 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise about 50% cationic lipid, about 10% non-cationic lipid, about 1.5% PEG lipid and 50 about 38.5% structural lipid. As yet another non-limiting example, the lipid nanoparticle may comprise about 55% cationic lipid, about 10% non-cationic lipid, about 2.5% PEG lipid and about 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described 55 herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and L319.

In some embodiments, the lipid nanoparticle formulations described herein may comprise a cationic lipid, a noncationic lipid, a PEG lipid and a structural lipid. As a 60 non-limiting example, the lipid nanoparticle comprise about 50% of the cationic lipid DLin-KC2-DMA, about 10% of the non-cationic lipid DSPC, about 1.5% of the PEG lipid PEG-DOMG and about 38.5% of the structural lipid cholesterol. As a non-limiting example, the lipid nanoparticle 65 comprise about 50% of the cationic lipid DLin-MC3-DMA, about 10% of the non-cationic lipid DSPC, about 1.5% of

the PEG lipid PEG-DOMG and about 38.5% of the structural lipid cholesterol. As a non-limiting example, the lipid nanoparticle comprise about 50% of the cationic lipid DLin-MC3-DMA, about 10% of the non-cationic lipid DSPC, about 1.5% of the PEG lipid PEG-DMG and about 38.5% of the structural lipid cholesterol. As yet another non-limiting example, the lipid nanoparticle comprise about 55% of the cationic lipid L319, about 10% of the non-cationic lipid DSPC, about 2.5% of the PEG lipid PEG-DMG and about 32.5% of the structural lipid cholesterol.

As a non-limiting example, the cationic lipid may be selected from (20Z,23Z)-N,N-dimethylnonacosa-20,23dien-10-amine, (17Z,20Z)-N,N-dimemylhexacosa-17,20dien-9-amine. (1Z,19Z)-N5N-dimethylpentacosa-16, 19-dien-8-amine. (13Z,16Z)-N,N-dimethyldocosa-13,16dien-5-amine, (12Z, 15Z)-N,N-dimethylhenicosa-12,15dien-4-amine, (14Z, 17Z)-N,N-dimethyltricosa-14,17-dien-6-amine, (15Z, 18Z)-N,N-dimethyltetracosa-15,18-dien-7amine, (18Z,21Z)-N,N-dimethylheptacosa-18,21-dien-10-(15Z, 18Z)-N.N-dimethyltetracosa-15,18-dien-5amine. amine, (14Z, 17Z)-N,N-dimethyltricosa-14,17-dien-4amine, (19Z,22Z)-N,N-dimeihyloctacosa-19,22-dien-9-(18Z,21 Z)-N,N-dimethylheptacosa-18,21-dien-8amine, amine, (17Z,20Z)-N,N-dimethylhexacosa-17,20-dien-7amine, (16Z, 19Z)-N,N-dimethylpentacosa-16,19-dien-6-(22Z,25Z)-N,N-dimethylhentriaconta-22,25-dienamine, 10-amine, (21 Z,24Z)-N,N-dimethyltriaconta-21,24-dien-9amine, (18Z)-N,N-dimetylheptacos-18-en-10-amine, (17Z)-N,N-dimethylhexacos-17-en-9-amine, (19Z,22Z)-N,Ndimethyloctacosa-19,22-dien-7-amine, N.N-(20Z,23Z)-N-ethyl-Ndimethylheptacosan-10-amine, methylnonacosa-20,23-dien-10-amine, 1-[(11Z,14Z)-1pyrrolidine, nonylicosa-11,14-dien-1-yl] (20Z)-N,Ndimethylheptacos-20-en-10-amine, (15Z)-N,N-dimethyl eptacos-15-en-10-amine, (14Z)-N,N-dimethylnonacos-14en-10-amine, (17Z)-N,N-dimethylnonacos-17-en-10-amine, (24Z)-N,N-dimethyltritriacont-24-en-10-amine, (20Z)-N,Ndimethylnonacos-20-en-10-amine, (22Z)-N,N-dimethylhentriacont-22-en-10-amine, (16Z)-N,N-dimethylpentacos-16-40 en-8-amine, (12Z, 15Z)-N,N-dimethyl-2-nonylhenicosa-12, 15-dien-1-amine, (13Z, 16Z)-N,N-dimethyl-3-nonyldocosa-N,N-dimethyl-1-[(1S,2R)-2-13,16-dien-1-amine, eptadecan-8-amine, octylcyclopropyl] 1-[(1S,2R)-2hexylcyclopropyl]-N,N-dimethylnonadecan-10-amine, N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]nonadecan-10-amine, N,N-dimethyl-21-[(1S,2R)-2-octylcyclopropyl] henicosan-10-amine,N,N-dimethyl-1-[(1S,2S)-2-{[(1R, 2R)-2-pentylcyclopropyl]methyl}cyclopropyl]nonadecan-10-amine,N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl] hexadecan-8-amine, N,N-dimethyl-[(1R,2S)-2undecylcyclopropyl]tetradecan-5-amine, N,N-dimethyl-3-{7-[(1S,2R)-2-octylcyclopropyl]heptyl} dodecan-1-amine, 1-[(1R,2S)-2-heptylcyclopropyl]-N,N-dimethyloctadecan-1-[(1S,2R)-2-decylcyclopropyl]-N,N-dimethyl-9-amine. pentadecan-6-amine, N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]pentadecan-8-amine, R-N,N-dimethyl-1-[(9Z, 12Z)-octadeca-9,12-dien-1-yloxy]-3-(octyloxy)propan-2amine, S-N,N-dimethyl-1-[(9Z, 12Z)-octadeca-9,12-dien-1yloxy]-3-(octyloxy)propan-2-amine, 1-{2-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-1-[(octyloxy)methyl] ethyl}pyrrolidine. (2S)-N,N-dimethyl-1-[(9Z, 12Z)octadeca-9,12-dien-1-yloxy]-3-[(5Z)-oct-5-en-1-yloxy] propan-2-amine, 1-{2-[(9Z, 12Z)-octadeca-9,12-dien-1-(2S)-1yloxy]-1-[(octyloxy)methyl]ethyl}azetidine,

(hexyloxy)-N,N-dimethyl-3-[(9Z, 12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, (2S)-1-(heptyloxy)-N,Ndimethyl-3-[(9Z, 12Z)-octadeca-9,12-dien-1-yloxy]propan-

N,N-dimethyl-1-(nonyloxy)-3-[(9Z, 12Z)-2-amine. octadeca-9,12-dien-1-yloxy]propan-2-amine, N,Ndimethyl-1-[(9Z)-octadec-9-en-1-yloxy]-3-(octyloxy) propan-2-amine; (2S)-N,N-dimethyl-1-[(6Z,9Z, 12Z)-5 octadeca-6,9,12-trien-1-yloxy]-3-(octyloxy)propan-2amine, (2S)-1-[(11Z,14Z)-icosa-11,14-dien-1-yloxy]-N,Ndimethyl-3-(pentyloxy)propan-2-amine, (2S)-1-(hexyloxy)-3-[(11Z,14Z)-icosa-11,14-dien-1-yloxy]-N,Ndimethylpropan-2-amine, 1-[(11Z,14Z)-icosa-11,14-dien-1-10 yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-amine, 1-[(13Z, 16Z)-docosa-13,16-dien-1-yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-amine, (2S)-1-[(13Z,16Z)-docosa-13, 16-dien-1-yloxy]-3-(hexyloxy)-N,N-dimethylpropan-2amine, (2S)-1-[(13Z)-docos-13-en-1-yloxy]-3-(hexyloxy)-N,N-dimethylpropan-2-amine, 1-[(13Z)-docos-13-en-1yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-amine, 1-[(9Z)hexadec-9-en-1-yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-amine. (2R)-N,N-dimethyl-H(1-metoylo ctyl)oxy]-3-[(9Z, 12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, 20 (2R)-1-[(3,7-dimethyloctyl)oxy]-N,N-dimethyl-3-[(9Z, 12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, N,N-dimethyl-1-(octyloxy)-3-({8-[(1S,2S)-2-{[(1R,2R)-2-pentylcyclopropyl]methyl}cyclopropyl]octyl}oxy)propan-2-N,N-dimethyl-1-{[8-(2-oc1ylcyclopropyl)octyl] 25 amine, oxy}-3-(octyloxy)propan-2-amine and (11E,20Z,23Z)-N,Ndimethylnonacosa-11,20,2-trien-10-amine or pharmaceutically acceptable salt or stereoisomer thereof.

In some embodiments, the LNP formulations of the RNA (e.g., mRNA) vaccines may contain PEG-c-DOMG at 3% 30 lipid molar ratio. In some embodiments, the LNP formulations of the RNA (e.g., mRNA) vaccines may contain PEG-c-DOMG at 1.5% lipid molar ratio.

In some embodiments, the pharmaceutical compositions of the RNA (e.g., mRNA) vaccines may include at least one 35 of the PEGylated lipids described in International Publication No. WO2012099755, the contents of which are herein incorporated by reference in their entirety.

In some embodiments, the LNP formulation may contain PEG-DMG 2000 (1,2-dimyristoyl-sn-glycero-3-phophoe- 40 thanolamine-N-[methoxy(polyethylene glycol)-2000). In some embodiments, the LNP formulation may contain PEG-DMG 2000, a cationic lipid known in the art and at least one other component. In some embodiments, the LNP formulation may contain PEG-DMG 2000, a cationic lipid known in 45 the art, DSPC and cholesterol. As a non-limiting example, the LNP formulation may contain PEG-DMG 2000, DLin-DMA, DSPC and cholesterol. As another non-limiting example the LNP formulation may contain PEG-DMG 2000, DLin-DMA, DSPC and cholesterol in a molar ratio of 50 2:40:10:48 (see e.g., Geall et al., Nonviral delivery of self-amplifying RNA (e.g., mRNA) vaccines, PNAS 2012; PMID: 22908294, the contents of each of which are herein incorporated by reference in their entirety).

The lipid nanoparticles described herein may be made in 55 a sterile environment.

In some embodiments, the LNP formulation may be formulated in a nanoparticle such as a nucleic acid-lipid particle. As a non-limiting example, the lipid particle may comprise one or more active agents or therapeutic agents; 60 one or more cationic lipids comprising from about 50 mol % to about 85 mol % of the total lipid present in the particle; one or more non-cationic lipids comprising from about 13 mol % to about 49.5 mol % of the total lipid present in the particle; and one or more conjugated lipids that inhibit 65 aggregation of particles comprising from about 0.5 mol % to about 2 mol % of the total lipid present in the particle.

The nanoparticle formulations may comprise a phosphate conjugate. The phosphate conjugate may increase in vivo circulation times and/or increase the targeted delivery of the nanoparticle. As a non-limiting example, the phosphate conjugates may include a compound of any one of the formulas described in International Application No. WO2013033438, the contents of which are herein incorporated by reference in its entirety.

The nanoparticle formulation may comprise a polymer conjugate. The polymer conjugate may be a water soluble conjugate. The polymer conjugate may have a structure as described in U.S. Patent Application No. 20130059360, the contents of which are herein incorporated by reference in its entirety. In some embodiments, polymer conjugates with the polynucleotides of the present disclosure may be made using the methods and/or segmented polymeric reagents described in U.S. Patent Application No. 20130072709, the contents of which are herein incorporated by reference in its entirety. In some embodiments, the polymer conjugate may have pendant side groups comprising ring moieties such as, but not limited to, the polymer conjugates described in U.S. Patent Publication No. US20130196948, the contents which are herein incorporated by reference in its entirety.

The nanoparticle formulations may comprise a conjugate to enhance the delivery of nanoparticles of the present disclosure in a subject. Further, the conjugate may inhibit phagocytic clearance of the nanoparticles in a subject. In one aspect, the conjugate may be a "self" peptide designed from the human membrane protein CD47 (e.g., the "self" particles described by Rodriguez et al. (Science 2013 339, 971-975), herein incorporated by reference in its entirety). As shown by Rodriguez et al., the self peptides delayed macrophagemediated clearance of nanoparticles which enhanced delivery of the nanoparticles. In another aspect, the conjugate may be the membrane protein CD47 (e.g., see Rodriguez et al. Science 2013 339, 971-975, herein incorporated by reference in its entirety). Rodriguez et al. showed that, similarly to "self" peptides, CD47 can increase the circulating particle ratio in a subject as compared to scrambled peptides and PEG coated nanoparticles.

In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure are formulated in nanoparticles which comprise a conjugate to enhance the delivery of the nanoparticles of the present disclosure in a subject. The conjugate may be the CD47 membrane or the conjugate may be derived from the CD47 membrane protein, such as the "self" peptide described previously. In some embodiments, the nanoparticle may comprise PEG and a conjugate of CD47 or a derivative thereof. In some embodiments, the nanoparticle may comprise both the "self" peptide described above and the membrane protein CD47.

In some embodiments, a "self" peptide and/or CD47 protein may be conjugated to a virus-like particle or pseudovirion, as described herein for delivery of the RNA (e.g., mRNA) vaccines of the present disclosure.

In some embodiments, RNA (e.g., mRNA) vaccine pharmaceutical compositions comprising the polynucleotides of the present disclosure and a conjugate that may have a degradable linkage. Non-limiting examples of conjugates include an aromatic moiety comprising an ionizable hydrogen atom, a spacer moiety, and a water-soluble polymer. As a non-limiting example, pharmaceutical compositions comprising a conjugate with a degradable linkage and methods for delivering such pharmaceutical compositions are described in U.S. Patent Publication No. US20130184443, the contents of which are herein incorporated by reference in their entirety. The nanoparticle formulations may be a carbohydrate nanoparticle comprising a carbohydrate carrier and a RNA (e.g., mRNA) vaccine. As a non-limiting example, the carbohydrate carrier may include, but is not limited to, an anhydride-modified phytoglycogen or glycogen-type material, phtoglycogen octenyl succinate, phytoglycogen betadextrin, anhydride-modified phytoglycogen beta-dextrin. (See e.g., International Publication No. WO2012109121; the contents of which are herein incorporated by reference in their entirety).

Nanoparticle formulations of the present disclosure may be coated with a surfactant or polymer in order to improve the delivery of the particle. In some embodiments, the nanoparticle may be coated with a hydrophilic coating such as, but not limited to, PEG coatings and/or coatings that have 15 a neutral surface charge. The hydrophilic coatings may help to deliver nanoparticles with larger payloads such as, but not limited to, RNA (e.g., mRNA) vaccines within the central nervous system. As a non-limiting example nanoparticles comprising a hydrophilic coating and methods of making 20 such nanoparticles are described in U.S. Patent Publication No. US20130183244, the contents of which are herein incorporated by reference in their entirety.

In some embodiments, the lipid nanoparticles of the present disclosure may be hydrophilic polymer particles. 25 Non-limiting examples of hydrophilic polymer particles and methods of making hydrophilic polymer particles are described in U.S. Patent Publication No. US20130210991, the contents of which are herein incorporated by reference in their entirety. 30

In some embodiments, the lipid nanoparticles of the present disclosure may be hydrophobic polymer particles.

Lipid nanoparticle formulations may be improved by replacing the cationic lipid with a biodegradable cationic lipid which is known as a rapidly eliminated lipid nanopar- 35 ticle (reLNP). Ionizable cationic lipids, such as, but not limited to, DLinDMA, DLin-KC2-DMA, and DLin-MC3-DMA, have been shown to accumulate in plasma and tissues over time and may be a potential source of toxicity. The rapid metabolism of the rapidly eliminated lipids can 40 improve the tolerability and therapeutic index of the lipid nanoparticles by an order of magnitude from a 1 mg/kg dose to a 10 mg/kg dose in rat. Inclusion of an enzymatically degraded ester linkage can improve the degradation and metabolism profile of the cationic component, while still 45 maintaining the activity of the reLNP formulation. The ester linkage can be internally located within the lipid chain or it may be terminally located at the terminal end of the lipid chain. The internal ester linkage may replace any carbon in the lipid chain.

In some embodiments, the internal ester linkage may be located on either side of the saturated carbon.

In some embodiments, an immune response may be elicited by delivering a lipid nanoparticle which may include a nanospecies, a polymer and an immunogen. (U.S. Publi-55 cation No. 20120189700 and International Publication No. WO2012099805; each of which is herein incorporated by reference in their entirety). The polymer may encapsulate the nanospecies or partially encapsulate the nanospecies. The immunogen may be a recombinant protein, a modified 60 RNA and/or a polynucleotide described herein. In some embodiments, the lipid nanoparticle may be formulated for use in a vaccine such as, but not limited to, against a pathogen.

Lipid nanoparticles may be engineered to alter the surface 65 properties of particles so the lipid nanoparticles may penetrate the mucosal barrier. Mucus is located on mucosal 86

tissue such as, but not limited to, oral (e.g., the buccal and esophageal membranes and tonsil tissue), ophthalmic, gastrointestinal (e.g., stomach, small intestine, large intestine, colon, rectum), nasal, respiratory (e.g., nasal, pharyngeal, tracheal and bronchial membranes), genital (e.g., vaginal, cervical and urethral membranes). Nanoparticles larger than 10-200 nm which are preferred for higher drug encapsulation efficiency and the ability to provide the sustained delivery of a wide array of drugs have been thought to be too large to rapidly diffuse through mucosal barriers. Mucus is continuously secreted, shed, discarded or digested and recycled so most of the trapped particles may be removed from the mucosa tissue within seconds or within a few hours. Large polymeric nanoparticles (200 nm-500 nm in diameter) which have been coated densely with a low molecular weight polyethylene glycol (PEG) diffused through mucus only 4 to 6-fold lower than the same particles diffusing in water (Lai et al. PNAS 2007 104(5):1482-487; Lai et al. Adv Drug Deliv Rev. 2009 61(2): 158-171; each of which is herein incorporated by reference in their entirety). The transport of nanoparticles may be determined using rates of permeation and/or fluorescent microscopy techniques including, but not limited to, fluorescence recovery after photobleaching (FRAP) and high resolution multiple particle tracking (MPT). As a non-limiting example, compositions which can penetrate a mucosal barrier may be made as described in U.S. Pat. No. 8,241,670 or International Patent Publication No. WO2013110028, the contents of each of which are herein incorporated by reference in its entirety.

The lipid nanoparticle engineered to penetrate mucus may comprise a polymeric material (i.e. a polymeric core) and/or a polymer-vitamin conjugate and/or a tri-block co-polymer. The polymeric material may include, but is not limited to, polyamines, polyethers, polyamides, polyesters, polycarbamates, polyureas, polycarbonates, poly(styrenes), polyimides, polysulfones, polyurethanes, polyacetylenes, polyethylenes, polyethyeneimines, polyisocyanates, polyacrylates, polymethacrylates, polyacrylonitriles, and polyarylates. The polymeric material may be biodegradable and/or biocompatible. Non-limiting examples of biocompatible polymers are described in International Patent Publication No. WO2013116804, the contents of which are herein incorporated by reference in their entirety. The polymeric material may additionally be irradiated. As a non-limiting example, the polymeric material may be gamma irradiated (see e.g., International App. No. WO201282165, herein incorporated by reference in its entirety). Non-limiting examples of specific polymers include poly(caprolactone) (PCL), ethylene vinyl acetate polymer (EVA), poly(lactic acid) (PLA), poly(L-lactic acid) (PLLA), poly(glycolic acid) (PGA), poly (lactic acid-co-glycolic acid) (PLGA), poly(L-lactic acidco-glycolic acid) (PLLGA), poly(D,L-lactide) (PDLA), poly (L-lactide) (PLLA), poly(D,L-lactide-co-caprolactone), poly(D,L-lactide-co-caprolactone-co-glycolide), poly(D,Llactide-co-PEO-co-D,L-lactide), poly(D,L-lactide-co-PPOco-D,L-lactide), polyalkyl cyanoacralate, polyurethane, poly-L-lysine (PLL), hydroxypropyl methacrylate (HPMA), polyethyleneglycol, poly-L-glutamic acid, poly(hydroxy acids), polyanhydrides, polyorthoesters, poly(ester amides), polyamides, poly(ester ethers), polycarbonates, polyalkylenes such as polyethylene and polypropylene, polyalkylene glycols such as poly(ethylene glycol) (PEG), polyalkylene oxides (PEO), polyalkylene terephthalates such as poly (ethylene terephthalate), polyvinyl alcohols (PVA), polyvinyl ethers, polyvinyl esters such as poly(vinyl acetate), polyvinyl halides such as poly(vinyl chloride) (PVC), poly-

vinylpyrrolidone, polysiloxanes, polystyrene (PS), polyurethanes, derivatized celluloses such as alkyl celluloses, hydroxyalkyl celluloses, cellulose ethers, cellulose esters, nitro celluloses, hydroxypropylcellulose, carboxymethylcellulose, polymers of acrylic acids, such as poly(methyl(meth) 5 acrylate) (PMMA), poly(ethyl(meth)acrylate), poly(butyl (meth)acrylate), poly(isobutyl(meth)acrylate), poly(hexyl (meth)acrylate), poly(isodecyl(meth)acrylate), poly(lauryl (meth)acrylate), poly(phenyl(meth)acrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), 10 poly(octadecyl acrylate) and copolymers and mixtures thereof, polydioxanone and its copolymers, polyhydroxyalkanoates, polypropylene fumarate, polyoxymethylene, poloxamers, poly(ortho)esters, poly(butyric acid), poly(valeric acid), poly(lactide-co-caprolactone), PEG-PLGA-PEG 15 and trimethylene carbonate, polyvinylpyrrolidone. The lipid nanoparticle may be coated or associated with a co-polymer such as, but not limited to, a block co-polymer (such as a branched polyether-polyamide block copolymer described in International Publication No. WO2013012476, herein 20 incorporated by reference in its entirety), and (poly(ethylene glycol))-(poly(propylene oxide))-(poly(ethylene glycol)) triblock copolymer (see e.g., U.S. Publication 20120121718 and U.S. Publication 20100003337 and U.S. Pat. No. 8,263, 665, the contents of each of which is herein incorporated by 25 reference in their entirety). The co-polymer may be a polymer that is generally regarded as safe (GRAS) and the formation of the lipid nanoparticle may be in such a way that no new chemical entities are created. For example, the lipid nanoparticle may comprise poloxamers coating PLGA nano- 30 particles without forming new chemical entities which are still able to rapidly penetrate human mucus (Yang et al. Angew. Chem. Int. Ed. 2011 50:2597-2600; the contents of which are herein incorporated by reference in their entirety). A non-limiting scalable method to produce nanoparticles 35 which can penetrate human mucus is described by Xu et al. (see, e.g., J Control Release 2013, 170(2):279-86; the contents of which are herein incorporated by reference in their entirety).

The vitamin of the polymer-vitamin conjugate may be 40 vitamin E. The vitamin portion of the conjugate may be substituted with other suitable components such as, but not limited to, vitamin A, vitamin E, other vitamins, cholesterol, a hydrophobic moiety, or a hydrophobic component of other surfactants (e.g., sterol chains, fatty acids, hydrocarbon 45 chains and alkylene oxide chains).

The lipid nanoparticle engineered to penetrate mucus may include surface altering agents such as, but not limited to, polynucleotides, anionic proteins (e.g., bovine serum albumin), surfactants (e.g., cationic surfactants such as for 50 example dimethyldioctadecyl-ammonium bromide), sugars or sugar derivatives (e.g., cyclodextrin), nucleic acids, polymers (e.g., heparin, polyethylene glycol and poloxamer), mucolytic agents (e.g., N-acetylcysteine, mugwort, bromelain, papain, clerodendrum, acetylcysteine, bromhexine, car- 55 bocisteine, eprazinone, mesna, ambroxol, sobrerol, domiodol, letosteine, stepronin, tiopronin, gelsolin, thymosin 34 dornase alfa, neltenexine, erdosteine) and various DNases including rhDNase. The surface altering agent may be embedded or enmeshed in the particle's surface or disposed 60 (e.g., by coating, adsorption, covalent linkage, or other process) on the surface of the lipid nanoparticle. (see e.g., U.S. Publication 20100215580 and U.S. Publication 20080166414 and US20130164343; the contents of each of which are herein incorporated by reference in their entirety). 65

In some embodiments, the mucus penetrating lipid nanoparticles may comprise at least one polynucleotide described herein. The polynucleotide may be encapsulated in the lipid nanoparticle and/or disposed on the surface of the particle. The polynucleotide may be covalently coupled to the lipid nanoparticle. Formulations of mucus penetrating lipid nanoparticles may comprise a plurality of nanoparticles. Further, the formulations may contain particles which may interact with the mucus and alter the structural and/or adhesive properties of the surrounding mucus to decrease mucoadhesion, which may increase the delivery of the mucus penetrating lipid nanoparticles to the mucosal tissue.

In some embodiments, the mucus penetrating lipid nanoparticles may be a hypotonic formulation comprising a mucosal penetration enhancing coating. The formulation may be hypotonice for the epithelium to which it is being delivered. Non-limiting examples of hypotonic formulations may be found in International Patent Publication No. WO2013110028, the contents of which are herein incorporated by reference in their entirety.

In some embodiments, in order to enhance the delivery through the mucosal barrier the RNA (e.g., mRNA) vaccine formulation may comprise or be a hypotonic solution.

Hypotonic solutions were found to increase the rate at which mucoinert particles such as, but not limited to, mucus-penetrating particles, were able to reach the vaginal epithelial surface (see e.g., Ensign et al. Biomaterials 2013 34(28):6922-9, the contents of which are herein incorporated by reference in their entirety).

In some embodiments, the RNA (e.g., mRNA) vaccine is formulated as a lipoplex, such as, without limitation, the ATUPLEX[™] system, the DACC system, the DBTC system and other siRNA-lipoplex technology from Silence Therapeutics (London, United Kingdom), STEMFECT[™] from STEMGENT® (Cambridge, Mass.), and polyethylenimine (PEI) or protamine-based targeted and non-targeted delivery of nucleic acids acids (Aleku et al. Cancer Res. 2008 68:9788-9798; Strumberg et al. Int J Clin Pharmacol Ther 2012 50:76-78; Santel et al., Gene Ther 2006 13:1222-1234; Santel et al., Gene Ther 2006 13:1360-1370; Gutbier et al., Pulm Pharmacol. Ther. 2010 23:334-344; Kaufmann et al. Microvasc Res 2010 80:286-293 Weide et al. J Immunother. 2009 32:498-507; Weide et al. J Immunother. 2008 31:180-188; Pascolo Expert Opin. Biol. Ther. 4:1285-1294; Fotin-Mleczek et al., 2011 J. Immunother. 34:1-15; Song et al., Nature Biotechnol. 2005, 23:709-717; Peer et al., Proc Natl Acad Sci USA. 2007 6; 104:4095-4100; deFougerolles Hum Gene Ther. 2008 19:125-132, the contents of each of which are incorporated herein by reference in their entirety).

In some embodiments, such formulations may also be constructed or compositions altered such that they passively or actively are directed to different cell types in vivo, including but not limited to hepatocytes, immune cells, tumor cells, endothelial cells, antigen presenting cells, and leukocytes (Akinc et al. Mol Ther. 2010 18:1357-1364; Song et al., Nat Biotechnol. 2005 23:709-717; Judge et al., J Clin Invest. 2009 119:661-673; Kaufmann et al., Microvasc Res 2010 80:286-293; Santel et al., Gene Ther 2006 13:1222-1234; Santel et al., Gene Ther 2006 13:1360-1370; Gutbier et al., Pulm Pharmacol. Ther. 2010 23:334-344; Basha et al., Mol. Ther. 2011 19:2186-2200; Fenske and Cullis, Expert Opin Drug Deliv. 2008 5:25-44; Peer et al., Science. 2008 319:627-630; Peer and Lieberman, Gene Ther. 2011 18:1127-1133, the contents of each of which are incorporated herein by reference in their entirety). One example of passive targeting of formulations to liver cells includes the DLin-DMA, DLin-KC2-DMA and DLin-MC3-DMA-based lipid nanoparticle formulations, which have been shown to bind to apolipoprotein E and promote binding

and uptake of these formulations into hepatocytes in vivo (Akinc et al. Mol Ther. 2010 18:1357-1364, the contents of which are incorporated herein by reference in their entirety). Formulations can also be selectively targeted through expression of different ligands on their surface as exempli-5 fied by, but not limited by, folate, transferrin, N-acetylgalactosamine (GalNAc), and antibody targeted approaches (Kolhatkar et al., Curr Drug Discov Technol. 2011 8:197-206; Musacchio and Torchilin, Front Biosci. 2011 16:1388-1412; Yu et al., Mol Membr Biol. 2010 27:286-298; Patil et 10 al., Crit Rev Ther Drug Carrier Syst. 2008 25:1-61; Benoit et al., Biomacromolecules. 2011 12:2708-2714; Zhao et al., Expert Opin Drug Deliv. 2008 5:309-319; Akinc et al., Mol Ther. 2010 18:1357-1364; Srinivasan et al., Methods Mol Biol. 2012 820:105-116; Ben-Arie et al., Methods Mol Biol. 15 may include, but is not limited to, tri-block co-polymers. As 2012 757:497-507; Peer 2010 J Control Release. 20:63-68; Peer et al., Proc Natl Acad Sci USA. 2007 104:4095-4100; Kim et al., Methods Mol Biol. 2011 721:339-353; Subramanya et al., Mol Ther. 2010 18:2028-2037; Song et al., Nat Biotechnol. 2005 23:709-717; Peer et al., Science. 2008 20 319:627-630; Peer and Lieberman, Gene Ther. 2011 18:1127-1133, the contents of each of which are incorporated herein by reference in their entirety).

In some embodiments, the RNA (e.g., mRNA) vaccine is formulated as a solid lipid nanoparticle. A solid lipid nano- 25 particle (SLN) may be spherical with an average diameter between 10 to 1000 nm. SLN possess a solid lipid core matrix that can solubilize lipophilic molecules and may be stabilized with surfactants and/or emulsifiers. In some embodiments, the lipid nanoparticle may be a self-assembly 30 lipid-polymer nanoparticle (see Zhang et al., ACS Nano, 2008, 2 (8), pp 1696-1702; the contents of which are herein incorporated by reference in their entirety). As a nonlimiting example, the SLN may be the SLN described in International Patent Publication No. WO2013105101, the 35 contents of which are herein incorporated by reference in their entirety. As another non-limiting example, the SLN may be made by the methods or processes described in International Patent Publication No. WO2013105101, the contents of which are herein incorporated by reference in 40 their entirety.

Liposomes, lipoplexes, or lipid nanoparticles may be used to improve the efficacy of polynucleotides directed protein production as these formulations may be able to increase cell transfection by the RNA (e.g., mRNA) vaccine; and/or 45 increase the translation of encoded protein. One such example involves the use of lipid encapsulation to enable the effective systemic delivery of polyplex plasmid DNA (Heyes et al., Mol Ther. 2007 15:713-720; the contents of which are incorporated herein by reference in their entirety). 50 The liposomes, lipoplexes, or lipid nanoparticles may also be used to increase the stability of the polynucleotide.

In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure can be formulated for controlled release and/or targeted delivery. As used herein, "controlled 55 release" refers to a pharmaceutical composition or compound release profile that conforms to a particular pattern of release to effect a therapeutic outcome. In some embodiments, the RNA (e.g., mRNA) vaccines may be encapsulated into a delivery agent described herein and/or known in 60 the art for controlled release and/or targeted delivery. As used herein, the term "encapsulate" means to enclose, surround or encase. As it relates to the formulation of the compounds of the disclosure, encapsulation may be substantial, complete or partial. The term "substantially encapsu- 65 lated" means that at least greater than 50, 60, 70, 80, 85, 90, 95, 96, 97, 98, 99, 99.9, 99.9 or greater than 99.999% of the

pharmaceutical composition or compound of the disclosure may be enclosed, surrounded or encased within the delivery agent. "Partially encapsulation" means that less than 10, 10, 20, 30, 40 50 or less of the pharmaceutical composition or compound of the disclosure may be enclosed, surrounded or encased within the delivery agent. Advantageously, encapsulation may be determined by measuring the escape or the activity of the pharmaceutical composition or compound of the disclosure using fluorescence and/or electron micrograph. For example, at least 1, 5, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 95, 96, 97, 98, 99, 99.9, 99.99 or greater than 99.99% of the pharmaceutical composition or compound of the disclosure are encapsulated in the delivery agent.

In some embodiments, the controlled release formulation a non-limiting example, the formulation may include two different types of tri-block co-polymers (International Pub. No. WO2012131104 and WO2012131106, the contents of each of which are incorporated herein by reference in their entirety).

In some embodiments, the RNA (e.g., mRNA) vaccines may be encapsulated into a lipid nanoparticle or a rapidly eliminated lipid nanoparticle and the lipid nanoparticles or a rapidly eliminated lipid nanoparticle may then be encapsulated into a polymer, hydrogel and/or surgical sealant described herein and/or known in the art. As a non-limiting example, the polymer, hydrogel or surgical sealant may be PLGA, ethylene vinyl acetate (EVAc), poloxamer, GELSITE® (Nanotherapeutics, Inc. Alachua, Fla.), HYL-ENEX® (Halozyme Therapeutics, San Diego Calif.), surgical sealants such as fibrinogen polymers (Ethicon Inc. Cornelia, Ga.), TISSELL® (Baxter International, Inc Deerfield, Ill.), PEG-based sealants, and COSEAL® (Baxter International, Inc Deerfield, Ill.).

In some embodiments, the lipid nanoparticle may be encapsulated into any polymer known in the art which may form a gel when injected into a subject. As another nonlimiting example, the lipid nanoparticle may be encapsulated into a polymer matrix which may be biodegradable.

In some embodiments, the RNA (e.g., mRNA) vaccine formulation for controlled release and/or targeted delivery may also include at least one controlled release coating. Controlled release coatings include, but are not limited to, OPADRY®, polyvinylpyrrolidone/vinyl acetate copolymer, polyvinylpyrrolidone, hydroxypropyl methylcellulose, hydroxyethyl hydroxypropyl cellulose, cellulose. EUDRAGIT RL®, EUDRAGIT RS® and cellulose derivatives such as ethylcellulose aqueous dispersions (AQUA-COAT® and SURELEASE®).

In some embodiments, the RNA (e.g., mRNA) vaccine controlled release and/or targeted delivery formulation may comprise at least one degradable polyester which may contain polycationic side chains. Degradeable polyesters include, but are not limited to, poly(serine ester), poly(Llactide-co-L-lysine), poly(4-hydroxy-L-proline ester), and combinations thereof. In some embodiments, the degradable polyesters may include a PEG conjugation to form a PEGylated polymer.

In some embodiments, the RNA (e.g., mRNA) vaccine controlled release and/or targeted delivery formulation comprising at least one polynucleotide may comprise at least one PEG and/or PEG related polymer derivatives as described in U.S. Pat. No. 8,404,222, the contents of which are incorporated herein by reference in their entirety.

In some embodiments, the RNA (e.g., mRNA) vaccine controlled release delivery formulation comprising at least one polynucleotide may be the controlled release polymer system described in US20130130348, the contents of which are incorporated herein by reference in their entirety.

In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be encapsulated in a therapeutic nanoparticle, referred to herein as "therapeutic nanoparticle⁵ RNA (e.g., mRNA) vaccines." Therapeutic nanoparticles may be formulated by methods described herein and known in the art such as, but not limited to, International Pub Nos. WO2010005740, WO2010030763, WO2010005721, WO2010005723, WO2012054923, U.S. Publication Nos. US20110262491, US20100104645, US20100087337, US20100068285, US20110274759, US20100068286, US20120288541, US20130123351 and US20130230567 and U.S. Pat. Nos. 8,206,747, 8,293,276, 8,318,208 and 15 8,318,211; the contents of each of which are herein incorporated by reference in their entirety. In some embodiments, therapeutic polymer nanoparticles may be identified by the methods described in US Pub No. US20120140790, the contents of which are herein incorporated by reference in 20 their entirety.

In some embodiments, the therapeutic nanoparticle RNA (e.g., mRNA) vaccine may be formulated for sustained release. As used herein, "sustained release" refers to a pharmaceutical composition or compound that conforms to 25 a release rate over a specific period of time. The period of time may include, but is not limited to, hours, days, weeks, months and years. As a non-limiting example, the sustained release nanoparticle may comprise a polymer and a therapeutic agent such as, but not limited to, the polynucleotides 30 of the present disclosure (see International Pub No. 2010075072 and US Pub No. US20100216804, US20110217377 and US20120201859, the contents of each of which are incorporated herein by reference in their entirety). In another non-limiting example, the sustained 35 release formulation may comprise agents which permit persistent bioavailability such as, but not limited to, crystals, macromolecular gels and/or particulate suspensions (see U.S. Patent Publication No US20130150295, the contents of each of which are incorporated herein by reference in their 40 entirety).

In some embodiments, the therapeutic nanoparticle RNA (e.g., mRNA) vaccines may be formulated to be target specific. As a non-limiting example, the therapeutic nanoparticles may include a corticosteroid (see International Pub. 45 No. WO2011084518, the contents of which are incorporated herein by reference in their entirety). As a non-limiting example, the therapeutic nanoparticles may be formulated in nanoparticles described in International Pub No. WO2008121949, WO2010005726, WO2010005725, so WO2011084521 and US Pub No. US20100069426, US20120004293 and US20100104655, the contents of each of which are incorporated herein by reference in their entirety.

In some embodiments, the nanoparticles of the present 55 disclosure may comprise a polymeric matrix. As a nonlimiting example, the nanoparticle may comprise two or more polymers such as, but not limited to, polyethylenes, polycarbonates, polyanhydrides, polyhydroxyacids, polypropylfumerates, polycaprolactones, polyamides, polyac- 60 etals, polyethers, polyesters, poly(orthoesters), polycyanoacrylates, polyvinyl alcohols, polyurethanes, polyphosphazenes, polyacrylates, polymethacrylates, polycyanoacrylates, polyureas, polystyrenes, polyamines, polylysine, poly(ethylene imine), poly(serine ester), poly(L- 65 lactide-co-L-lysine), poly(4-hydroxy-L-proline ester) or combinations thereof.

In some embodiments, the therapeutic nanoparticle comprises a diblock copolymer. In some embodiments, the diblock copolymer may include PEG in combination with a polymer such as, but not limited to, polyethylenes, polycarbonates, polyanhydrides, polyhydroxyacids, polypropylfumerates, polycaprolactones, polyamides, polyacetals, polyethers, polyesters, poly(orthoesters), polycyanoacrylates, polyvinyl alcohols, polyurethanes, polyphosphazenes, polyacrylates, polymethacrylates, polycyanoacrylates, polyureas, polystyrenes, polyamines, polylysine, poly(ethylene imine), poly(serine ester), poly(L-lactide-co-L-lysine), poly(4-hydroxy-L-proline ester) or combinations thereof. In yet another embodiment, the diblock copolymer may be a high-X diblock copolymer such as those described in International Patent Publication No. WO2013120052, the contents of which are incorporated herein by reference in their entirety.

As a non-limiting example the therapeutic nanoparticle comprises a PLGA-PEG block copolymer (see U.S. Publication No. US20120004293 and U.S. Pat. No. 8,236,330, each of which is herein incorporated by reference in their entirety). In another non-limiting example, the therapeutic nanoparticle is a stealth nanoparticle comprising a diblock copolymer of PEG and PLA or PEG and PLGA (see U.S. Pat. No. 8,246,968 and International Publication No. WO2012166923, the contents of each of which are herein incorporated by reference in their entirety). In yet another non-limiting example, the therapeutic nanoparticle is a stealth nanoparticle or a target-specific stealth nanoparticle as described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety.

In some embodiments, the therapeutic nanoparticle may comprise a multiblock copolymer (see e.g., U.S. Pat. Nos. 8,263,665 and 8,287,910 and U.S. Patent Pub. No. US20130195987, the contents of each of which are herein incorporated by reference in their entirety).

In yet another non-limiting example, the lipid nanoparticle comprises the block copolymer PEG-PLGA-PEG (see e.g., the thermosensitive hydrogel (PEG-PLGA-PEG) was used as a TGF-beta1 gene delivery vehicle in Lee et al. Thermosensitive Hydrogel as a Tgf-ß1 Gene Delivery Vehicle Enhances Diabetic Wound Healing. Pharmaceutical Research, 2003 20(12): 1995-2000; as a controlled gene delivery system in Li et al. Controlled Gene Delivery System Based on Thermosensitive Biodegradable Hydrogel. Pharmaceutical Research 2003 20(6):884-888; and Chang et al., Non-ionic amphiphilic biodegradable PEG-PLGA-PEG copolymer enhances gene delivery efficiency in rat skeletal muscle. J Controlled Release. 2007 118:245-253, the contents of each of which are herein incorporated by reference in their entirety). The RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in lipid nanoparticles comprising the PEG-PLGA-PEG block copolymer.

In some embodiments, the therapeutic nanoparticle may comprise a multiblock copolymer (see e.g., U.S. Pat. Nos. 8,263,665 and 8,287,910 and U.S. Patent Pub. No. US20130195987, the contents of each of which are herein incorporated by reference in their entirety).

In some embodiments, the block copolymers described herein may be included in a polyion complex comprising a non-polymeric micelle and the block copolymer. (see e.g., U.S. Publication No. 20120076836, the contents of which are herein incorporated by reference in their entirety).

In some embodiments, the therapeutic nanoparticle may comprise at least one acrylic polymer. Acrylic polymers include but are not limited to, acrylic acid, methacrylic acid,

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acrylic acid and methacrylic acid copolymers, methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl methacrylate, amino alkyl methacrylate copolymer, poly (acrylic acid), poly(methacrylic acid), polycyanoacrylates and combinations thereof.

In some embodiments, the therapeutic nanoparticles may comprise at least one poly(vinyl ester) polymer. The poly (vinyl ester) polymer may be a copolymer such as a random copolymer. As a non-limiting example, the random copolymer may have a structure such as those described in Inter- 10 national Application No. WO2013032829 or U.S. Patent Publication No US20130121954, the contents of each of which are herein incorporated by reference in their entirety. In some embodiments, the poly(vinyl ester) polymers may be conjugated to the polynucleotides described herein.

In some embodiments, the therapeutic nanoparticle may comprise at least one diblock copolymer. The diblock copolymer may be, but it not limited to, a poly(lactic) acid-poly (ethylene)glycol copolymer (see, e.g., International Patent Publication No. WO2013044219, the contents of which are 20 herein incorporated by reference in their entirety).

As a non-limiting example, the therapeutic nanoparticle may be used to treat cancer (see International publication No. WO2013044219, the contents of which are herein incorporated by reference in their entirety).

In some embodiments, the therapeutic nanoparticles may comprise at least one cationic polymer described herein and/or known in the art.

In some embodiments, the therapeutic nanoparticles may comprise at least one amine-containing polymer such as, but 30 not limited to polylysine, polyethylene imine, poly(amidoamine) dendrimers, poly(beta-amino esters) (see, e.g., U.S. Pat. No. 8,287,849, the contents of which are herein incorporated by reference in their entirety) and combinations thereof.

In some embodiments, the nanoparticles described herein may comprise an amine cationic lipid such as those described in International Patent Application No. WO2013059496, the contents of which are herein incorporated by reference in their entirety. In some embodiments, 40 the cationic lipids may have an amino-amine or an aminoamide moiety.

In some embodiments, the therapeutic nanoparticles may comprise at least one degradable polyester which may contain polycationic side chains. Degradeable polyesters 45 include, but are not limited to, poly(serine ester), poly(Llactide-co-L-lysine), poly(4-hydroxy-L-proline ester), and combinations thereof. In some embodiments, the degradable polyesters may include a PEG conjugation to form a PEGylated polymer. 50

In some embodiments, the synthetic nanocarriers may contain an immunostimulatory agent to enhance the immune response from delivery of the synthetic nanocarrier. As a non-limiting example, the synthetic nanocarrier may comprise a Th1 immunostimulatory agent, which may enhance 55 a Th1-based response of the immune system (see International Pub No. WO2010123569 and U.S. Publication No. US20110223201, the contents of each of which are herein incorporated by reference in their entirety).

In some embodiments, the synthetic nanocarriers may be 60 formulated for targeted release. In some embodiments, the synthetic nanocarrier is formulated to release the polynucleotides at a specified pH and/or after a desired time interval. As a non-limiting example, the synthetic nanoparticle may be formulated to release the RNA (e.g., mRNA) vaccines 65 after 24 hours and/or at a pH of 4.5 (see International Publication Nos. WO2010138193 and WO2010138194 and

US Pub Nos. US20110020388 and US20110027217, each of which is herein incorporated by reference in their entireties).

In some embodiments, the synthetic nanocarriers may be formulated for controlled and/or sustained release of the polynucleotides described herein. As a non-limiting example, the synthetic nanocarriers for sustained release may be formulated by methods known in the art, described herein and/or as described in International Pub No. WO2010138192 and US Pub No. 20100303850, each of which is herein incorporated by reference in their entirety.

In some embodiments, the RNA (e.g., mRNA) vaccine may be formulated for controlled and/or sustained release wherein the formulation comprises at least one polymer that is a crystalline side chain (CYSC) polymer. CYSC polymers are described in U.S. Pat. No. 8,399,007, herein incorporated by reference in its entirety.

In some embodiments, the synthetic nanocarrier may be formulated for use as a vaccine. In some embodiments, the synthetic nanocarrier may encapsulate at least one polynucleotide which encode at least one antigen. As a nonlimiting example, the synthetic nanocarrier may include at least one antigen and an excipient for a vaccine dosage form (see International Publication No. WO2011150264 and U.S. Publication No. US20110293723, the contents of each of which are herein incorporated by reference in their entirety). As another non-limiting example, a vaccine dosage form may include at least two synthetic nanocarriers with the same or different antigens and an excipient (see International Publication No. WO2011150249 and U.S. Publication No. US20110293701, the contents of each of which are herein incorporated by reference in their entirety). The vaccine dosage form may be selected by methods described herein, known in the art and/or described in International Publica-35 tion No. WO2011150258 and U.S. Publication No. US20120027806, the contents of each of which are herein incorporated by reference in their entirety).

In some embodiments, the synthetic nanocarrier may comprise at least one polynucleotide which encodes at least one adjuvant. As non-limiting example, the adjuvant may comprise dimethyldioctadecylammonium-bromide, dimethyldioctadecylammonium-chloride, dimethyldioctadecylammonium-phosphate or dimethyldioctadecylammonium-acetate (DDA) and an apolar fraction or part of said apolar fraction of a total lipid extract of a mycobacterium (see, e.g., U.S. Pat. No. 8,241,610, the content of which is herein incorporated by reference in its entirety). In some embodiments, the synthetic nanocarrier may comprise at least one polynucleotide and an adjuvant. As a non-limiting example, the synthetic nanocarrier comprising and adjuvant may be formulated by the methods described in International Publication No. WO2011150240 and U.S. Publication No. US20110293700, the contents of each of which are herein incorporated by reference in their entirety.

In some embodiments, the synthetic nanocarrier may encapsulate at least one polynucleotide that encodes a peptide, fragment or region from a virus. As a non-limiting example, the synthetic nanocarrier may include, but is not limited to, any of the nanocarriers described in International WO2012024621, WO201202629. Publication No. WO2012024632 and U.S. Publication No. US20120064110, US20120058153 and US20120058154, the contents of each of which are herein incorporated by reference in their entirety.

In some embodiments, the synthetic nanocarrier may be coupled to a polynucleotide which may be able to trigger a humoral and/or cytotoxic T lymphocyte (CTL) response

(see, e.g., International Publication No. WO2013019669, the contents of which are herein incorporated by reference in their entirety).

In some embodiments, the RNA (e.g., mRNA) vaccine may be encapsulated in, linked to and/or associated with 5 zwitterionic lipids. Non-limiting examples of zwitterionic lipids and methods of using zwitterionic lipids are described in U.S. Patent Publication No. US20130216607, the contents of which are herein incorporated by reference in their entirety.

In some aspects, the zwitterionic lipids may be used in the liposomes and lipid nanoparticles described herein.

In some embodiments, the RNA (e.g., mRNA) vaccine may be formulated in colloid nanocarriers as described in U.S. Patent Publication No. US20130197100, the contents 15 of which are herein incorporated by reference in their entirety.

In some embodiments, the nanoparticle may be optimized for oral administration. The nanoparticle may comprise at least one cationic biopolymer such as, but not limited to, 20 chitosan or a derivative thereof. As a non-limiting example, the nanoparticle may be formulated by the methods described in U.S. Publication No. 20120282343, the contents of which are herein incorporated by reference in their entirety. 25

In some embodiments, LNPs comprise the lipid KL52 (an amino-lipid disclosed in U.S. Application Publication No. 2012/0295832, the contents of which are herein incorporated by reference in their entirety. Activity and/or safety (as measured by examining one or more of ALT/AST, white 30 blood cell count and cytokine induction, for example) of LNP administration may be improved by incorporation of such lipids. LNPs comprising KL52 may be administered intravenously and/or in one or more doses. In some embodiments, administration of LNPs comprising KL52 results in 35 equal or improved mRNA and/or protein expression as compared to LNPs comprising MC3.

In some embodiments, RNA (e.g., mRNA) vaccine may be delivered using smaller LNPs. Such particles may comprise a diameter from below 0.1 um up to 100 nm such as, 40 but not limited to, less than 0.1 um, less than 1.0 um, less than 5 um, less than 10 um, less than 15 um, less than 20 um, less than 25 um, less than 30 um, less than 35 um, less than 40 um, less than 50 um, less than 55 um, less than 60 um, less than 65 um, less than 70 um, less than 75 um, less than 45 80 um, less than 85 um, less than 90 um, less than 95 um, less than 100 um, less than 125 um, less than 150 um, less than 175 um, less than 200 um, less than 225 um, less than 250 um, less than 275 um, less than 300 um, less than 325 um, less than 350 um, less than 375 um, less than 400 um, 50 less than 425 um, less than 450 um, less than 475 um, less than 500 um, less than 525 um, less than 550 um, less than 575 um, less than 600 um, less than 625 um, less than 650 um, less than 675 um, less than 700 um, less than 725 um, less than 750 um, less than 775 um, less than 800 um, less 55 than 825 um, less than 850 um, less than 875 um, less than 900 um, less than 925 um, less than 950 um, less than 975 um, or less than 1000 um.

In some embodiments, RNA (e.g., mRNA) vaccines may be delivered using smaller LNPs, which may comprise a 60 diameter from about 1 nm to about 100 nm, from about 1 nm to about 10 nm, about 1 nm to about 20 nm, from about 1 nm to about 30 nm, from about 1 nm to about 40 nm, from about 1 nm to about 50 nm, from about 1 nm to about 60 nm, from about 1 nm to about 70 nm, from about 1 nm to about 65 80 nm, from about 1 nm to about 90 nm, from about 5 nm to about from 100 nm, from about 5 nm to about 10 nm,

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about 5 nm to about 20 nm, from about 5 nm to about 30 nm, from about 5 nm to about 40 nm, from about 5 nm to about 50 nm, from about 5 nm to about 60 nm, from about 5 nm to about 70 nm, from about 5 nm to about 80 nm, from about 5 nm to about 90 nm, about 10 to about 50 nm, from about 20 to about 50 nm, from about 30 to about 50 nm, from about 40 to about 50 nm, from about 20 to about 60 nm, from about 30 to about 60 nm, from about 40 to about 60 nm, from about 20 to about 70 nm, from about 30 to about 70 nm, from about 40 to about 70 nm, from about 50 to about 70 nm, from about 60 to about 70 nm, from about 20 to about 80 nm, from about 30 to about 80 nm, from about 40 to about 80 nm, from about 50 to about 80 nm, from about 60 to about 80 nm, from about 20 to about 90 nm, from about 30 to about 90 nm, from about 40 to about 90 nm, from about 50 to about 90 nm, from about 60 to about 90 nm and/or from about 70 to about 90 nm.

In some embodiments, such LNPs are synthesized using methods comprising microfluidic mixers. Examples of microfluidic mixers may include, but are not limited to, a slit interdigital micromixer including, but not limited to those manufactured by Microinnova (Allerheiligen bei Wildon, Austria) and/or a staggered herringbone micromixer (SHM) (Zhigaltsev, I. V. et al., Bottom-up design and synthesis of limit size lipid nanoparticle systems with aqueous and triglyceride cores using millisecond microfluidic mixing have been published (Langmuir. 2012. 28:3633-40; Belliveau, N. M. et al., Microfluidic synthesis of highly potent limit-size lipid nanoparticles for in vivo delivery of siRNA. Molecular Therapy-Nucleic Acids. 2012. 1:e37; Chen, D. et al., Rapid discovery of potent siRNA-containing lipid nanoparticles enabled by controlled microfluidic formulation. J Am Chem Soc. 2012. 134(16):6948-51, the contents of each of which are herein incorporated by reference in their entirety). In some embodiments, methods of LNP generation comprising SHM, further comprise the mixing of at least two input streams wherein mixing occurs by microstructureinduced chaotic advection (MICA). According to this method, fluid streams flow through channels present in a herringbone pattern causing rotational flow and folding the fluids around each other. This method may also comprise a surface for fluid mixing wherein the surface changes orientations during fluid cycling. Methods of generating LNPs using SHM include those disclosed in U.S. Application Publication Nos. 2004/0262223 and 2012/0276209, the contents of each of which are herein incorporated by reference in their entirety.

In some embodiments, the RNA (e.g., mRNA) vaccine of the present disclosure may be formulated in lipid nanoparticles created using a micromixer such as, but not limited to, a Slit Interdigital Microstructured Mixer (SIMM-V2) or a Standard Slit Interdigital Micro Mixer (SSIMM) or Caterpillar (CPMM) or Impinging-jet (IJMM) from the Institut fiir Mikrotechnik Mainz GmbH, Mainz Germany).

In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in lipid nanoparticles created using microfluidic technology (see, e.g., Whitesides, George M. The Origins and the Future of Microfluidics. Nature, 2006 442: 368-373; and Abraham et al. Chaotic Mixer for Microchannels. Science, 2002 295: 647-651; each of which is herein incorporated by reference in its entirety). As a non-limiting example, controlled microfluidic formulation includes a passive method for mixing streams of steady pressure-driven flows in micro channels at a low Reynolds number (see, e.g., Abraham et al. Chaotic Mixer for Microchannels. Science, 2002 295: 647-651, the contents of which are herein incorporated by reference in their entirety).

In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in lipid nanoparticles created using a micromixer chip such as, but not limited to, those from Harvard Apparatus (Holliston, Mass.) or Dolomite Microfluidics (Royston, UK). A micromixer 5 chip can be used for rapid mixing of two or more fluid streams with a split and recombine mechanism.

In some embodiments, the RNA (e.g., mRNA) vaccines of the disclosure may be formulated for delivery using the drug encapsulating microspheres described in International Pat-10 ent Publication No. WO2013063468 or U.S. Pat. No. 8,440, 614, the contents of each of which are herein incorporated by reference in their entirety. The microspheres may comprise a compound of the formula (I), (II), (II), (IV), (V) or (VI) as described in International Patent Publication No. 15 WO2013063468, the contents of which are herein incorporated by reference in their entirety. In some embodiments, the amino acid, peptide, polypeptide, lipids (APPL) are useful in delivering the RNA (e.g., mRNA) vaccines of the disclosure to cells (see International Patent Publication No. 20 WO2013063468, the contents of which are herein incorporated by reference in their entirety.

In some embodiments, the RNA (e.g., mRNA) vaccines of the disclosure may be formulated in lipid nanoparticles having a diameter from about 10 to about 100 nm such as, 25 but not limited to, about 10 to about 20 nm, about 10 to about 30 nm, about 10 to about 40 nm, about 10 to about 50 nm, about 10 to about 60 nm, about 10 to about 70 nm, about 10 to about 80 nm, about 10 to about 90 nm, about 20 to about 30 nm, about 20 to about 40 nm, about 20 to about 50 nm, 30 about 20 to about 60 nm, about 20 to about 70 nm, about 20 to about 80 nm, about 20 to about 90 nm, about 20 to about 100 nm, about 30 to about 40 nm, about 30 to about 50 nm, about 30 to about 60 nm, about 30 to about 70 nm, about 30 to about 80 nm, about 30 to about 90 nm, about 30 to about 35 100 nm, about 40 to about 50 nm, about 40 to about 60 nm, about 40 to about 70 nm, about 40 to about 80 nm, about 40 to about 90 nm, about 40 to about 100 nm, about 50 to about 60 nm, about 50 to about 70 nm about 50 to about 80 nm, about 50 to about 90 nm, about 50 to about 100 nm, about 40 60 to about 70 nm, about 60 to about 80 nm, about 60 to about 90 nm, about 60 to about 100 nm, about 70 to about 80 nm, about 70 to about 90 nm, about 70 to about 100 nm, about 80 to about 90 nm, about 80 to about 100 nm and/or about 90 to about 100 nm.

In some embodiments, the lipid nanoparticles may have a diameter from about 10 to 500 nm.

In some embodiments, the lipid nanoparticle may have a diameter greater than 100 nm, greater than 150 nm, greater than 200 nm, greater than 250 nm, greater than 300 nm, 50 greater than 350 nm, greater than 400 nm, greater than 450 nm, greater than 500 nm, greater than 550 nm, greater than 600 nm, greater than 650 nm, greater than 750 nm, greater than 550 nm, greater 550 nm, greater 550 nm, greater 550 nm, greater 550 nm, grea

In some embodiments, the lipid nanoparticle may be a limit size lipid nanoparticle described in International Patent Publication No. WO2013059922, the contents of which are herein incorporated by reference in their entirety. The limit 60 size lipid nanoparticle may comprise a lipid bilayer surrounding an aqueous core or a hydrophobic core; where the lipid bilayer may comprise a phospholipid such as, but not limited to, diacylphosphatidylcholine, a diacylphosphatidylethanolamine, a ceramide, a sphingomyelin, a dihy- 65 drosphingomyelin, a cephalin, a cerebroside, a C8-C20 fatty acid diacylphophatidylcholine, and 1-palmitoyl-2-oleoyl

phosphatidylcholine (POPC). In some embodiments, the limit size lipid nanoparticle may comprise a polyethylene glycol-lipid such as, but not limited to, DLPE-PEG, DMPE-PEG, DPPC-PEG and DSPE-PEG.

In some embodiments, the RNA (e.g., mRNA) vaccines may be delivered, localized and/or concentrated in a specific location using the delivery methods described in International Patent Publication No. WO2013063530, the contents of which are herein incorporated by reference in their entirety. As a non-limiting example, a subject may be administered an empty polymeric particle prior to, simultaneously with or after delivering the RNA (e.g., mRNA) vaccines to the subject. The empty polymeric particle undergoes a change in volume once in contact with the subject and becomes lodged, embedded, immobilized or entrapped at a specific location in the subject.

In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in an active substance release system (see, e.g., U.S. Patent Publication No. US20130102545, the contents of which are herein incorporated by reference in their entirety). The active substance release system may comprise 1) at least one nanoparticle bonded to an oligonucleotide inhibitor strand which is hybridized with a catalytically active nucleic acid and 2) a compound bonded to at least one substrate molecule bonded to a therapeutically active substance (e.g., polynucleotides described herein), where the therapeutically active substance is released by the cleavage of the substrate molecule by the catalytically active nucleic acid.

In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a nanoparticle comprising an inner core comprising a non-cellular material and an outer surface comprising a cellular membrane. The cellular membrane may be derived from a cell or a membrane derived from a virus. As a non-limiting example, the nanoparticle may be made by the methods described in International Patent Publication No. WO2013052167, the contents of which are herein incorporated by reference in their entirety. As another non-limiting example, the nanoparticle described in International Patent Publication No. WO2013052167, the contents of which are herein incorporated by reference in their entirety, may be used to deliver the RNA (e.g., mRNA) vaccines described herein.

In some embodiments, the RNA (e.g., mRNA) vaccines 45 may be formulated in porous nanoparticle-supported lipid bilayers (protocells). Protocells are described in International Patent Publication No. WO2013056132, the contents of which are herein incorporated by reference in their entirety.

In some embodiments, the RNA (e.g., mRNA) vaccines described herein may be formulated in polymeric nanoparticles as described in or made by the methods described in U.S. Pat. Nos. 8,420,123 and 8,518,963 and European Patent No. EP2073848B1, the contents of each of which are herein incorporated by reference in their entirety. As a non-limiting example, the polymeric nanoparticle may have a high glass transition temperature such as the nanoparticles described in U.S. Pat. No. 8,518,963, the contents of which are herein incorporated by reference in their entirety. As another non-limiting example, the polymer nanoparticle for oral and parenteral formulations may be made by the methods described in European Patent No. EP2073848B1, the contents of which are herein incorporated by reference in their entirety.

In some embodiments, the RNA (e.g., mRNA) vaccines described herein may be formulated in nanoparticles used in imaging. The nanoparticles may be liposome nanoparticles

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such as those described in U.S. Patent Publication No US20130129636, herein incorporated by reference in its entirety. As a non-limiting example, the liposome may comprise gadolinium(III)2-{4,7-bis-carboxymethyl-10-[(N, N-distearylamidomethyl-N'-amido-methyl]-1,4,7,10-tetra-azacyclododec-1-yl}-acetic acid and a neutral, fully saturated phospholipid component (see, e.g., U.S. Patent Publication No US20130129636, the contents of which are herein incorporated by reference in their entirety).

In some embodiments, the nanoparticles which may be used in the present disclosure are formed by the methods described in U.S. Patent Application No. US20130130348, the contents of which are herein incorporated by reference in their entirety.

The nanoparticles of the present disclosure may further include nutrients such as, but not limited to, those which deficiencies can lead to health hazards from anemia to neural tube defects (see, e.g., the nanoparticles described in International Patent Publication No WO2013072929, the con-20 tents of which are herein incorporated by reference in their entirety). As a non-limiting example, the nutrient may be iron in the form of ferrous, ferric salts or elemental iron, iodine, folic acid, vitamins or micronutrients.

In some embodiments, the RNA (e.g., mRNA) vaccines of 25 the present disclosure may be formulated in a swellable nanoparticle. The swellable nanoparticle may be, but is not limited to, those described in U.S. Pat. No. 8,440,231, the contents of which are herein incorporated by reference in their entirety. As a non-limiting embodiment, the swellable 30 nanoparticle may be used for delivery of the RNA (e.g., mRNA) vaccines of the present disclosure to the pulmonary system (see, e.g., U.S. Pat. No. 8,440,231, the contents of which are herein incorporated by reference in their entirety).

The RNA (e.g., mRNA) vaccines of the present disclosure 35 may be formulated in polyanhydride nanoparticles such as, but not limited to, those described in U.S. Pat. No. 8,449, 916, the contents of which are herein incorporated by reference in their entirety.

The nanoparticles and microparticles of the present dis- 40 closure may be geometrically engineered to modulate macrophage and/or the immune response. In some embodiments, the geometrically engineered particles may have varied shapes, sizes and/or surface charges in order to incorporated the polynucleotides of the present disclosure for targeted 45 delivery such as, but not limited to, pulmonary delivery (see, e.g., International Publication No WO2013082111, the contents of which are herein incorporated by reference in their entirety). Other physical features the geometrically engineering particles may have include, but are not limited to, 50 fenestrations, angled arms, asymmetry and surface roughness, charge which can alter the interactions with cells and tissues. As a non-limiting example, nanoparticles of the present disclosure may be made by the methods described in International Publication No WO2013082111, the contents 55 of which are herein incorporated by reference in their entirety.

In some embodiments, the nanoparticles of the present disclosure may be water soluble nanoparticles such as, but not limited to, those described in International Publication 60 No. WO2013090601, the contents of which are herein incorporated by reference in their entirety. The nanoparticles may be inorganic nanoparticles which have a compact and zwitterionic ligand in order to exhibit good water solubility. The nanoparticles may also have small hydrodynamic diam-65 eters (HD), stability with respect to time, pH, and salinity and a low level of non-specific protein binding.

In some embodiments the nanoparticles of the present disclosure may be developed by the methods described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety.

In some embodiments, the nanoparticles of the present disclosure are stealth nanoparticles or target-specific stealth nanoparticles such as, but not limited to, those described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety. The nanoparticles of the present disclosure may be made by the methods described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety.

In some embodiments, the stealth or target-specific stealth nanoparticles may comprise a polymeric matrix. The polymeric matrix may comprise two or more polymers such as, but not limited to, polyethylenes, polycarbonates, polyanhydrides, polyhydroxyacids, polypropylfumerates, polycaprolactones, polyamides, polyacetals, polyethers, polyesters, poly(orthoesters), polycyanoacrylates, polyvinyl alcohols, polyurethanes, polyphosphazenes, polyacrylates, polymethacrylates, polycyanoacrylates, polystyrenes, polyamines, polyesters, polyanhydrides, polyethers, polyurethanes, polymethacrylates, polyacrylates, polyurethanes, polymethacrylates, polyacrylates, polycyanoacrylates, polycyanoacrylates, polycyanoacrylates or combinations thereof.

In some embodiments, the nanoparticle may be a nanoparticle-nucleic acid hybrid structure having a high density nucleic acid layer. As a non-limiting example, the nanoparticle-nucleic acid hybrid structure may made by the methods described in U.S. Patent Publication No. US20130171646, the contents of which are herein incorporated by reference in their entirety. The nanoparticle may comprise a nucleic acid such as, but not limited to, polynucleotides described herein and/or known in the art.

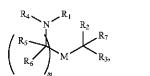
At least one of the nanoparticles of the present disclosure may be embedded in in the core a nanostructure or coated with a low density porous 3-D structure or coating which is capable of carrying or associating with at least one payload within or on the surface of the nanostructure. Non-limiting examples of the nanostructures comprising at least one nanoparticle are described in International Patent Publication No. WO2013123523, the contents of which are herein incorporated by reference in their entirety.

In some embodiments the RNA (e.g., mRNA) vaccine may be associated with a cationic or polycationic compounds, including protamine, nucleoline, spermine or spermidine, or other cationic peptides or proteins, such as poly-L-lysine (PLL), polyarginine, basic polypeptides, cell penetrating peptides (CPPs), including HIV-binding peptides, HIV-1 Tat (HIV), Tat-derived peptides, Penetratin, VP²² derived or analog peptides, Pestivirus Erns, HSV, VP²² (Herpes simplex), MAP, KALA or protein transduction domains (PTDs), PpT620, prolin-rich peptides, arginine-rich peptides, lysine-rich peptides, MPG-peptide(s), Pep-1, L-oligomers, Calcitonin peptide(s), Antennapedia-derived peptides (particularly from Drosophila antennapedia), pAntp, pIsl, FGF, Lactoferrin, Transportan, Buforin-2, Bac715-24, SynB, SynB(1), pVEC, hCT-derived peptides, SAP, histones, cationic polysaccharides, for example chitosan, polybrene, cationic polymers, e.g. polyethyleneimine (PEI), cationic lipids, e.g. DOTMA: [1-(2,3-sioleyloxy) propyl)]-N,N,N-trimethylammonium chloride, DMRIE, di-C14-amidine, DOTIM, SAINT, DC-Chol, BGTC, CTAP, DOPC, DODAP, DOPE: Dioleyl phosphatidylethanolamine, DOSPA, DODAB, DOIC, DMEPC, DOGS: Dioctadecylamidoglicylspermin, DIMRI: Dimyristooxypropyl

dimethyl hydroxyethyl ammonium bromide, DOTAP: dioleoyloxy-3-(trimethylammonio)propane, DC-6-14: O,Oditetradecanoyl-N-.alpha.-trimethylammonioacetyl)diethanolamine chloride, CLIP 1: rac-[(2,3-dioctadecyloxypropyl) (2-hydroxyethyl)]-dimethylammonium chloride, CLIP6: 5 rac-[2(2,3-dihexadecvloxvpropyloxymethyloxy)ethyl]trimethylammonium, CLIP9: rac-[2(2,3-dihexadecvloxypropyloxysuccinyloxy)ethyl]-trimethylammonium, oligofectamine, or cationic or polycationic polymers, e.g. modified polyaminoacids, such as beta-aminoacid-polymers or reversed polyamides, etc., modified polyethylenes, such as PVP (poly(N-ethyl-4-vinylpyridinium bromide)), etc., modified acrylates, such as pDMAEMA (poly(dimethylaminoethyl methylacrylate)), etc., modified amidoamines such as pAMAM (poly(amidoamine)), etc., modified polybetaminoester (PBAE), such as diamine end modified 1,4 butanediol diacrylate-co-5-amino-1-pentanol polymers, etc., dendrimers, such as polypropylamine dendrimers or pAMAM based dendrimers, etc., polyimine(s), such as PEI: 20 poly(ethyleneimine), poly(propyleneimine), etc., polyallylamine, sugar backbone based polymers, such as cyclodextrin based polymers, dextran based polymers, chitosan, etc., silan backbone based polymers, such as PMOXA-PDMS copolymers, etc., blockpolymers consisting of a combina- 25 tion of one or more cationic blocks (e.g. selected from a cationic polymer as mentioned above) and of one or more hydrophilic or hydrophobic blocks (e.g. polyethyleneglycole), etc.

In other embodiments the RNA (e.g., mRNA) vaccine is not associated with a cationic or polycationic compounds.

In some embodiments, a nanoparticle comprises compounds of Formula (I):



or a salt or isomer thereof, wherein:

 R_1 is selected from the group consisting of C_{5-30} alkyl, 45 C₅₋₂₀ alkenyl, -R*YR", -YR", and -R"M'R';

 \mathbf{R}_2 and \mathbf{R}_3 are independently selected from the group consisting of H, C_{1-14} alkyl, C_{2-14} alkenyl, -R*YR", -YR", and -R*OR", or R_2 and R_3 , together with the atom to which they are attached, form a heterocycle or carbocycle; 50 R₄ is selected from the group consisting of a C₃₋₆ carbo-

cycle, $-(CH_2)_n Q$, $-(CH_2)_n CHQR$,

-CHQR, --CQ(R)₂, and unsubstituted C₁₋₆ alkyl, where Q is selected from a carbocycle, heterocycle, -OR, $-O(CH_2)_n N(R)_2$, -C(O)OR, -OC(O)R, —CX₃, 55 $-CX_2H, -CXH_2, -CN, -N(R)_2, -C(O)N(R)_2, -N(R)$ C(O)R, $-N(R)S(O)_2R$, $-N(R)C(O)N(R)_2$, -N(R)C(S)N $(R)_{2}, -N(R)R_{8}, -O(CH_{2})_{\mu}OR, -N(R)C(=NR_{9})N(R)_{2},$ $-N(R)C(=CHR_9)N(R)_2$, $-OC(O)N(R)_2$, -N(R)C(O)OR, -N(OR)C(O)R, $-N(OR)S(O)_2R$, -N(OR)C(O)OR, 60 ing of C_{1-3} alkyl, C_{2-3} alkenyl, and H; $-N(OR)C(O)N(R)_2$, $-N(OR)C(S)N(R)_2$, -N(OR)C $(=NR_9)N(R)_2, -N(OR)C(=CHR_9)N(R)_2, -C(=NR_9)N(R)_2$ $(R)_2$, $-C(=NR_9)R$, -C(O)N(R)OR, and $-C(R)N(R)_2C$ (O)OR, and each n is independently selected from 1, 2, 3, 4, and 5; 65

each R5 is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

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each R₆ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

M and M' are independently selected from -C(O)O, -OC(O), -C(O)N(R'),

-N(R')C(O), -C(O), -C(S), -C(S)S, -SC(S)--, --CH(OH)--, --P(O)(OR')O--, --S(O)₂--, --S--

S—, an aryl group, and a heteroaryl group; R_7 is selected from the group consisting of $\rm C_{1-3}$ alkyl, $\rm C_{2-3}$

alkenyl, and H; R₈ is selected from the group consisting of C_{3-6} carbocycle and heterocycle;

 R_9 is selected from the group consisting of H, CN, NO₂, C_{1-6} alkyl, -OR, $-S(O)_2R$, $-S(O)_2N(R)_2$, C_{2-6} alkenyl, C_{3-6} carbocycle and heterocycle;

each R is independently selected from the group consist-15 ing of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R' is independently selected from the group consisting of C₁₋₁₈ alkyl, C₂₋₁₈ alkenyl, —R*YR", —YR", and H; each R" is independently selected from the group con-

sisting of C₃₋₁₄ alkyl and C₃₋₁₄ alkenyl; each R* is independently selected from the group consisting of C₁₋₁₂ alkyl and C₂₋₁₂ alkenyl;

each Y is independently a C_{3-6} carbocycle;

each X is independently selected from the group consisting of F, Cl, Br, and I; and

m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13.

In some embodiments, a subset of compounds of Formula (I) includes those in which when R_4 is $-(CH_2)_n Q$, $-(CH_2)_n$ CHQR, —CHQR, or $-CQ(R)_2$, then (i) Q is not $-N(R)_2$ when n is 1, 2, 3, 4 or 5, or (ii) Q is not 5, 6, or 7-membered heterocycloalkyl when n is 1 or 2.

In some embodiments, another subset of compounds of Formula (I) includes those in which

 $R_{\rm 1}$ is selected from the group consisting of $C_{\rm 5-30}$ alkyl, C₅₋₂₀ alkenyl, ---R*YR", ---YR", and ----R"M'R';

 R_2 and R_3 are independently selected from the group consisting of H, C_{1-14} alkyl, C_{2-14} alkenyl, -R*YR", -YR", and -R*OR", or R_2 and R_3 , together with the atom to which they are attached, form a heterocycle or carbocycle; R_4 is selected from the group consisting of a C_{3-6} carbo-40 cycle, $-(CH_2)_n Q$, $-(CH_2)_n CHQR$,

-CHQR, -CQ(R)2, and unsubstituted C1-6 alkyl, where Q is selected from a C₃₋₆ carbocycle, a 5- to 14-membered heteroaryl having one or more heteroatoms selected from N, O, and S, -OR,

 $\begin{array}{l} - O(CH_2)N(R)_2, - C(O)OR, - OC(O)R, - CX_3, - CX_2H, \\ - CXH_2, - CN, - C(O)N(R)_2, - N(R)C(O)R, - N(R)S \end{array}$ $(O)_2 R$, $-N(R)C(O)N(R)_2$, $-N(R)C(S)N(R)_2$, $-CRN(R)_2$ $C(O)OR, -N(R)R_8, -O(CH_2)_nOR, -N(R)C(=NR_9)N$ $(R)_{2}, -N(R)C(=CHR_{9})N(R)_{2}, -OC(O)N(R)_{2}, -N(R)C(R)C(R)_{2}, -N(R)C(R)C(R)C(R)_{2}, -N(R)C(R)C(R)C(R)_{2}, -N(R)C(R)C(R)C(R)_{2}, -N(R)C(R)C(R)C(R)C(R)_{2}, -N(R)C(R)C(R)C(R)C(R)C(R))$ $(O)OR, -N(OR)C(O)R, -N(OR)S(O)_2R, -N(OR)C(O)$ $(=NR_9)N(R)_2, -N(OR)C(=CHR_9)N(R)_2, -C(=NR_9)N(R)_2$ $(R)_2$, $-C(=NR_9)R$, -C(O)N(R)O R, and a 5- to 14-membered heterocycloalkyl having one or more heteroatoms selected from N, O, and S which is substituted with one or more substituents selected from oxo (=O), OH, amino, mono- or di-alkylamino, and $\mathrm{C}_{1\text{-}3}$ alkyl, and each n is independently selected from 1, 2, 3, 4, and 5;

each R5 is independently selected from the group consist-

each R₆ is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

M and M' are independently selected from -C(O)O-, -OC(O), -C(O)N(R'), -N(R')C(O), -C(O), -C(S), -C(S)S, -SC(S), -CH(OH), -P(O)(OR')O-, $-S(O)_2$, -S-S-, an aryl group, and a heteroaryl group;

(I)

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R7 is selected from the group consisting of C1-3 alkyl, C2-3 alkenyl, and H;

 R_8 is selected from the group consisting of C_{3-6} carbocycle and heterocycle;

 R_9 is selected from the group consisting of H, CN, NO₂, ⁵ C_{1-6} alkyl, -OR, $-S(O)_2R$, $-S(O)_2N(R)_2$, C_{2-6} alkenyl, C3-6 carbocycle and heterocycle;

each R is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

each R' is independently selected from the group consisting of C₁₋₁₈ alkyl, C₂₋₁₈ alkenyl, -R*YR", -YR", and H;

each R" is independently selected from the group consisting of C₃₋₁₄ alkyl and C₃₋₁₄ alkenyl;

each R* is independently selected from the group con- $_{15}$ sisting of C_{1-12} alkyl and C_{2-12} alkenyl;

each Y is independently a C_{3-6} carbocycle;

each X is independently selected from the group consisting of F, Cl, Br, and I; and

m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13, or salts or isomers thereof.

In some embodiments, another subset of compounds of Formula (I) includes those in which

 $R_{\rm 1}$ is selected from the group consisting of $C_{\text{5-30}}$ alkyl, C₅₋₂₀ alkenyl, —R*YR", —YR", and —R"M'R';

R₂ and R₃ are independently selected from the group consisting of H, C_{1-14} alkyl, C_{2-14} alkenyl, -R*YR", -YR", and -R*OR", or R_2 and R_3 , together with the atom

to which they are attached, form a heterocycle or carbocycle; R_{Δ} is selected from the group consisting of a C_{3-6} carbo- 30

cycle, $-(CH_2)_n Q$, $-(CH_2)_n CHQR$,

-CHQR, -CQ(R)₂, and unsubstituted C₁₋₆ alkyl, where Q is selected from a C_{3-6} carbocycle, a 5- to 14-membered heterocycle having one or more heteroatoms selected from N, O, and S, -OR,

 $-O(CH_2)_n N(R)_2$ -C(O)OR,-OC(O)R, ----CX,, $-CX_2H$, $-CXH_2$, -CN, $-C(O)N(R)_2$, -N(R)C(O)R,

 $-N(\overline{R})S(O)_2R$, $-N(R)C(O)N(R)_2$, $-N(R)C(S)N(R)_2$,

 $-CRN(R)_2C(O)OR, -N(R)R_8,$

 $-N(R)C(=NR_9)N(R)_2,$ $-O(CH_2)_nOR$, -N(R)C 40 -N(R)C(O)OR, $(=CHR_9)N(R)_2$ $-OC(O)N(R)_2$ $-N(OR)S(O)_2R$, -N(OR)C(O)OR, -N(OR)C(O)R $-N(OR)C(O)N(R)_2$, $-N(OR)C(S)N(R)_2,$ -N(OR)C $(=NR_9)N(R)_2, -N(OR)C(=CHR_9)N(R)_2, -C(=NR_9)R,$ C(O)N(R)OR, and $-C(=NR_9)N(R)_2$, and each n is 45 independently selected from 1, 2, 3, 4, and 5; and when Q is a 5- to 14-membered heterocycle and (i) R_4 is $-(CH_2)_n Q$ in which n is 1 or 2, or (ii) R_4 is $-(CH_2)_n$ CHQR in which n is 1, or (iii) R_4 is —CHQR, and —CQ(R)₂, then Q is either

a 5- to 14-membered heteroaryl or 8- to 14-membered 50 heterocycloalkyl;

each R₅ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R₆ is independently selected from the group consisting of C1-3 alkyl, C2-3 alkenyl, and H;

M and M' are independently selected from ---C(O)O---, -OC(O), -C(O)N(R'), -N(R')C(O), -C(O)--C(S), -C(S)S, -SC(S), -CH(OH), -P(O)(OR)O, $-S(O)_2$, -S, an aryl group, and a heteroaryl group;

R7 is selected from the group consisting of C1-3 alkyl, C2-3 alkenyl, and H;

 R_8 is selected from the group consisting of C_{3-6} carbocycle and heterocycle;

R₉ is selected from the group consisting of H, CN, NO₂, 65 ing of F, Cl, Br, and I; and C_{1-6} alkyl, -OR, $-S(O)_2R$, $-S(O)_2N(R)_2$, C_{2-6} alkenyl, C_{3-6} carbocycle and heterocycle;

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each R is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R' is independently selected from the group consisting of C₁₋₁₈ alkyl, C₂₋₁₈ alkenyl, ---R*YR", ---YR", and H;

each R" is independently selected from the group consisting of C₃₋₁₄ alkyl and C₃₋₁₄ alkenyl;

each R* is independently selected from the group consisting of C₁₋₁₂ alkyl and C₂₋₁₂ alkenyl;

each Y is independently a C3-6 carbocycle;

each X is independently selected from the group consisting of F, Cl, Br, and I; and

m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

or salts or isomers thereof. In some embodiments, another subset of compounds of

Formula (I) includes those in which

 R_1 is selected from the group consisting of C_{5-30} alkyl, C₅₋₂₀ alkenyl, —R*YR", —YR", and —R"M'R';

 R_2 and R_3 are independently selected from the group 20 consisting of H, C1-14 alkyl, C2-14 alkenyl, -R*YR",

-YR", and -R*OR", or R₂ and R₃, together with the atom to which they are attached, form a heterocycle or carbocycle;

 R_4 is selected from the group consisting of a C_{3-6} carbocycle, $-(CH_2)_n Q$, $-(CH_2)_n CHQR$,

-CHQR, $-CQ(R)_2$, and unsubstituted C_{1-6} alkyl, where Q is selected from a C3-6 carbocycle, a 5- to 14-membered heteroaryl having one or more heteroatoms selected from N, O, and S, -OR,

 $-O(CH_2)_n N(R)_2,$ —C(O)OR, -OC(O)R, ----CX3, $-CX_2H$, $-CXH_2$, -CN, $-C(O)N(R)_2$, -N(R)C(O)R, $-N(R)C(O)N(R)_2$, $-N(R)C(S)N(R)_2$, $-N(R)S(O)_2R$ $-CRN(R)_2C(O)OR, -N(R)R_8, -O(CH_2)_nOR, -N(R)C$ $(=NR_9)N(R)_2, -N(R)C(=CHR_9)N(R)_2, -OC(O)N(R)_2,$ -N(R)C(O)OR, -N(OR)C(O)R, $-N(OR)S(O)_2R$ 35 -N(OR)C(O)OR, $-N(OR)C(O)N(R)_2$, -N(OR)C(S)N $(R)_2, -N(OR)C(=NR_9)N(R)_2, -N(OR)C(=CHR_9)N(R)$ $_{2}$, $-C(=NR_{9})R$, -C(O)N(R)OR, and $-C(=NR_{9})N(R)_{2}$, and each n is independently selected from 1, 2, 3, 4, and 5; each R5 is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R₆ is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

M and M' are independently selected from -C(O)O-, -OC(O), -C(O)N(R'), -N(R')C(O), -C(O)--C(S), -C(S)S, -SC(S), -CH(OH), -P(O)(OR')O, $-S(O)_2$, -S, an aryl group, and a heteroaryl group;

 R_7 is selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

 R_8 is selected from the group consisting of C_{3-6} carbocycle and heterocycle;

 R_9 is selected from the group consisting of H, CN, NO₂, C_{1-6} alkyl, -OR, $-S(O)_2R$, $-S(O)_2N(R)_2$, C_{2-6} alkenyl, C_{3-6} carbocycle and heterocycle;

each R is independently selected from the group consisting of C1-3 alkyl, C2-3 alkenyl, and H;

each R' is independently selected from the group consisting of C₁₋₁₈ alkyl, C₂₋₁₈ alkenyl, ---R*YR", ---YR", and H; each R" is independently selected from the group con-

60 sisting of C_{3-14} alkyl and C_{3-14} alkenyl; each R* is independently selected from the group consisting of C_{1-12} alkyl and C_{2-12} alkenyl;

each Y is independently a C_{3-6} carbocycle;

each X is independently selected from the group consist-

m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13, or salts or isomers thereof.

In some embodiments, another subset of compounds of Formula (I) includes those in which

 R_1 is selected from the group consisting of C_{5-30} alkyl, C_{5-20} alkenyl, -R*YR'', -YR'', and -R''M'R';

R₂ and R₃ are independently selected from the group -5 consisting of H, C2-14 alkyl, C2-14 alkenyl, -R*YR",

-YR", and —R*OR", or R₂ and R₃, together with the atom to which they are attached, form a heterocycle or carbocycle;

 R_4 is $-(CH_2)_n Q$ or $-(CH_2)_n CHQR$, where Q is -N(R)2, and n is selected from 3, 4, and 5; 10

each R5 is independently selected from the group consisting of C1-3 alkyl, C2-3 alkenyl, and H;

each R₆ is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

M and M are independently selected from -C(O)O-, 15

-OC(O)-, -C(O)N(R')-, -N(R')C(O)-, -C(O)-, -C(S)-, -C(S)S-, -SC(S)-, -CH(OH)-, -P(O)(OR')O-, $-S(O)_2-$, -S-S-, an aryl group, and a heteroaryl group;

 R_7 is selected from the group consisting of C_{1-3} alkyl, C_{2-3} 20 alkenyl, and H;

each R is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R' is independently selected from the group consist-

ing of C_{1-18} alkyl, C_{2-18} alkenyl, -R*YR", -YR", and H; 25 each R" is independently selected from the group consisting of C_{3-14} alkyl and C_{3-14} alkenyl;

each R* is independently selected from the group consisting of C_{1-12} alkyl and C_{1-12} alkenyl;

each Y is independently a C_{3-6} carbocycle;

each X is independently selected from the group consisting of F, Cl, Br, and I; and

m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13, or salts or isomers thereof.

In some embodiments, another subset of compounds of 35 Formula (I) includes those in which

 $R_{\rm 1}$ is selected from the group consisting of $C_{\rm 5\text{-}30}$ alkyl, C_{5-20} alkenyl, -R*YR'', -YR'', and -R''M'R';

 $\overline{R_2}$ and $\overline{R_3}$ are independently selected from the group consisting of C1-14 alkyl, C2-14 alkenyl, -R*YR", -YR", 40 and -R*OR", or R_2 and R_3 , together with the atom to which

they are attached, form a heterocycle or carbocycle;

 R_4 is selected from the group consisting of $-(CH_2)_n Q$, $-(CH_2)_n CHQR$, --CHQR, and $--CQ(R)_2$, where Q is

 $-N(R)_2$, and n is selected from 1, 2, 3, 4, and 5;

each R5 is independently selected from the group consisting of C1-3 alkyl, C2-3 alkenyl, and H;

each R₆ is independently selected from the group consisting of C1-3 alkyl, C2-3 alkenyl, and H;

M and M are independently selected from ---C(O)O---, 50 -OC(O), -C(O)N(R'), -N(R')C(O), -C(O)-C(S), -C(S)S, -SC(S), -CH(OH), -P(O)(OR')O, $-S(O)_2$, -S, an aryl group, and a heteroaryl group;

 R_7 is selected from the group consisting of C_{1-3} alkyl, C_{2-3} 55 alkenyl, and H;

each R is independently selected from the group consisting of C₁₋₃ alkyl, C₂₋₃ alkenyl, and H;

each R' is independently selected from the group consist-

ing of C_{1-18} alkyl, C_{2-18} alkenyl, --R*YR", --YR", and H; 60 each R" is independently selected from the group consisting of C3-14 alkyl and C3-14 alkenyl;

each R* is independently selected from the group consisting of C_{1-12} alkyl and C_{1-12} alkenyl;

each Y is independently a C₃₋₆ carbocycle;

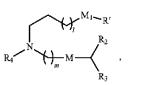
each X is independently selected from the group consist-

ing of F, Cl, Br, and I; and

m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

or salts or isomers thereof.

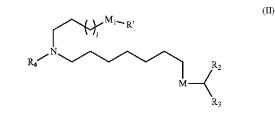
In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IA):



or a salt or isomer thereof, wherein 1 is selected from 1, 2, 3, 4, and 5; m is selected from 5, 6, 7, 8, and 9; M_1 is a bond or M'; R_4 is unsubstituted C_{1-3} alkyl, or $-(CH_2)_n Q$, in which Q is OH, --NHC(S)N(R)2, --NHC(O)N(R)2, --N(R) $C(O)R, -N(R)S(O)_2R, -N(R)R_8, -NHC(=NR_9)N(R)_2,$ $-NHC(=CHR_9)N(R)_2$, $-OC(O)N(R)_2$, -N(R)C(O)OR, heteroaryl or heterocycloalkyl; M and M' are independently selected

from -C(O)O-, -OC(O)-, -C(O)N(R')-, -P(O)(OR')O-, -S-S-, an aryl group, and a heteroaryl group; and R_2 and R_3 are independently selected from the group consisting of H, C_{1-14} alkyl, and C_{2-14} alkenyl.

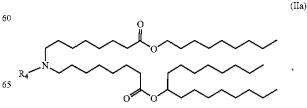
In some embodiments, a subset of compounds of Formula ₃₀ (I) includes those of Formula (II):

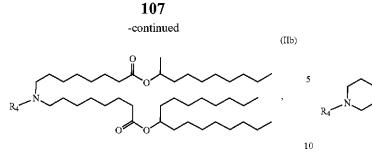


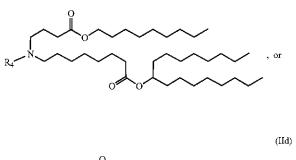
or a salt or isomer thereof, wherein 1 is selected from 1, 2, 3, 4, and 5; M_1 is a bond or M'; R_4 is unsubstituted C_{1-3} alkyl, or $-(CH_2)_n Q$, in which n is 2, 3, or 4, and Q is OH, -NHC(S)N(R)₂, -NHC(O)N(R)₂, -N(R)C(O)R, -N(R) $-N(R)R_8$, $-NHC(=NR_9)N(R)_2$, $S(O)_{2}R_{1}$ ----NHC $(=CHR_9)N(R)_2$, $-OC(O)N(R)_2$, -N(R)C(O)OR, heteroaryl or heterocycloalkyl; M and M' are independently selected

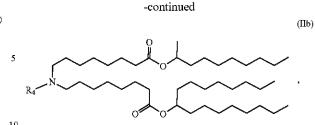
from -C(O)O, -OC(O), -C(O)N(R'), -P(O)(OR')O—, —S—S—, an aryl group, and a heteroaryl group; and R2 and R3 are independently selected from the group consisting of H, C1-14 alkyl, and C2-14 alkenyl.

In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIa), (IIb), (IIc), or (IIe):





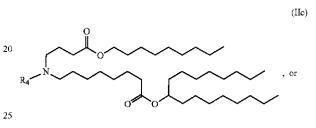




(IIc)

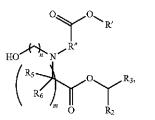
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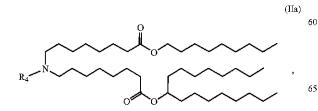
or a salt or isomer thereof, wherein R_4 is as described herein.

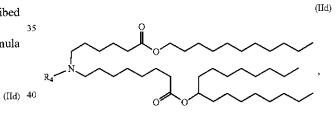
In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IId):



or a salt or isomer thereof, wherein n is 2, 3, or 4; and m, R', R", and R₂ through R₆ are as described herein. For example, each of R₂ and R₃ may be independently selected from the group consisting of C_{5-14} alkyl and C_{5-14} alkenyl.

In some embodiments, a subset of compounds of Formula ⁵⁵ (I) includes those of Formula (IIa), (IIb), (IIc), or (IIe):

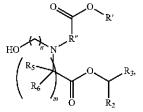




or a salt or isomer thereof, wherein R_4 is as described herein. $^{\rm 45}$

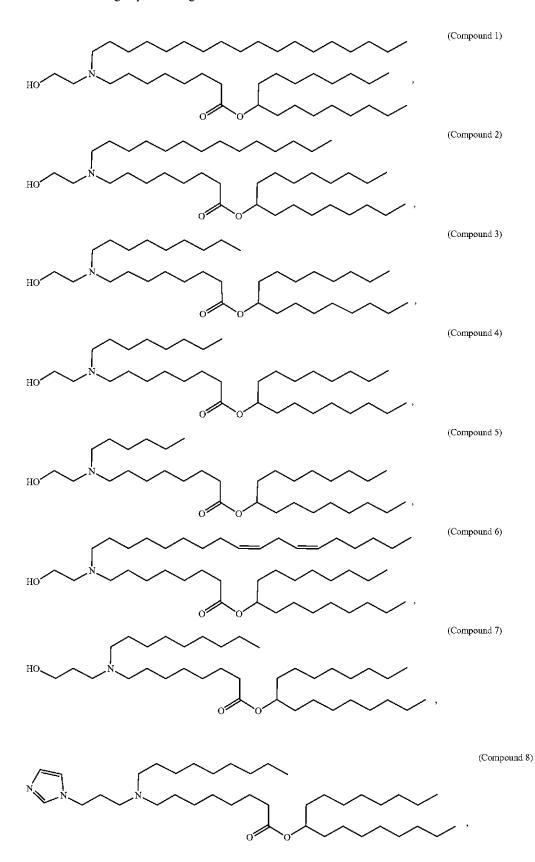
In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IId):

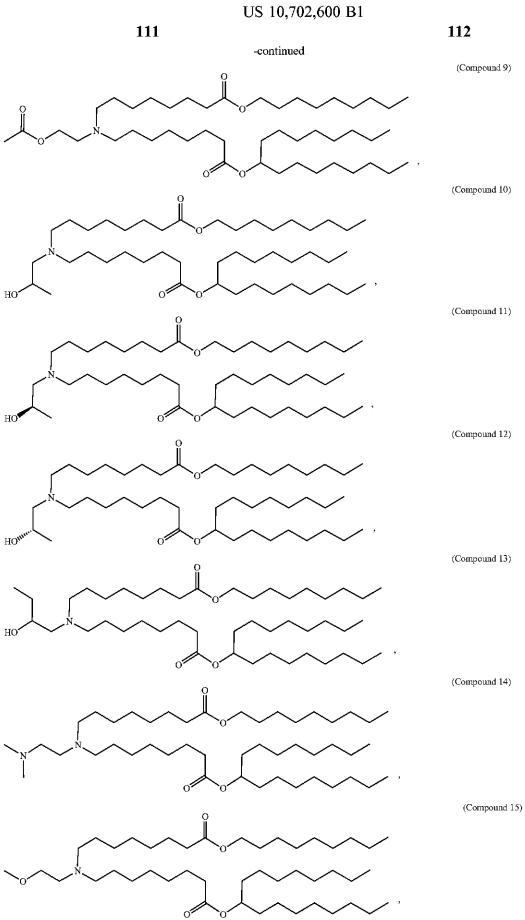
(IId)

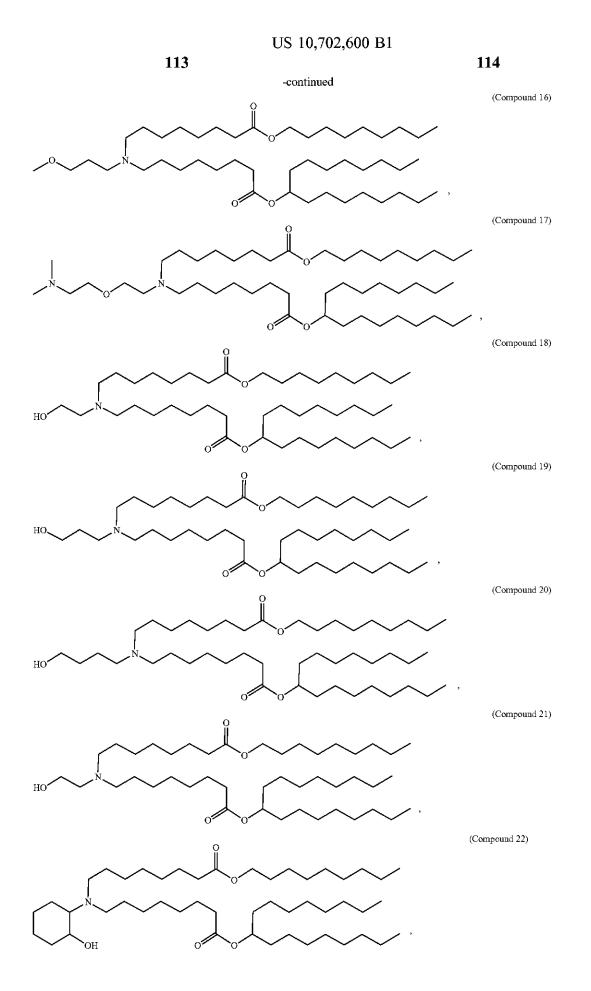


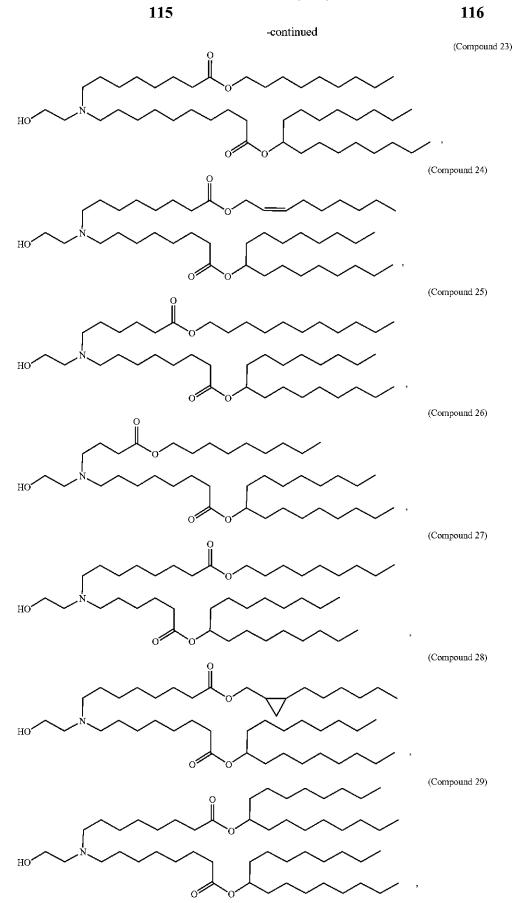
or a salt or isomer thereof, wherein n is 2, 3, or 4; and m, 65 R', R", and R₂ through R₆ are as described herein. For example, each of R₂ and R₃ may be independently selected from the group consisting of C_{5-14} alkyl and C_{5-14} alkenyl.

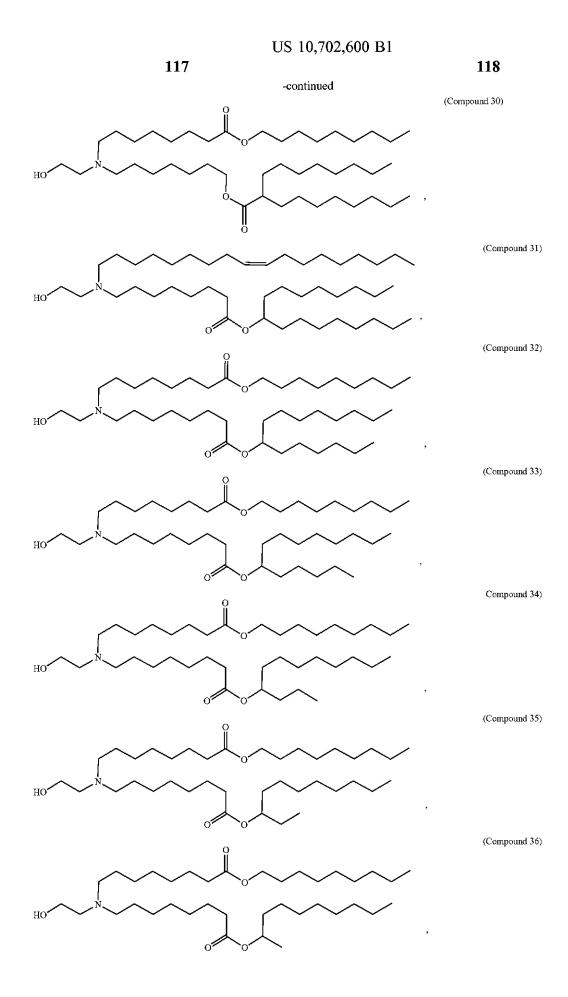
109 In some embodiments, the compound of Formula (I) is selected from the group consisting of:

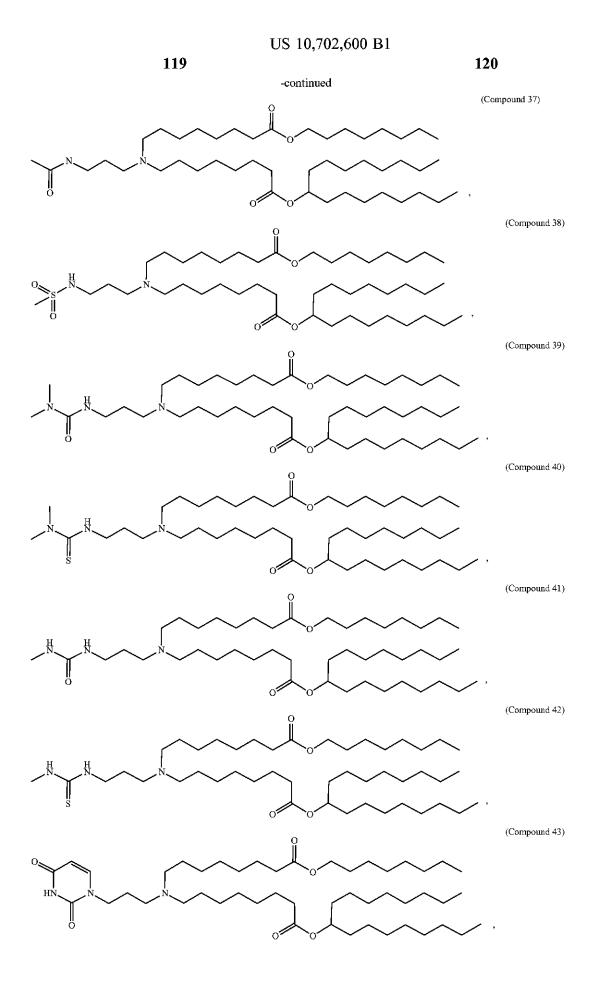


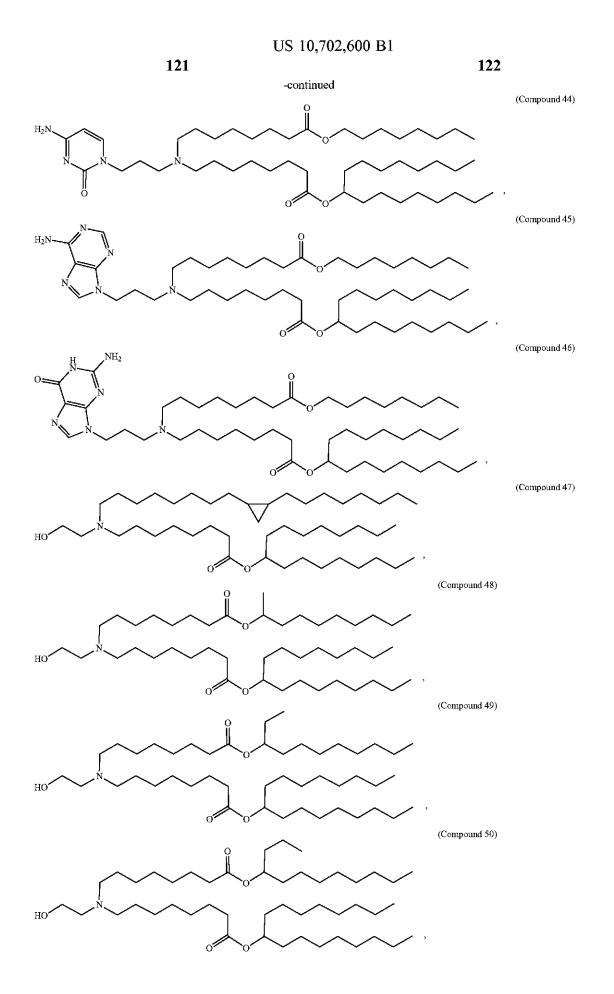


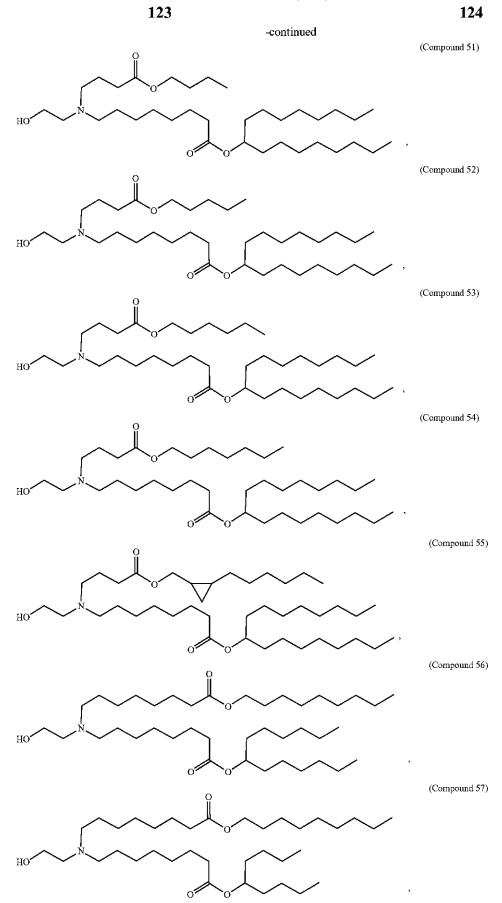


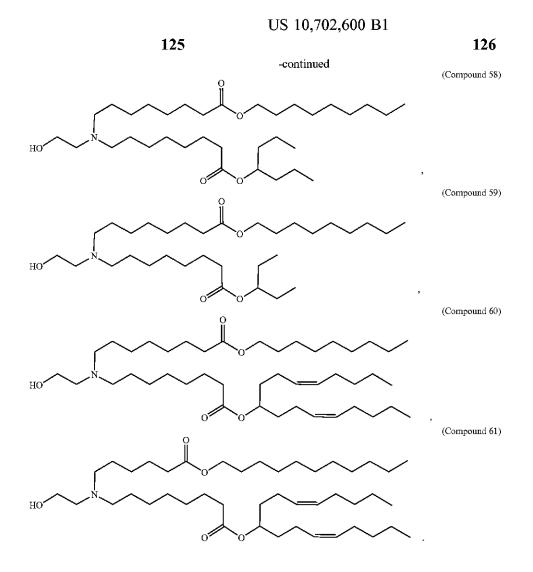




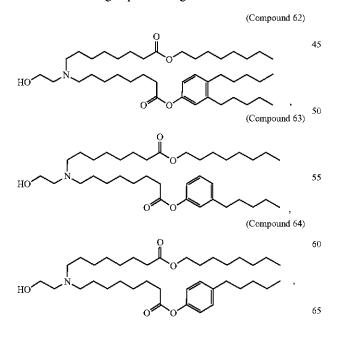


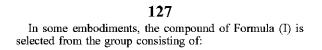


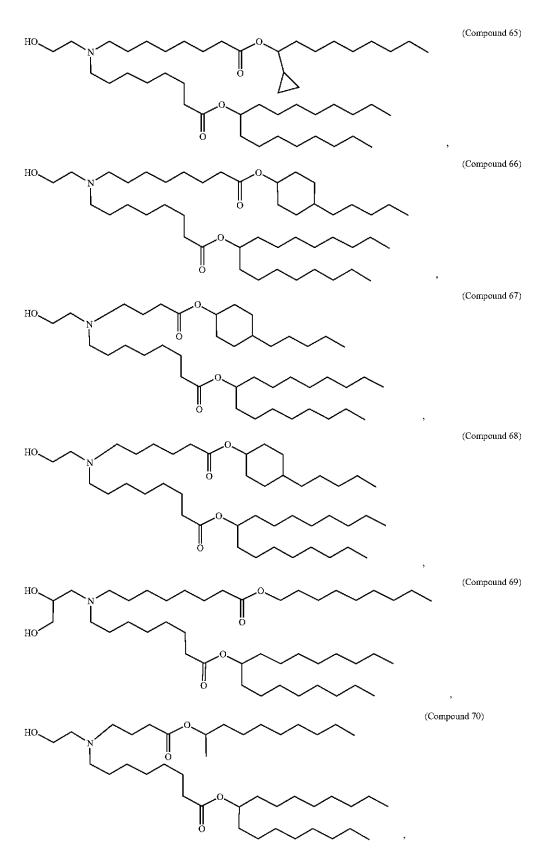


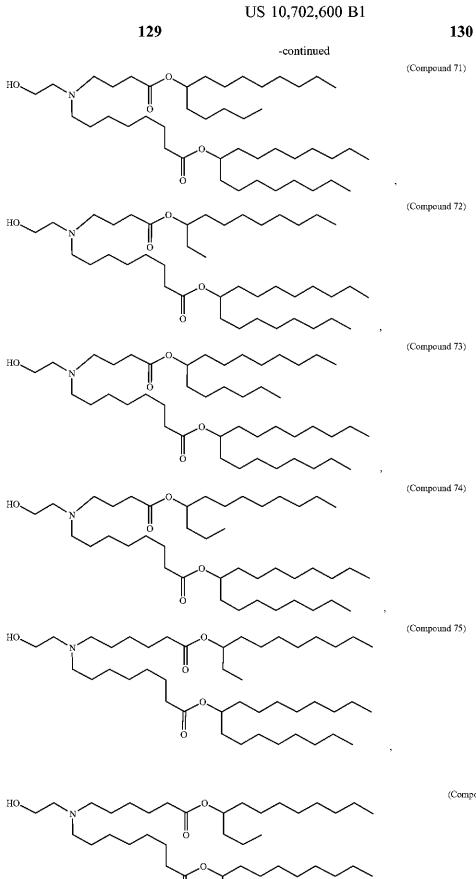


In further embodiments, the compound of Formula (I) is 40 selected from the group consisting of:



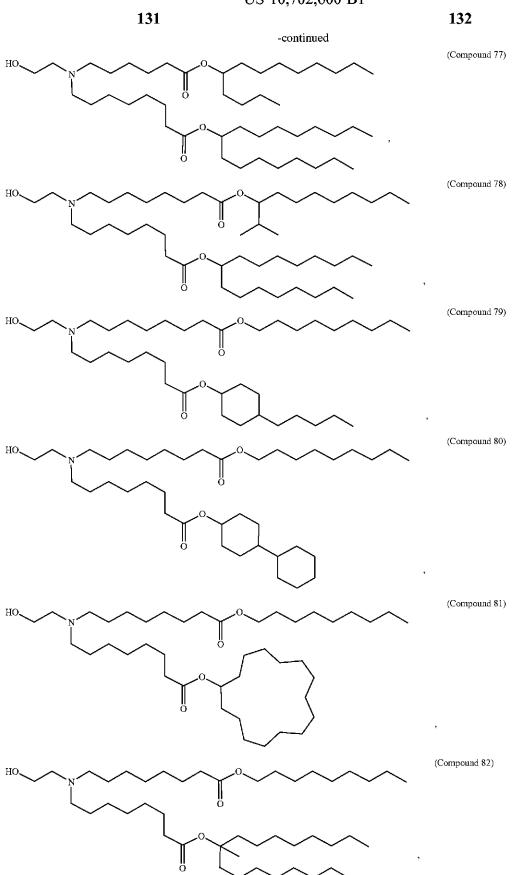




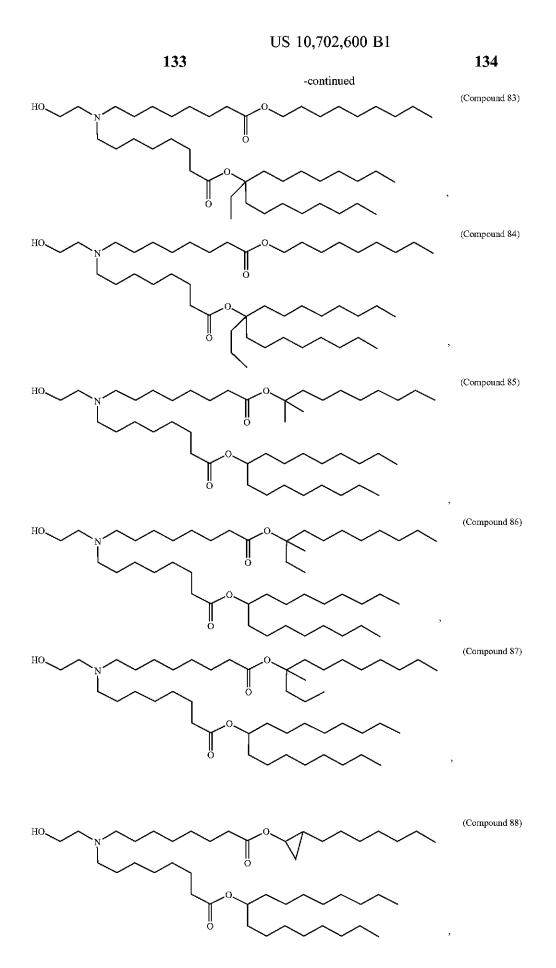


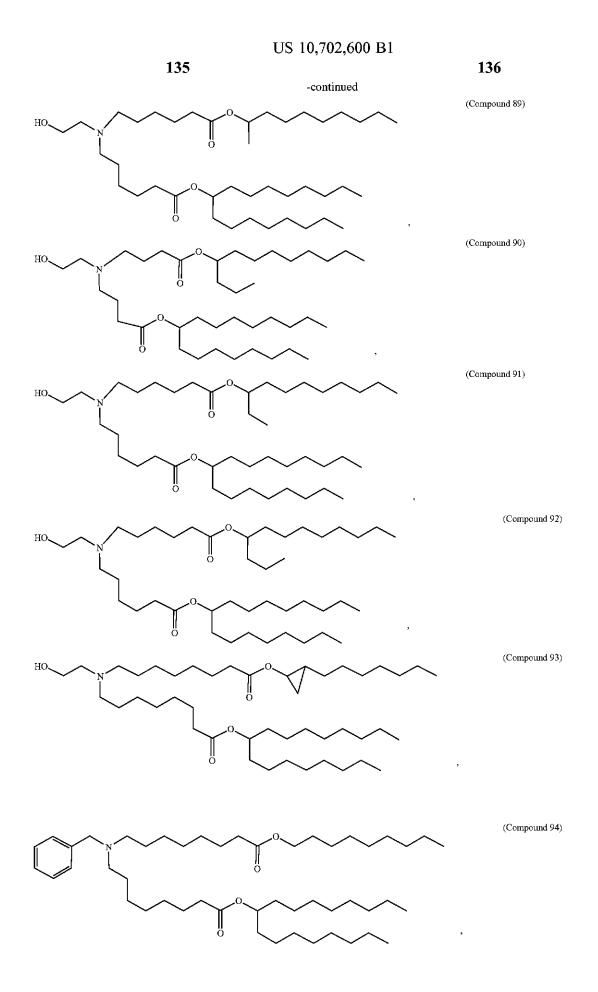
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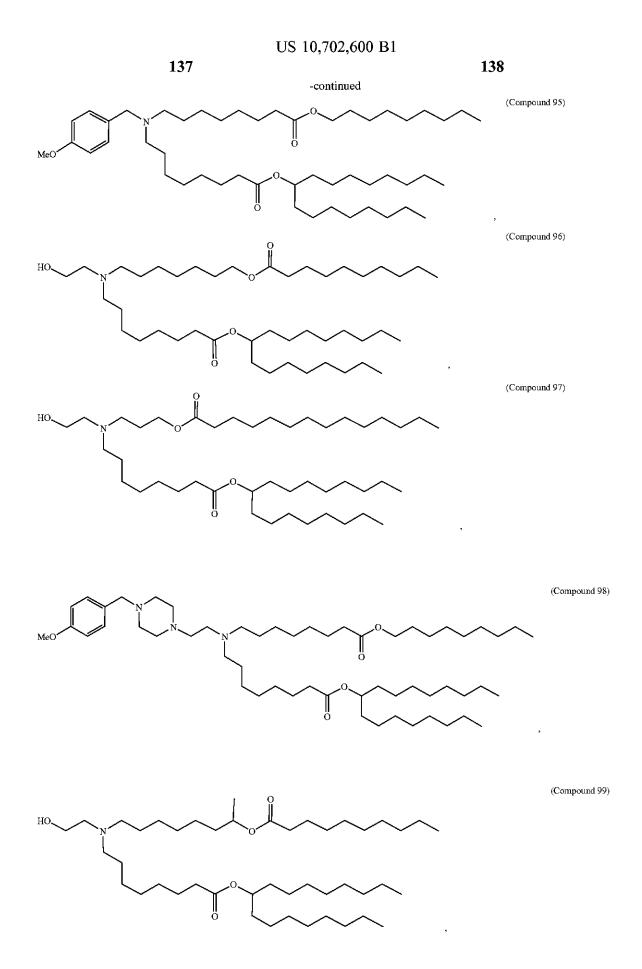
(Compound 76)

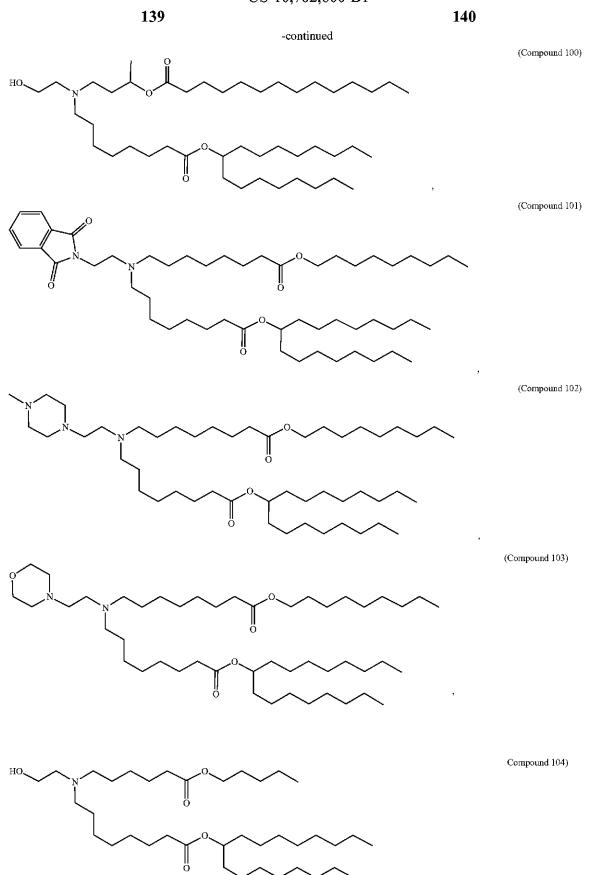


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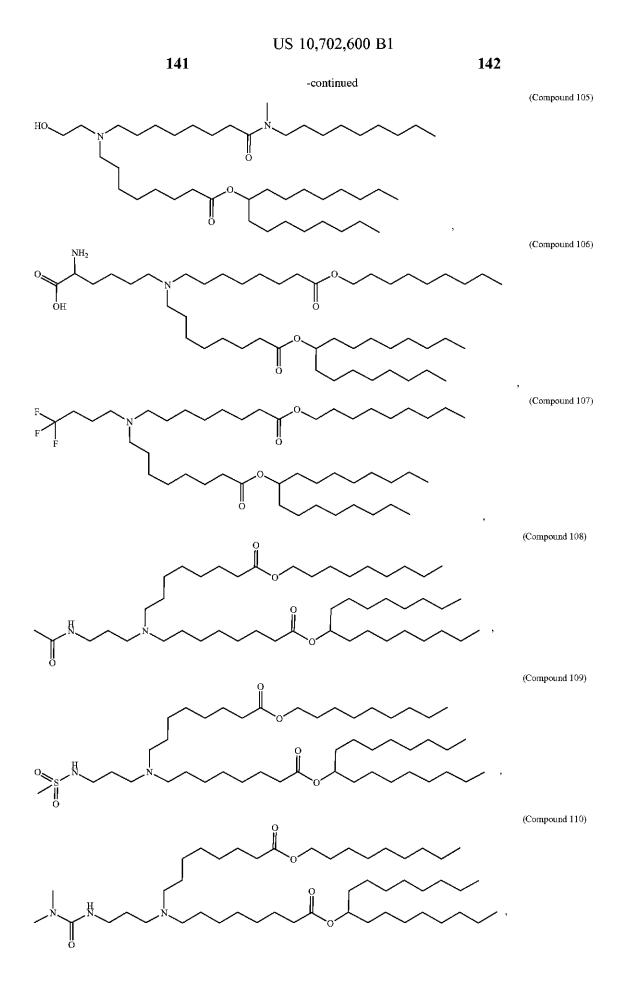


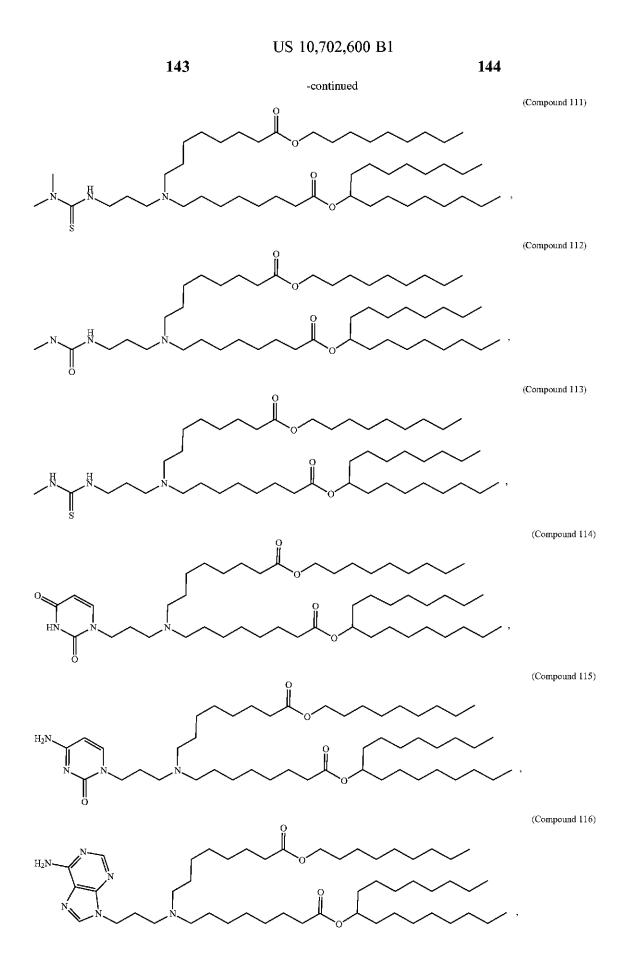


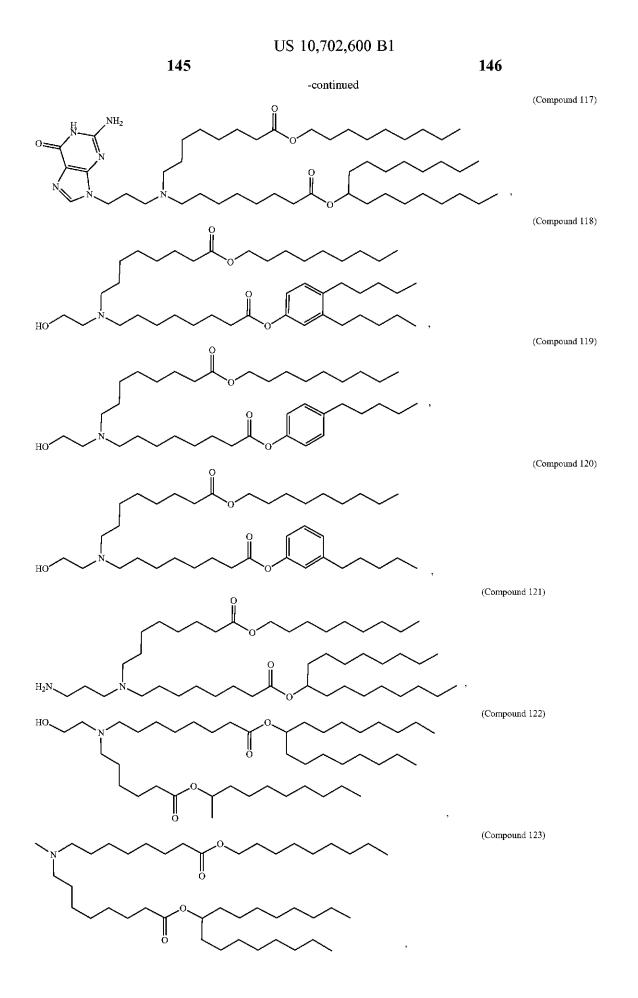


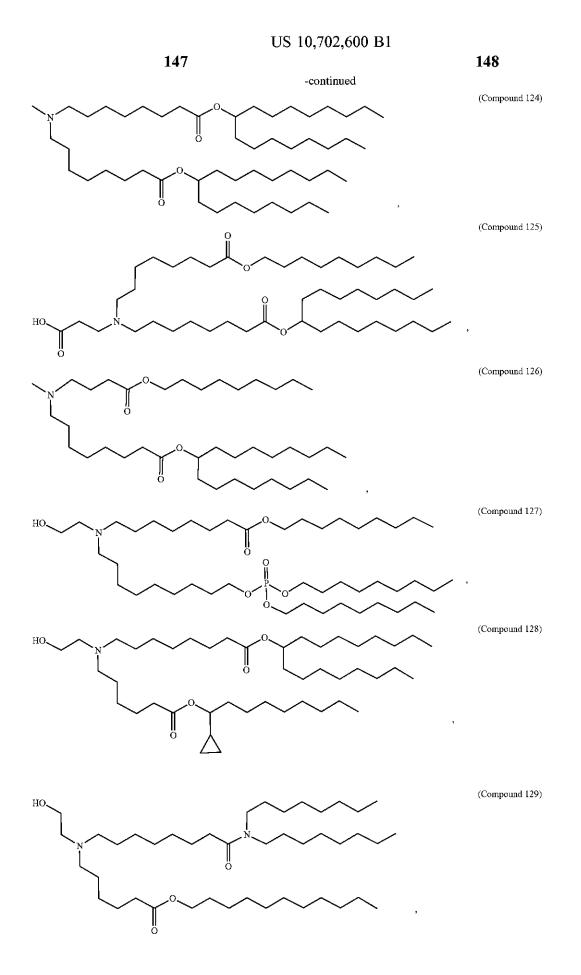


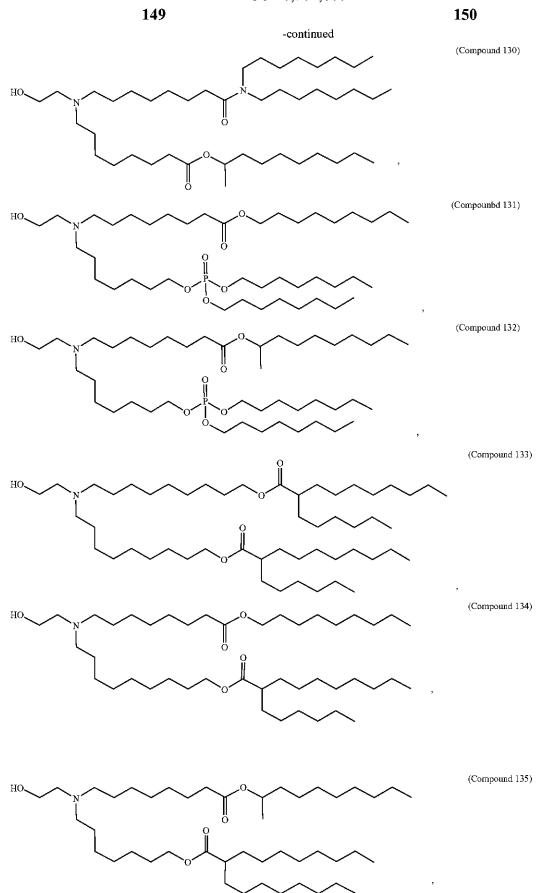
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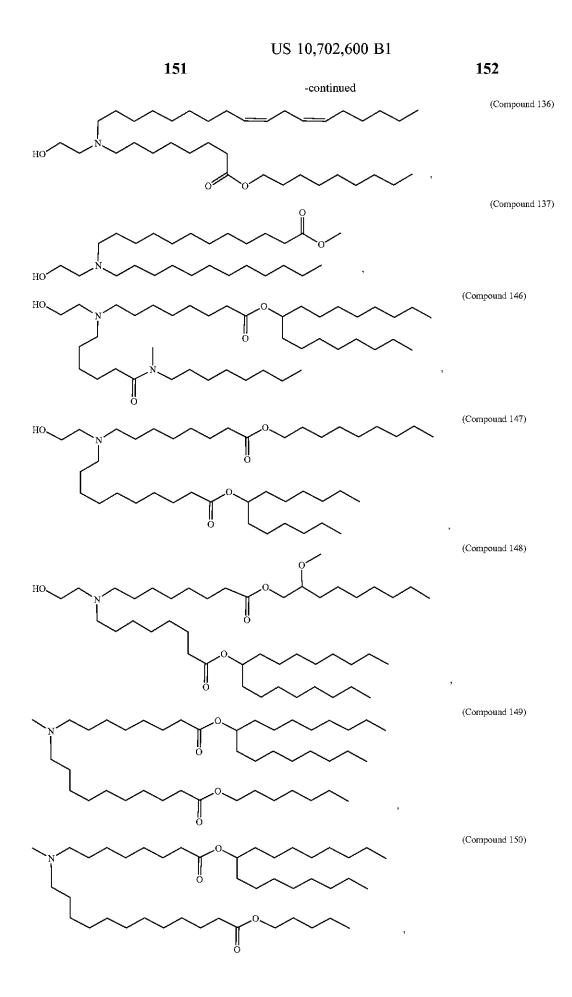


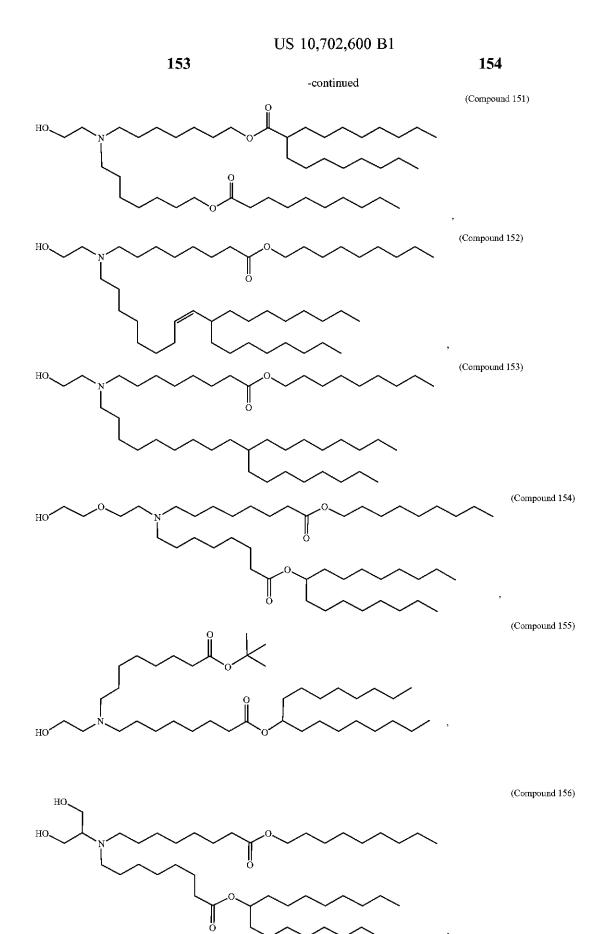


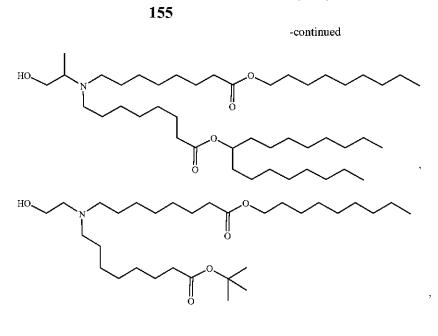










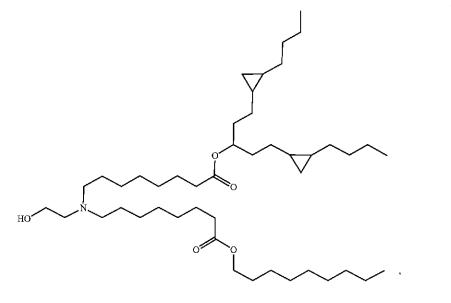


(Compound 158)

(Compound 157)

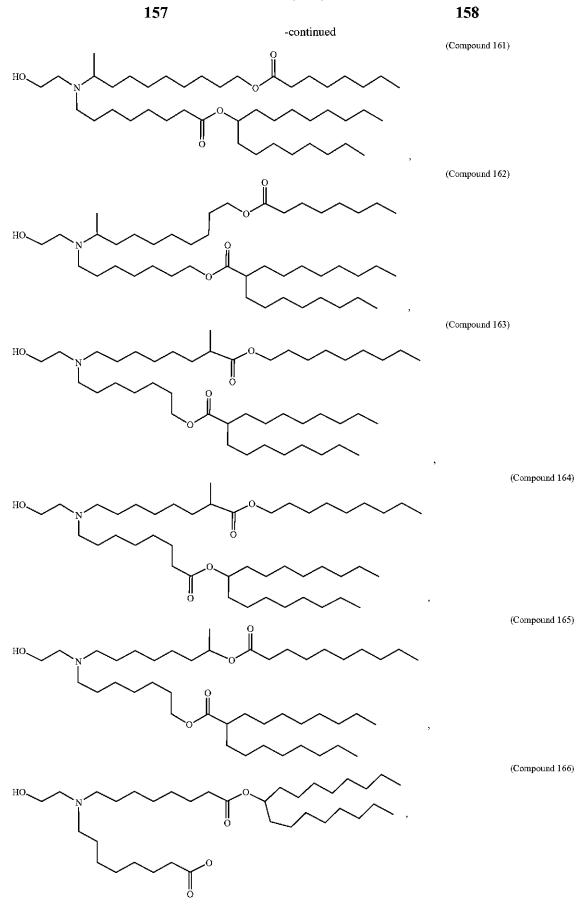
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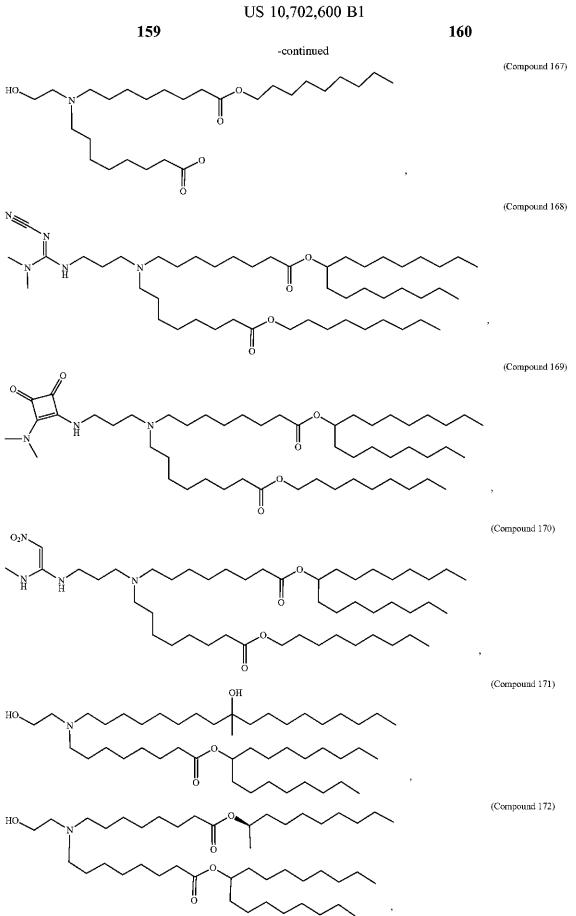
(Compound 159)

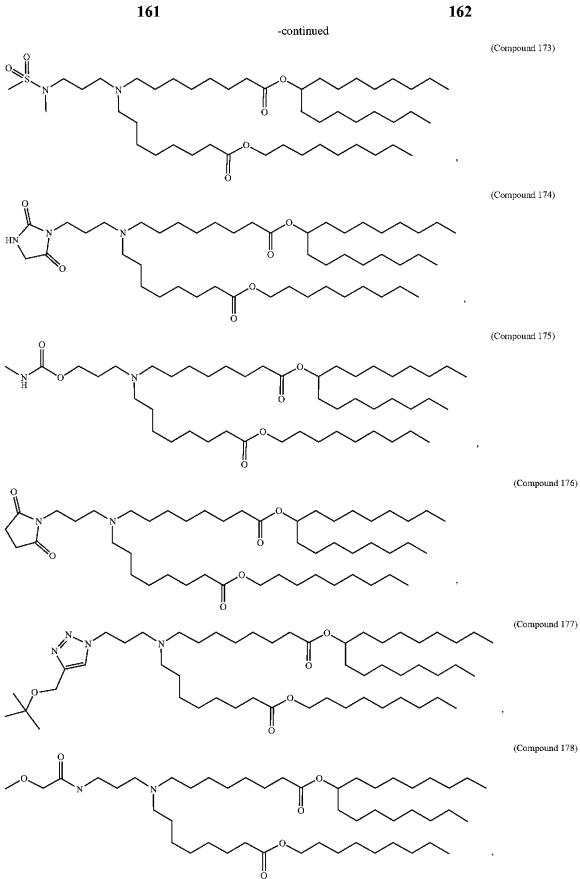


(Compound 160)

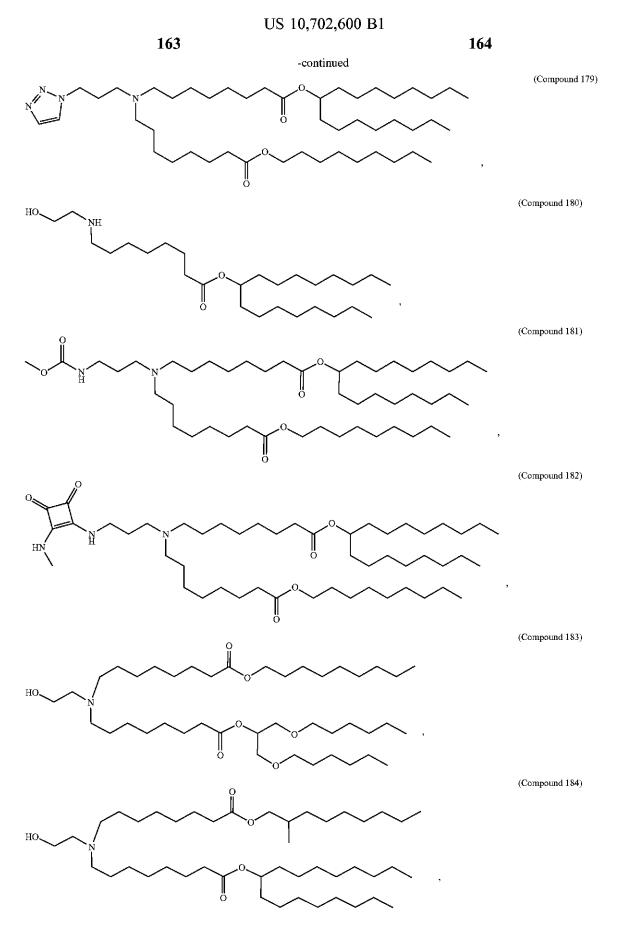
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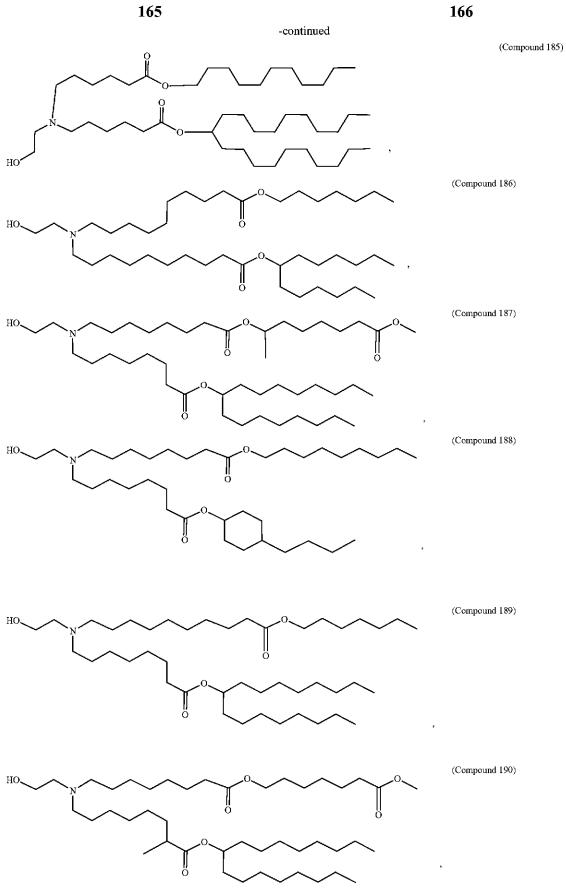


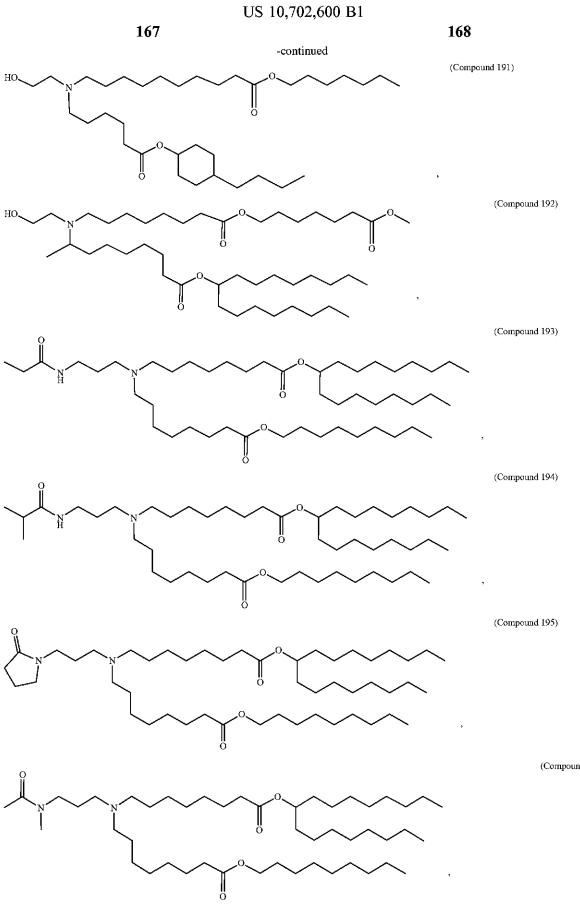




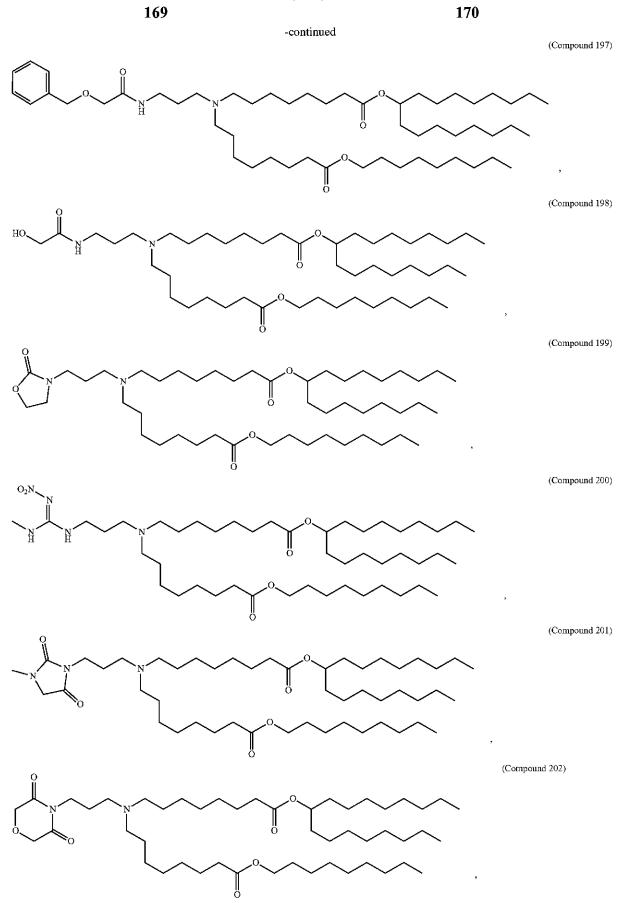


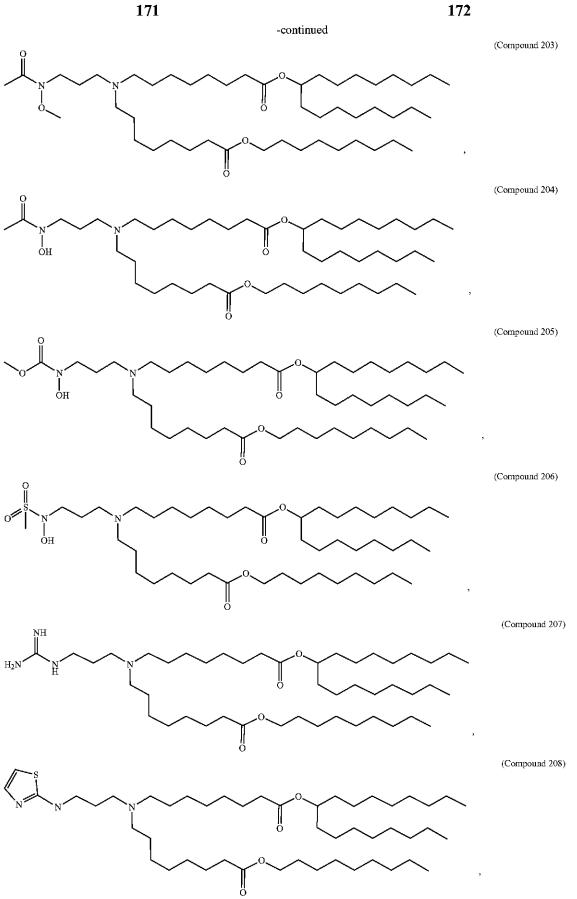


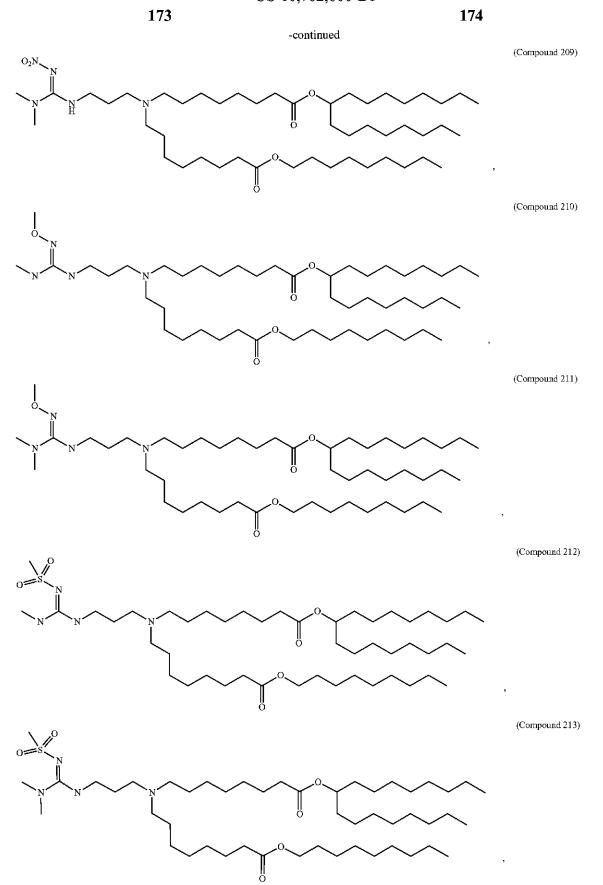




(Compound 196)

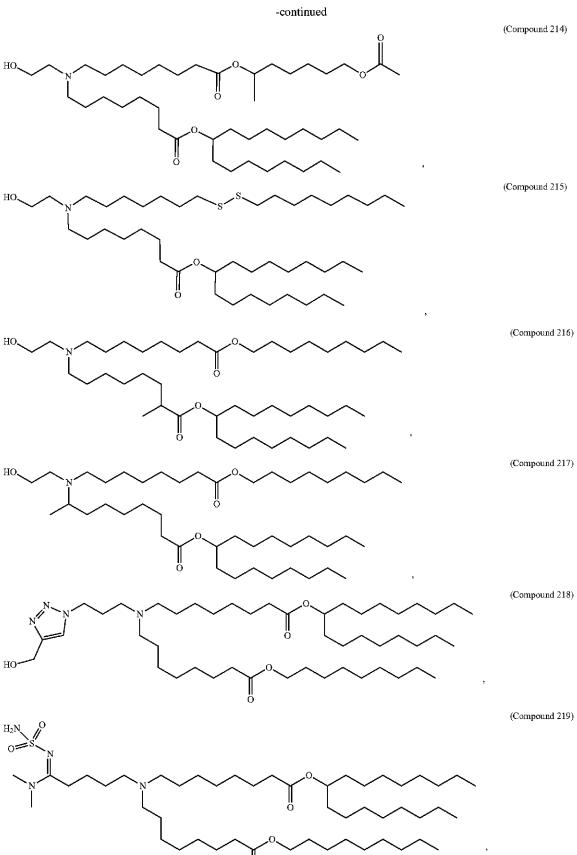


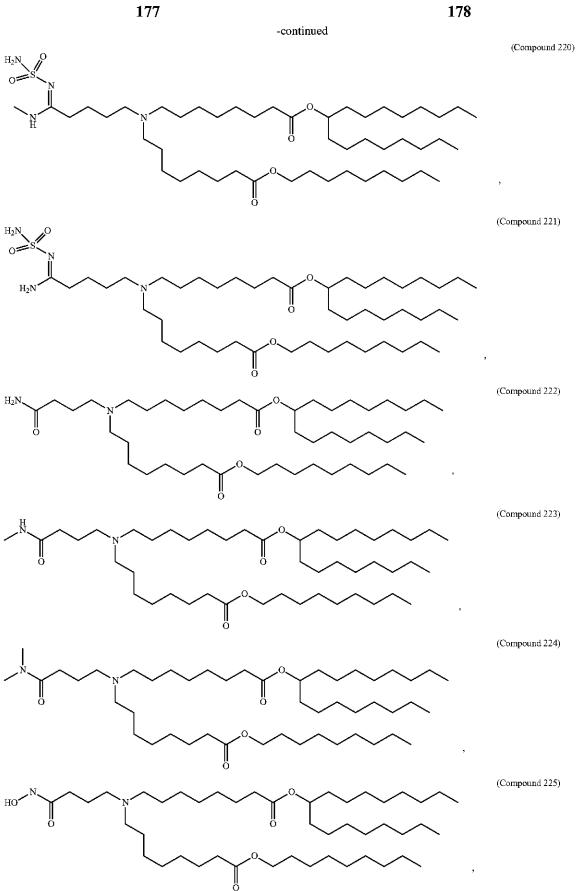


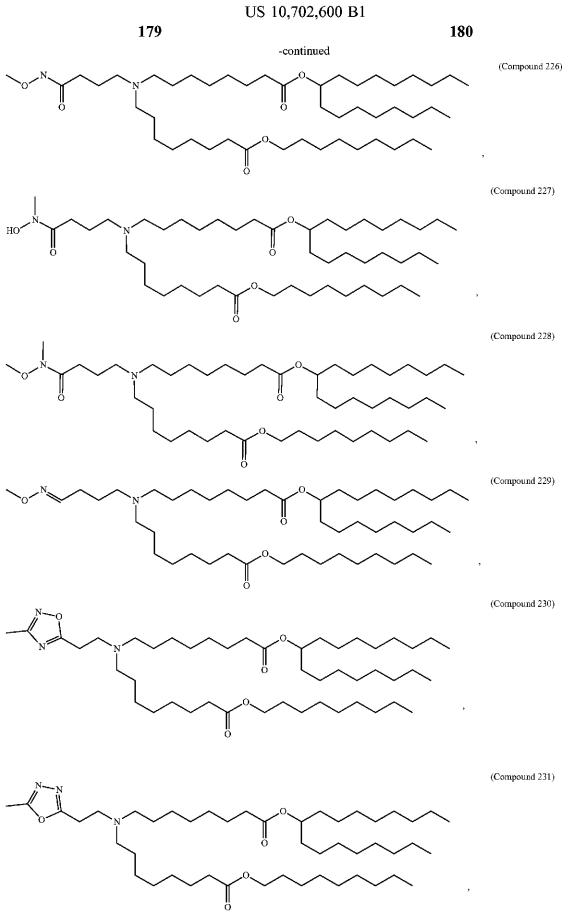


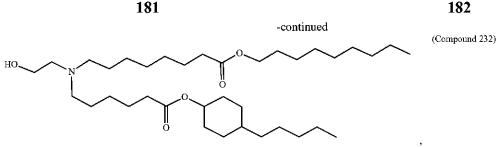
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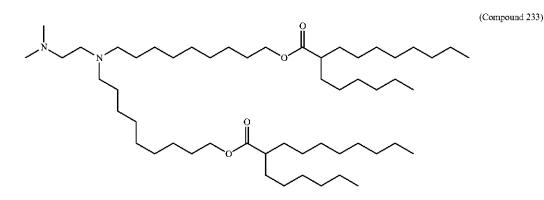




and salts and isomers thereof.

In some embodiments, a nanoparticle comprises the following compound:

ing the cell with a nanoparticle composition including (i) a lipid component including a phospholipid (such as a polyunsaturated lipid), a PEG lipid, a structural lipid, and a



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or salts and isomers thereof.

In some embodiments, the disclosure features a nanoparticle composition including a lipid component comprising a compound as described herein (e.g., a compound according to Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe)).

In some embodiments, the disclosure features a pharmaceutical composition comprising a nanoparticle composition $_{\Delta 0}$ according to the preceding embodiments and a pharmaceutically acceptable carrier. For example, the pharmaceutical composition is refrigerated or frozen for storage and/or shipment (e.g., being stored at a temperature of 4° C. or lower, such as a temperature between about -150° C. and 45 about 0° C. or between about -80° C. and about -20° C. (e.g., about -5° C., -10° C., -15° C., -20° C., -25° C., -30° C., -40° C., -50° C., -60° C., -70° C., -80° C., -90° C., -130° C. or -150° C.). For example, the pharmaceutical composition is a solution that is refrigerated for storage 50 and/or shipment at, for example, about -20° C., -30° C., -40° C., -50° C., -60° C., -70° C., or -80° C.

In some embodiments, the disclosure provides a method of delivering a therapeutic and/or prophylactic (e.g., RNA, such as mRNA) to a cell (e.g., a mammalian cell). This 55 method includes the step of administering to a subject (e.g., a mammal, such as a human) a nanoparticle composition including (i) a lipid component including a phospholipid (such as a polyunsaturated lipid), a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), 60 (IIc), (IId) or (IIe) and (ii) a therapeutic and/or prophylactic, in which administering involves contacting the cell with the nanoparticle composition, whereby the therapeutic and/or prophylactic is delivered to the cell.

In some embodiments, the disclosure provides a method 65 of producing a polypeptide of interest in a cell (e.g., a mammalian cell). The method includes the step of contact-

compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe) and (ii) an mRNA encoding the polypeptide of interest, whereby the mRNA is capable of being translated in the cell to produce the polypeptide.

In some embodiments, the disclosure provides a method of treating a disease or disorder in a mammal (e.g., a human) in need thereof. The method includes the step of administering to the mammal a therapeutically effective amount of a nanoparticle composition including (i) a lipid component including a phospholipid (such as a polyunsaturated lipid), a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe) and (ii) a therapeutic and/or prophylactic (e.g., an mRNA).

In some embodiments, the disease or disorder is characterized by dysfunctional or aberrant protein or polypeptide activity. For example, the disease or disorder is selected from the group consisting of rare diseases, infectious diseases, cancer and proliferative diseases, genetic diseases (e.g., cystic fibrosis), autoimmune diseases, diabetes, neurodegenerative diseases, cardio- and reno-vascular diseases, and metabolic diseases.

In some embodiments, the disclosure provides a method of delivering (e.g., specifically delivering) a therapeutic and/or prophylactic to a mammalian organ (e.g., a liver, spleen, lung, or femur). This method includes the step of administering to a subject (e.g., a mammal) a nanoparticle composition including (i) a lipid component including a phospholipid, a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe) and (ii) a therapeutic and/or prophylactic (e.g., an mRNA), in which administering involves contacting the cell with the nanoparticle composition, whereby the therapeutic and/or prophylactic is delivered to the target organ (e.g., a liver, spleen, lung, or femur).

In some embodiments, the disclosure features a method for the enhanced delivery of a therapeutic and/or prophylactic (e.g., an mRNA) to a target tissue (e.g., a liver, spleen, lung, or femur). This method includes administering to a subject (e.g., a mammal) a nanoparticle composition, the 5 composition including (i) a lipid component including a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe), a phospholipid, a structural lipid, and a PEG lipid; and (ii) a therapeutic and/or prophylactic, the administering including contacting the target tissue with the nanoparticle 10 composition, whereby the therapeutic and/or prophylactic is delivered to the target tissue.

In some embodiments, the disclosure features a method of lowering immunogenicity comprising introducing the nanoparticle composition of the disclosure into cells, wherein the 15 nanoparticle composition reduces the induction of the cellular immune response of the cells to the nanoparticle composition, as compared to the induction of the cellular immune response in cells induced by a reference composition which comprises a reference lipid instead of a com- 20 pound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe). For example, the cellular immune response is an innate immune response, an adaptive immune response, or both.

The disclosure also includes methods of synthesizing a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) 25 or (IIe) and methods of making a nanoparticle composition including a lipid component comprising the compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe). Modes of Vaccine Administration

Respiratory virus RNA (e.g. mRNA) vaccines may be 30 administered by any route which results in a therapeutically effective outcome. These include, but are not limited, to intradermal, intramuscular, and/or subcutaneous administration. The present disclosure provides methods comprising administering RNA (e.g., mRNA) vaccines to a subject in 35 need thereof. The exact amount required will vary from subject to subject, depending on the species, age, and general condition of the subject, the severity of the disease, the particular composition, its mode of administration, its mode of activity, and the like. Respiratory virus RNA (e.g., 40 mRNA) vaccines compositions are typically formulated in dosage unit form for ease of administration and uniformity of dosage. It will be understood, however, that the total daily usage of RNA (e.g., mRNA) vaccine compositions may be decided by the attending physician within the scope of sound 45 medical judgment. The specific therapeutically effective, prophylactically effective, or appropriate imaging dose level for any particular patient will depend upon a variety of factors including the disorder being treated and the severity of the disorder; the activity of the specific compound 50 employed; the specific composition employed; the age, body weight, general health, sex and diet of the patient; the time of administration, route of administration, and rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with 55 5 years later, or Day 0 and 10 years later) at a total dose of the specific compound employed; and like factors well known in the medical arts.

In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines compositions may be administered at dosage levels sufficient to deliver 0.0001 mg/kg to 100 60 mg/kg, 0.001 mg/kg to 0.05 mg/kg, 0.005 mg/kg to 0.05 mg/kg, 0.001 mg/kg to 0.005 mg/kg, 0.05 mg/kg to 0.5 mg/kg, 0.01 mg/kg to 50 mg/kg, 0.1 mg/kg to 40 mg/kg, 0.5 mg/kg to 30 mg/kg, 0.01 mg/kg to 10 mg/kg, 0.1 mg/kg to 10 mg/kg, or 1 mg/kg to 25 mg/kg, of subject body weight 65 per day, one or more times a day, per week, per month, etc. to obtain the desired therapeutic, diagnostic, prophylactic, or

imaging effect (see, e.g., the range of unit doses described in International Publication No WO2013078199, the contents of which are herein incorporated by reference in their entirety). The desired dosage may be delivered three times a day, two times a day, once a day, every other day, every third day, every week, every two weeks, every three weeks, every four weeks, every 2 months, every three months, every 6 months, etc. In some embodiments, the desired dosage may be delivered using multiple administrations (e.g., two, three, four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, or more administrations). When multiple administrations are employed, split dosing regimens such as those described herein may be used. In exemplary embodiments, respiratory virus RNA (e.g., mRNA) vaccines compositions may be administered at dosage levels sufficient to deliver 0.0005 mg/kg to 0.01 mg/kg, e.g., about 0.0005 mg/kg to about 0.0075 mg/kg, e.g., about 0.0005 mg/kg, about 0.001 mg/kg, about 0.002 mg/kg, about 0.003 mg/kg, about 0.004 mg/kg or about 0.005 mg/kg.

In some embodiments, respiratory virus RNA (e.g., mRNA) vaccine compositions may be administered once or twice (or more) at dosage levels sufficient to deliver 0.025 mg/kg to 0.250 mg/kg, 0.025 mg/kg to 0.500 mg/kg, 0.025 mg/kg to 0.750 mg/kg, or 0.025 mg/kg to 1.0 mg/kg.

In some embodiments, respiratory virus RNA (e.g., mRNA) vaccine compositions may be administered twice (e.g., Day 0 and Day 7, Day 0 and Day 14, Day 0 and Day 21, Day 0 and Day 28, Day 0 and Day 60, Day 0 and Day 90, Day 0 and Day 120, Day 0 and Day 150, Day 0 and Day 180, Day 0 and 3 months later, Day 0 and 6 months later, Day 0 and 9 months later, Day 0 and 12 months later, Day 0 and 18 months later, Day 0 and 2 years later, Day 0 and 5 years later, or Day 0 and 10 years later) at a total dose of or at dosage levels sufficient to deliver a total dose of 0.0100 mg, 0.025 mg, 0.050 mg, 0.075 mg, 0.100 mg, 0.125 mg, 0.150 mg, 0.175 mg, 0.200 mg, 0.225 mg, 0.250 mg, 0.275 mg, 0.300 mg, 0.325 mg, 0.350 mg, 0.375 mg, 0.400 mg, 0.425 mg, 0.450 mg, 0.475 mg, 0.500 mg, 0.525 mg, 0.550 mg, 0.575 mg, 0.600 mg, 0.625 mg, 0.650 mg, 0.675 mg, 0.700 mg, 0.725 mg, 0.750 mg, 0.775 mg, 0.800 mg, 0.825 mg, 0.850 mg, 0.875 mg, 0.900 mg, 0.925 mg, 0.950 mg, 0.975 mg, or 1.0 mg. Higher and lower dosages and frequency of administration are encompassed by the present disclosure. For example, a respiratory virus RNA (e.g., mRNA) vaccine composition may be administered three or four times.

In some embodiments, respiratory virus RNA (e.g., mRNA) vaccine compositions may be administered twice (e.g., Day 0 and Day 7, Day 0 and Day 14, Day 0 and Day 21, Day 0 and Day 28, Day 0 and Day 60, Day 0 and Day 90, Day 0 and Day 120, Day 0 and Day 150, Day 0 and Day 180, Day 0 and 3 months later, Day 0 and 6 months later, Day 0 and 9 months later, Day 0 and 12 months later, Day 0 and 18 months later, Day 0 and 2 years later, Day 0 and or at dosage levels sufficient to deliver a total dose of 0.010 mg, 0.025 mg, 0.100 mg or 0.400 mg.

In some embodiments, the respiratory virus RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as a single dosage of between 10 µg/kg and 400 µg/kg of the nucleic acid vaccine (in an effective amount to vaccinate the subject). In some embodiments the RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as a single dosage of between 10 μ g and 400 μ g of the nucleic acid vaccine (in an effective amount to vaccinate the subject). In some embodiments, a respiratory virus RNA (e.g.,

mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as a single dosage of 25-1000 μg (e.g., a single dosage of mRNA encoding hMPV, PIV3, RSV, MeV and/or BetaCoV antigen). In some embodiments, a respiratory virus RNA (e.g., mRNA) vaccine is adminis- 5 tered to the subject as a single dosage of 25, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 µg. For example, a respiratory virus RNA (e.g., mRNA) vaccine may be administered to a subject as a single dose of 25-100, 25-500, 50-100, 50-500, 10 50-1000, 100-500, 100-1000, 250-500, 250-1000, or 500-1000 µg. In some embodiments, a respiratory virus RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as two dosages, the combination of which equals 25-1000 µg of the respiratory 15 virus RNA (e.g., mRNA) vaccine.

A respiratory virus RNA (e.g. mRNA) vaccine pharmaceutical composition described herein can be formulated into a dosage form described herein, such as an intranasal, intratracheal, or injectable (e.g., intravenous, intraocular, 20 intravitreal, intramuscular, intradermal, intracardiac, intraperitoneal, and subcutaneous).

Respiratory Virus RNA (e.g., mRNA) Vaccine Formulations and Methods of Use

Some aspects of the present disclosure provide formula- 25 tions of the respiratory virus RNA (e.g., mRNA) vaccine, wherein the RNA (e.g., mRNA) vaccine is formulated in an effective amount to produce an antigen specific immune response in a subject (e.g., production of antibodies specific to an hMPV, PIV3, RSV, MeV and/or BetaCoV antigenic 30 polypeptide). "An effective amount" is a dose of an RNA (e.g., mRNA) vaccine effective to produce an antigenspecific immune response. Also provided herein are methods of inducing an antigen-specific immune response in a subject. 35

In some embodiments, the antigen-specific immune response is characterized by measuring an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide antibody titer produced in a subject administered a respiratory virus RNA (e.g., mRNA) vaccine as 40 provided herein. An antibody titer is a measurement of the amount of antibodies within a subject, for example, antibodies that are specific to a particular antigen (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) or epitope of an antigen. 45 Antibody titer is typically expressed as the inverse of the greatest dilution that provides a positive result. Enzymelinked immunosorbent assay (ELISA) is a common assay for determining antibody titers, for example.

In some embodiments, an antibody titer is used to assess 50 whether a subject has had an infection or to determine whether immunizations are required. In some embodiments, an antibody titer is used to determine the strength of an autoimmune response, to determine whether a booster immunization is needed, to determine whether a previous 55 vaccine was effective, and to identify any recent or prior infections. In accordance with the present disclosure, an antibody titer may be used to determine the strength of an immune response induced in a subject by the respiratory virus RNA (e.g., mRNA) vaccine. 60

In some embodiments, an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject is increased by at least 1 log relative to a control. For example, anti-antigenic polypeptide antibody titer pro-65 duced in a subject may be increased by at least 1.5, at least 2, at least 2.5, or at least 3 log relative to a control. In some

embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by 1, 1.5, 2, 2.5 or 3 log relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by 1-3 log relative to a control. For example, the anti-antigenic polypeptide antibody titer produced in a subject may be increased by 1-1.5, 1-2, 1-2.5, 1-3, 1.5-2, 1.5-2.5, 1.5-3, 2-2.5, 2-3, or 2.5-3 log relative to a control.

In some embodiments, the anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject is increased at least 2 times relative to a control. For example, the anti-antigenic polypeptide antibody titer produced in a subject may be increased at least 3 times, at least 4 times, at least 5 times, at least 6 times, at least 7 times, at least 8 times, at least 9 times, or at least 10 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased 2, 3, 4, 5, 6, 7, 8, 9, or 10 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in a subject is increased 2-10 times relative to a control. For example, the anti-antigenic polypeptide antibody titer produced in a subject may be increased 2-10, 2-9, 2-8, 2-7, 2-6, 2-5, 2-4, 2-3, 3-10, 3-9, 3-8, 3-7, 3-6, 3-5, 3-4, 4-10, 4-9, 4-8, 4-7, 4-6, 4-5, 5-10, 5-9, 5-8, 5-7, 5-6, 6-10, 6-9, 6-8, 6-7, 7-10, 7-9, 7-8, 8-10, 8-9, or 9-10 times relative to a control.

A control, in some embodiments, is the anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject who has not been administered a respiratory virus RNA (e.g., mRNA) vaccine of the present disclosure. In some embodiments, a control is an antiantigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject who has been administered a live attenuated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. An attenuated vaccine is a vaccine produced by reducing the virulence of a viable (live). An attenuated virus is altered in a manner that renders it harmless or less virulent relative to live, unmodified virus. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject administered inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an antihMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject administered a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. Recombinant protein vaccines typically include protein antigens that either have been produced in a heterologous expression system (e.g., bacteria or yeast) or purified from large amounts of the pathogenic organism. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject who has been administered an hMPV, PIV3, RSV, MeV and/or BetaCoV virus-like particle (VLP) vaccine. For example, an hMPV VLP vaccine used as a control may be a hMPV VLPs, comprising (or consisting of) viral matrix (M) and fusion (F) proteins, generated by expressing viral proteins in suspension-adapted human embryonic kidney epithelial (293-F) cells (see, e.g., Cox R G et al., J Virol. 2014 June; 88(11): 6368-6379, the contents of which are herein incorporated by reference).

In some embodiments, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose that is reduced compared to the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. A "standard of care," as provided herein, refers to 5 a medical or psychological treatment guideline and can be general or specific. "Standard of care" specifies appropriate treatment based on scientific evidence and collaboration between medical professionals involved in the treatment of a given condition. It is the diagnostic and treatment process 10 that a physician/clinician should follow for a certain type of patient, illness or clinical circumstance. A "standard of care dose," as provided herein, refers to the dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, or a live attenuated or inactivated hMPV, 15 PIV3, RSV, MeV and/or BetaCoV vaccine, that a physician/ clinician or other medical professional would administer to a subject to treat or prevent hMPV, PIV3, RSV, MeV and/or BetaCoV, or a hMPV-, PIV3-, RSV-, MeV- and/or BetaCoVrelated condition, while following the standard of care 20 guideline for treating or preventing hMPV, PIV3, RSV, MeV and/or BetaCoV, or a hMPV-, PIV3-, RSV-, MeV- and/or BetaCoV-related condition.

In some embodiments, the anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or 25 anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject administered an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is equivalent to an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic 30 polypeptide) antibody titer produced in a control subject administered a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine.

In some embodiments, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to an at least 2-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. For example, an effective amount 40 9 to 300-, 9 to 200-, 9 to 100-, 9 to 90-, 9 to 80-, 9 to 70-, of a respiratory virus RNA (e.g., mRNA) vaccine may be a dose equivalent to an at least 3-fold, at least 4-fold, at least 5-fold, at least 6-fold, at least 7-fold, at least 8-fold, at least 9-fold, or at least 10-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or 45 BetaCoV protein vaccine. In some embodiments, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to an at least at least 100-fold, at least 500-fold, or at least 1000-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, 50 MeV and/or BetaCoV protein vaccine. In some embodiments, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to a 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 20-, 50-, 100-, 250-, 500-, or 1000-fold reduction in a standard of care dose of a recombinant or 55 purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, the anti-antigenic polypeptide antibody titer produced in a subject administered an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is equivalent to an anti-antigenic polypeptide anti- 60 body titer produced in a control subject administered the standard of care dose of a recombinant or protein hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. In some embodiments, an effective 65 amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to a 2-fold to 1000-fold (e.g., 2-fold to

100-fold, 10-fold to 1000-fold) reduction in the standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, wherein the antiantigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine.

In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to a 2 to 1000-, 2 to 900-, 2 to 800-, 2 to 700-, 2 to 600-, 2 to 500-, 2 to 400-, 2 to 300-, 2 to 200-, 2 to 100-, 2 to 90-, 2 to 80-, 2 to 70-, 2 to 60-, 2 to 50-, 2 to 40-, 2 to 30-, 2 to 20-, 2 to 10-, 2 to 9-, 2 to 8-, 2 to 7-, 2 to 6-, 2 to 5-, 2 to 4-, 2 to 3-, 3 to 1000-, 3 to 900-, 3 to 800-, 3 to 700-, 3 to 600-, 3 to 500-, 3 to 400-, 3 to 3 to 00-, 3 to 200-, 3 to 100-, 3 to 90-, 3 to 80-, 3 to 70-, 3 to 60-, 3 to 50-, 3 to 40-, 3 to 30-, 3 to 20-, 3 to 10-, 3 to 9-, 3 to 8-, 3 to 7-, 3 to 6-, 3 to 5-, 3 to 4-, 4 to 1000-, 4 to 900-, 4 to 800-, 4 to 700-, 4 to 600-, 4 to 500-, 4 to 400-, 4 to 4 to 00-, 4 to 200-, 4 to 100-, 4 to 90-, 4 to 80-, 4 to 70-, 4 to 60-, 4 to 50-, 4 to 40-, 4 to 30-, 4 to 20-, 4 to 10-, 4 to 9-, 4 to 8-, 4 to 7-, 4 to 6-, 4 to 5-, 4 to 4-, 5 to 1000-, 5 to 900-, 5 to 800-, 5 to 700-, 5 to 600-, 5 to 500-, 5 to 400-, 5 to 300-, 5 to 200-, 5 to 100-, 5 to 90-, 5 to 80-, 5 to 70-, 5 to 60-, 5 to 50-, 5 to 40-, 5 to 30-, 5 to 20-, 5 to 10-, 5 to 9-, 5 to 8-, 5 to 7-, 5 to 6-, 6 to 1000-, 6 to 900-, 6 to 800-, 6 to 700-, 6 to 600-, 6 to 500-, 6 to 400-, 6 to 300-, 6 to 200-, 6 to 100-, 6 to 90-, 6 to 80-, 6 to 70-, 6 to 60-, 6 to 50-, 6 to 40-, 6 to 30-, 6 to 20-, 6 to 10-, 6 to 9-, 6 to 8-, 6 to 7-, 7 to 1000-, 7 to 900-, 7 to 800-, 7 to 700-, 7 to 600-, 7 to 500-, 7 to 400-, 7 to 300-, 7 to 200-, 7 to 100-, 7 to 90-, 7 to 80-, 7 to 70-, 7 to 60-, 7 to 50-, 7 to 40-, 7 to 30-, 7 to 20-, 7 to 10-, 7 to 9-, 7 to 8-, 8 to 1000-, 8 to 900-, 8 to 800-, 8 to 700-, 8 to 600-, 8 to 500-, 8 to 400-, 8 to 300-, 8 to 200-, 8 to 100-, 8 to 90-, 8 to 80-, 8 to 70-, 8 to 60-, 8 to 50-, 8 to 40-, 8 to 30-, 8 to 20-, 8 to 10-, 8 to 9-, 9 to 1000-, 9 to 900-, 9 to 800-, 9 to 700-, 9 to 600-, 9 to 500-, 9 to 400-, 9 to 60-, 9 to 50-, 9 to 40-, 9 to 30-, 9 to 20-, 9 to 10-, 10 to 1000-, 10 to 900-, 10 to 800-, 10 to 700-, 10 to 600-, 10 to 500-, 10 to 400-, 10 to 300-, 10 to 200-, 10 to 100-, 10 to 90-, 10 to 80-, 10 to 70-, 10 to 60-, 10 to 50-, 10 to 40-, 10 to 30-, 10 to 20-, 20 to 1000-, 20 to 900-, 20 to 800-, 20 to 700-, 20 to 600-, 20 to 500-, 20 to 400-, 20 to 300-, 20 to 200-, 20 to 100-, 20 to 90-, 20 to 80-, 20 to 70-, 20 to 60-, 20 to 50-, 20 to 40-, 20 to 30-, 30 to 1000-, 30 to 900-, 30 to 800-, 30 to 700-, 30 to 600-, 30 to 500-, 30 to 400-, 30 to 300-, 30 to 200-, 30 to 100-, 30 to 90-, 30 to 80-, 30 to 70-, 30 to 60-, 30 to 50-, 30 to 40-, 40 to 1000-, 40 to 900-, 40 to 800-, 40 to 700-, 40 to 600-, 40 to 500-, 40 to 400-, 40 to 300-, 40 to 200-, 40 to 100-, 40 to 90-, 40 to 80-, 40 to 70-, 40 to 60-, 40 to 50-, 50 to 1000-, 50 to 900-, 50 to 800-, 50 to 700-, 50 to 600-, 50 to 500-, 50 to 400-, 50 to 300-, 50 to 200-, 50 to 100-, 50 to 90-, 50 to 80-, 50 to 70-, 50 to 60-, 60 to 1000-, 60 to 900-, 60 to 800-, 60 to 700-, 60 to 600-, 60 to 500-, 60 to 400-, 60 to 300-, 60 to 200-, 60 to 100-, 60 to 90-, 60 to 80-, 60 to 70-, 70 to 1000-, 70 to 900-, 70 to 800-, 70 to 700-, 70 to 600-, 70 to 500-, 70 to 400-, 70 to 300-, 70 to 200-, 70 to 100-, 70 to 90-, 70 to 80-, 80 to 1000-, 80 to 900-, 80 to 800-, 80 to 700-, 80 to 600-, 80 to 500-, 80 to 400-, 80 to 300-, 80 to 200-, 80 to 100-, 80 to 90-, 90 to 1000-, 90 to 900-, 90 to 800-, 90 to 700-, 90 to 600-, 90 to 500-, 90 to 400-, 90 to 300-, 90 to 200-, 90 to 100-, 100 to 1000-, 100 to 900-, 100 to 800-, 100 to 700-, 100 to 600-, 100 to 500-, 100 to 400-, 100 to 300-, 100 to 200-, 200 to

1000-, 200 to 900-, 200 to 800-, 200 to 700-, 200 to 600-, 200 to 500-, 200 to 400-, 200 to 300-, 300 to 1000-, 300 to 900-, 300 to 800-, 300 to 700-, 300 to 600-, 300 to 500-, 300 to 400-, 400 to 1000-, 400 to 900-, 400 to 800-, 400 to 700-, 400 to 600-, 400 to 500-, 500 to 1000-, 500 to 900-, 500 to 5 800-, 500 to 700-, 500 to 600-, 600 to 1000-, 600 to 900-, 600 to 800-, 600 to 700-, 700 to 1000-, 700 to 900-, 700 to 800-, 800 to 1000-, 800 to 900-, or 900 to 1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. 10 In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or 15 encompassed by the following numbered paragraphs: BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. In some embodiments, the effective amount is a dose equivalent to (or equivalent to an at least) 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 20-, 30-, 40-, 50-, 60-, 70-, 80-, 90-, 100-, 110-, 120-, 130-, 20 140-, 150-, 160-, 170-, 1280-, 190-, 200-, 210-, 220-, 230-, 240-, 250-, 260-, 270-, 280-, 290-, 300-, 310-, 320-, 330-, 340-, 350-, 360-, 370-, 380-, 390-, 400-, 410-, 420-, 430-, 440-, 450-, 4360-, 470-, 480-, 490-, 500-, 510-, 520-, 530-, 540-, 550-, 560-, 5760-, 580-, 590-, 600-, 610-, 620-, 630-, 25 640-, 650-, 660-, 670-, 680-, 690-, 700-, 710-, 720-, 730-, 740-, 750-, 760-, 770-, 780-, 790-, 800-, 810-, 820-, 830-, 840-, 850-, 860-, 870-, 880-, 890-, 900-, 910-, 920-, 930-, 940-, 950-, 960-, 970-, 980-, 990-, or 1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, 30 RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant or 35 purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine.

In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a total dose of 40 hMPV antigenic polypeptide comprises an amino acid 50-1000 µg. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a total dose of 50-1000, 50-900, 50-800, 50-700, 50-600, 50-500, 50-400, 50-300, 50-200, 50-100, 50-90, 50-80, 50-70, 50-60, 60-1000, 60-900, 60-800, 60-700, 60-600, 60-500, 45 60-400, 60-300, 60-200, 60-100, 60-90, 60-80, 60-70, 70-1000, 70-900, 70-800, 70-700, 70-600, 70-500, 70-400, 70-300, 70-200, 70-100, 70-90, 70-80, 80-1000, 80-900, 80-800, 80-700, 80-600, 80-500, 80-400, 80-300, 80-200, 80-100, 80-90, 90-1000, 90-900, 90-800, 90-700, 90-600, 50 90-500, 90-400, 90-300, 90-200, 90-100, 100-1000, 100-900, 100-800, 100-700, 100-600, 100-500, 100-400, 100-300, 100-200, 200-1000, 200-900, 200-800, 200-700, 200-600, 200-500, 200-400, 200-300, 300-1000, 300-900, 300-800, 300-700, 300-600, 300-500, 300-400, 400-1000, 400- 55 reading frame encoding a hMPV antigenic polypeptide or an 900, 400-800, 400-700, 400-600, 400-500, 500-1000, 500-900, 500-800, 500-700, 500-600, 600-1000, 600-900, 600-900, 600-700, 700-1000, 700-900, 700-800, 800-1000, 800-900, or 900-1000 µg. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is 60 a total dose of 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 µg. In some embodiments, the effective amount is a dose of 25-500 µg administered to the subject a total of two times. In some embodiments, the effective amount of a respiratory 65 virus RNA (e.g., mRNA) vaccine is a dose of 25-500, 25-400, 25-300, 25-200, 25-100, 25-50, 50-500, 50-400,

50-300, 50-200, 50-100, 100-500, 100-400, 100-300, 100-200, 150-500, 150-400, 150-300, 150-200, 200-500, 200-400, 200-300, 250-500, 250-400, 250-300, 300-500, 300-400, 350-500, 350-400, 400-500 or 450-500 µg administered to the subject a total of two times. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a total dose of 25, 50, 100, 150, 200, 250, 300, 350, 400, 450, or 500 µg administered to the subject a total of two times.

EXAMPLES OF ADDITIONAL EMBODIMENTS OF THE DISCLOSURE

Additional embodiments of the present disclosure are

1. A respiratory virus vaccine, comprising: at least one ribonucleic acid (RNA) polynucleotide having an open reading frame encoding at least one, at least two, at least three, at least four or at least five antigenic polypeptides selected from human metapneumovirus (hMPV) antigenic polypeptides or immunogenic fragments thereof, human parainfluenza virus type 3 (PIV3) antigenic polypeptides or immunogenic fragments thereof, respiratory syncytial virus (RSV) antigenic polypeptides or immunogenic fragments thereof, measles virus (MeV) antigenic polypeptides or immunogenic fragments thereof, and betacoronavirus (Beta-CoV) antigenic polypeptides or immunogenic fragments thereof.

2. The respiratory virus vaccine of paragraph 1, comprising: at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and a PIV3 antigenic polypeptide or an immunogenic fragment thereof; or at least two RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof.

3. The respiratory virus vaccine of paragraph 2, wherein the sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13.

4. The respiratory virus vaccine of paragraph 1, comprising: at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and a RSV antigenic polypeptide or an immunogenic fragment thereof; or

at least two RNA polynucleotides, one having an open immunogenic fragment thereof and one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof.

5. The respiratory virus vaccine of paragraph 4, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8.

6. The respiratory virus vaccine of paragraph 1, comprising: at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and MeV antigenic polypeptide or an immunogenic fragment thereof; or

at least two RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and one having an open 5 reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

7. The respiratory virus vaccine of paragraph 6, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an 10 amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at 15 least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50.

8. The respiratory virus vaccine of paragraph 1, comprising: at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immu- 20 nogenic fragment thereof and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and one having an open 25 reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

9. The respiratory virus vaccine of paragraph 8, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an 30 amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at 35 least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34.

10. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading 40 frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and a RSV antigenic polypeptide or an immunogenic fragment thereof; or

at least two RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an 45 immunogenic fragment thereof and one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof.

11. The respiratory virus vaccine of paragraph 10, wherein the PIV3 antigenic polypeptide comprises an amino acid 50 sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13.

12. The respiratory virus vaccine of paragraph 1, compris- 55 ing:

at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and a MeV antigenic polypeptide or an immunogenic fragment thereof; or 60

at least two RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

13. The respiratory virus vaccine of paragraph 12, wherein the PIV3 antigenic polypeptide comprises an amino acid

sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50.

14. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

- 15. The respiratory virus vaccine of paragraph 14, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID
- NO: 12-13, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34.

16. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof and a MeV antigenic polypeptide or an immunogenic fragment thereof; or

at least two RNA polynucleotides, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

17. The respiratory virus vaccine of paragraph 16, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50.

18. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two RNA polynucleotides, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

19. The respiratory virus vaccine of paragraph 18, wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34.

20. The respiratory virus vaccine of paragraph 1, comprising:

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at least one RNA polynucleotide having an open reading frame encoding a MeV antigenic polypeptide or an immu-

nogenic fragment thereof and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two RNA polynucleotides, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof and one having an open 5 reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

21. The respiratory virus vaccine of paragraph 20, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an 10 amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at 15 least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34.

22. The respiratory virus vaccine of paragraph 1, comprising

at least one RNA polynucleotide having an open reading 20 frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and a RSV antigenic polypeptide or an immunogenic fragment thereof; or

at least two or three RNA polynucleotides, one having an 25 open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a RSV antigenic polypeptide or an 30 immunogenic fragment thereof.

23. The respiratory virus vaccine of paragraph 22, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to 35 an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence 40 open reading frame encoding a hMPV antigenic polypeptide identified by any one of SEQ ID NO: 12-13.

24. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immu- 45 nogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and a MeV antigenic polypeptide or an immunogenic fragment thereof; or

at least two or three RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide 50 or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

25. The respiratory virus vaccine of paragraph 24, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID 60 NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the MeV anti- 65 genic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid

sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50. 26. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two or three RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

27. The respiratory virus vaccine of paragraph 26, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13 and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34. 28. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a MeV antigenic polypeptide or an immunogenic fragment thereof; or

at least two or three RNA polynucleotides, one having an or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

29. The respiratory virus vaccine of paragraph 28, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence 55 identified by any one of SEQ ID NO: 47-50.

30. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two or three RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open

reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

31. The respiratory virus vaccine of paragraph 30, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an 5 amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEO ID NO: 5-8, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34.

32. The respiratory virus vaccine of paragraph 1, comprising

at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two or three RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open 25 reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

33. The respiratory virus vaccine of paragraph 32, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an 30 amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% 35 or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid sequence having at least 90% or 95% identity to an amino 40 acid sequence identified by any one of SEQ ID NO: 23-34. 34. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immu- 45 nogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a MeV antigenic polypeptide or an immunogenic fragment thereof; or

at least two or three RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide 50 or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

35. The respiratory virus vaccine of paragraph 34, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID 60 NO: 12-13, and/or wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50. 65

36. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two or three RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

37. The respiratory virus vaccine of paragraph 36, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one 20 of SEO ID NO: 23-34 or an amino acid sequence having at

least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34.

38. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two or three RNA polynucleotides, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

39. The respiratory virus vaccine of paragraph 38, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34.

40. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two or three RNA polynucleotides, one having an 55 open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

41. The respiratory virus vaccine of paragraph 40, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ

ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid 5 sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34. 42. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading 10 frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a MeV antigenic polypeptide or an immunogenic fragment thereof; 15 having an open reading frame encoding a hMPV antigenic or

at least two, three or four RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic 20 polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

43. The respiratory virus vaccine of paragraph 42, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID 30 NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the MeV anti- 35 genic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50. 44. The respiratory virus vaccine of paragraph 1, compris- 40 ing:

at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic poly- 45 peptide or an immunogenic fragment thereof, and a Beta-CoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two, three or four RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic 50 polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one hav- 55 ing an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

45. The respiratory virus vaccine of paragraph 44, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an 60 amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% 65 or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the BetaCoV

antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 46. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a Beta-CoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two, three or four RNA polynucleotides, one polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

47. The respiratory virus vaccine of paragraph 46, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEO ID NO: 5-8 or an 25 amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34.

48. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two, three or four RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

49. The respiratory virus vaccine of paragraph 48, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90%

or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino 5 acid sequence identified by any one of SEQ ID NO: 24-34. 50. The respiratory virus vaccine of paragraph 1, comprising:

at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or 15

at least two, three or four RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, one having an 20 open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

51. The respiratory virus vaccine of paragraph 50, wherein 25 the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, wherein the MeV antigenic polypeptide com- 30 prises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence 35 identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 52. The respiratory virus vaccine of paragraph 1, compris-40 ing:

at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

at least two, three, four or five RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic 50 polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, one having an 55 open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

53. The respiratory virus vaccine of paragraph 52, wherein 60 the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises 65 an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90%

or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34.

54. The vaccine of any one of paragraphs 1-53, wherein at least one RNA polynucleotide has less than 80% identity to wild-type mRNA sequence.

- 55. The vaccine of any one of paragraphs 1-53, wherein at least one RNA polynucleotide has at least 80% identity to wild-type mRNA sequence, but does not include wild-type mRNA sequence.
- 56. The vaccine of any one of paragraphs 1-55, wherein at least one antigenic polypeptide has membrane fusion activity, attaches to cell receptors, causes fusion of viral and cellular membranes, and/or is responsible for binding of the virus to a cell being infected.
- 57. The vaccine of any one of paragraphs 1-56, wherein at least one RNA polynucleotide comprises at least one chemical modification.
- 58. The vaccine of paragraph 57, wherein the chemical modification is selected from pseudouridine, N1-methylpseudouridine, N1-ethylpseudouridine, 2-thiouridine, 4'-thiouridine, 5-methylcyto sine, 5-methyluridine, 2-thio-1methyl-1-deaza-pseudouridine, 2-thio-1-methylpseudouridine, 2-thio-5-aza-uridine, 2-thiodihydropseudouridine, 2-thio-dihydrouridine, 2-thio-
- pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyl uridine.
- 59. The vaccine of paragraph 57 or 58, wherein the chemical modification is in the 5-position of the uracil.

60. The vaccine of any one of paragraphs 57-59, wherein the chemical modification is a N1-methylpseudouridine or N1-ethylpseudouridine.

61. The vaccine of any one of paragraphs 57-60, wherein at least 80%, at least 90% or 100% of the uracil in the open reading frame have a chemical modification.

62. The vaccine of any one of paragraphs 1-61, wherein at least one RNA polynucleotide further encodes at least one 5' terminal cap, optionally wherein the 5' terminal cap is 7mG(5')ppp(5')NImpNp.

63. The vaccine of any one of paragraphs 1-62, wherein at least one antigenic polypeptide or immunogenic fragment thereof is fused to a signal peptide selected from: a HuIgGk signal peptide (METPAQLLFLLLWLPDTTG; SEQ ID NO: 15); IgE heavy chain epsilon-1 signal peptide (MD-WTWILFLVAAATRVHS; SEQ ID NO: 16); Japanese encephalitis PRM signal sequence (MLGSNSGQRV-VFTILLLLVAPAYS; SEQ ID NO: 17), VSVg protein signal sequence (MKCLLYLAFLFIGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWLVS-LAIVTACAGA; SEQ ID NO: 19).

64. The vaccine of paragraph 63, wherein the signal peptide is fused to the N-terminus or the C-terminus of at least one antigenic polypeptide.

65. The vaccine of any one of paragraphs 1-64, wherein the antigenic polypeptide or immunogenic fragment thereof comprises a mutated N-linked glycosylation site.

66. The vaccine of any one of paragraphs 1-65 formulated in a nanoparticle, optionally a a lipid nanoparticle.

67. The vaccine of paragraph 66, wherein the lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid; optionally wherein the lipid 5 nanoparticle carrier comprises a molar ratio of about 20-60% cationic lipid, 0.5-15% PEG-modified lipid, 25-55% sterol, and 25% non-cationic lipid; optionally wherein the cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid, and the sterol is a 10 cholesterol; and optionally wherein the cationic lipid is selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate 15 (L319). Formula (II) 68. The vaccine of paragraph 66 or 67, wherein the nanoparticle (e.g., lipid nanoparticle) comprises a compound of Formula (I) and/or Formula (II), optionally Compound 3, 18, 20, 25, 26, 29, 30, 60, 108-112, or 122. 69. The vaccine of any one of paragraphs 1-68 further 20 comprising an adjuvant, optionally a flagellin protein or peptide that optionally comprises an amino acid sequence identified by any one of SEQ ID NO: 54-56.

70. The vaccine of any one of paragraphs 1-69, wherein the open reading frame is codon-optimized.

71. The vaccine of any one of paragraphs 1-70 formulated in an effective amount to produce an antigen-specific immune response.

72. A method of inducing an immune response in a subject, the method comprising administering to the subject the 30 vaccine of any one of paragraphs 1-71 in an amount effective to produce an antigen-specific immune response in the subject.

73. The method of paragraph 72, wherein the subject is administered a single dose of the vaccine, or wherein the 35 subject is administered a first dose and then a booster dose of the vaccine.

74. The method of paragraph 72 or 73, wherein the vaccine is administered to the subject by intradermal injection or intramuscular injection.

75. The method of any one of paragraphs 72-74, wherein an anti-antigenic polypeptide antibody titer produced in the subject is increased by at least 1 log relative to a control, and/or wherein the anti-antigenic polypeptide antibody titer produced in the subject is increased at least 2 times relative 45 to a control.

76. The method of any one of paragraphs 72-75, wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has not been administered a vaccine against the virus, and/or wherein the control is an anti- 50 antigenic polypeptide antibody titer produced in a subject who has been administered a live attenuated vaccine or an inactivated vaccine against the virus, and/or, wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a recombinant 55 protein vaccine or purified protein vaccine against the virus, and/or wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a VLP vaccine against the virus.

77. The method of any one of paragraphs 72-76, wherein the 60 effective amount is a dose equivalent to an at least 2-fold reduction in the standard of care dose of a recombinant protein vaccine or a purified protein vaccine against the virus, and wherein an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-anti- 65 genic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant

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protein vaccine or a purified protein vaccine against the virus, respectively; and/or wherein the effective amount is a dose equivalent to an at least 2-fold reduction in the standard of care dose of a live attenuated vaccine or an inactivated vaccine against the virus, and wherein an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a live attenuated vaccine or an inactivated vaccine against the virus, respectively; and/or wherein the effective amount is a dose equivalent to an at least 2-fold reduction in the standard of care dose of a VLP vaccine against the virus, and wherein an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a VLP vaccine against the virus.

78. The method of any one of paragraphs 72-77, wherein the effective amount is a total dose of 50 µg-1000 µg, optionally wherein the effective amount is a dose of 25 μ g, 100 μ g, 400 μ g, or 500 μ g administered to the subject a total of two times. 79. The method of any one of paragraphs 72-78, wherein the efficacy of the vaccine against the virus is greater than 65%; and/or wherein the vaccine immunizes the subject against the virus for up to 2 years or wherein the vaccine immunizes the subject against the virus for more than 2 years.

80. The method of any one of paragraphs 72-79, wherein the subject has an age of about 5 years old or younger or wherein the subject has an age of about 60 years old or older; and/or wherein the subject has a chronic pulmonary disease; and/or the subject has been exposed to the virus, wherein the subject is infected with the virus, or wherein the subject is at risk of infection by the virus; and/or wherein the subject is immunocompromised.

81. The respiratory virus vaccine of any one of paragraphs 1-71, comprising at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide having an 40 open reading frame encoding at least one (e.g., at least two, at least three, at least four, or at least five) antigenic polypeptide selected from hMPV antigenic polypeptides (SEQ ID NO: 5-8), PIV3 antigenic polypeptides (SEQ ID NO: 12-13), RSV antigenic polypeptides, MeV antigenic polypeptides (SEQ ID NO: 47-50) and BetaCoV antigenic polypeptides (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1; (SEQ ID NO: 24-34)), formulated in a cationic lipid nanoparticle

(a) having a molar ratio of about 20-60% cationic lipid, about 5-25% non-cationic lipid, about 25-55% sterol, and about 0.5-15% PEG-modified lipid, and/or

(b) comprising a compound of Formula (I) and/or Formula (II),

wherein the at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide comprises at least one chemical modification.

82. The respiratory virus vaccine of any one of paragraphs 1-71, comprising at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide having an open reading frame encoding at least one (e.g., at least two, at least three, at least four, or at least five) antigenic polypeptide selected from hMPV antigenic polypeptides (SEQ ID NO: 5-8), PIV3 antigenic polypeptides (SEQ ID NO: 12-13), RSV antigenic polypeptides, MeV antigenic polypeptides (SEQ ID NO: 47-50) and BetaCoV antigenic polypeptides (e.g., MERS-CoV, SARS-CoV, HCoV-OC43,

HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1; (SEQ ID NO: 24-34)), formulated in a cationic lipid nanoparticle

(a) having a molar ratio of about 20-60% cationic lipid, about 5-25% non-cationic lipid, about 25-55% sterol, and 5 about 0.5-15% PEG-modified lipid, and/or

(b) comprising at least one (e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14) Compound selected from Compounds 3, 18, 20, 25, 26, 29, 30, 60, 108-112 and 122. 83. The respiratory virus vaccine of paragraphs 81 or 82, wherein the at least one antigenic polypeptide is selected from hMPV antigentic polypeptides (e.g., SEQ ID NO: 5-8). 84. The respiratory virus vaccine of any one of paragraphs 81-83, wherein the at least one antigenic polypeptide is 15 selected from PIV3 antigentic polypeptides (e.g., SEQ ID NO: 12-13).

85. The respiratory virus vaccine of any one of paragraphs 81-84, wherein the at least one antigenic polypeptide is selected from RSV antigentic polypeptides.

86. The respiratory virus vaccine of any one of paragraphs 81-85, wherein the at least one antigenic polypeptide is selected from MeV antigentic polypeptides (e.g., SEQ ID NO: 47-50).

87. The respiratory virus vaccine of any one of paragraphs 25 81-86, wherein the at least one antigenic polypeptide is selected from BetaCoV antigentic polypeptides (e.g., SEQ ID NO: 24-34).

88. The respiratory virus vaccine of paragraph 87, wherein the BetaCoV antigentic polypeptides are MERS antigentic polypeptides.

89. The respiratory virus vaccine of paragraph 87, wherein the BetaCoV antigentic polypeptides are SARS antigentic polypeptides.

35 90. The respiratory virus vaccine of any one of paragraphs 81-89, wherein the at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide comprises at least one chemical modification (e.g., selected from pseudouridine, N1-methylpseudouridine, N1-ethylp- 40 seudouridine, 2-thiouridine, 4'-thiouridine, 5-methylcvtosine, 5-methyluridine, 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-4-methoxy-2-thio-pseudouridine, 45 pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyl uridine).

91. A respiratory virus vaccine, comprising:

at least one messenger ribonucleic acid (mRNA) poly- 50 nucleotide having a 5' terminal cap, an open reading frame encoding at least one respiratory virus antigenic polypeptide, and a 3' polyA tail.

92. The vaccine of paragraph 91, wherein the at least one mRNA polynucleotide comprises a sequence identified by 55 any one of SEQ ID NO: 57-80.

93. The vaccine of paragraph 91 or 92, wherein the 5' terminal cap is or comprises 7mG(5')ppp(5')NlmpNp. 94. The vaccine of any one of paragraphs 91-93, wherein 100% of the uracil in the open reading frame is modified to 60 include N1-methyl pseudouridine at the 5-position of the uracil.

95. The vaccine of any one of paragraphs 91-94, wherein the vaccine is formulated in a lipid nanoparticle comprising: DLin-MC3-DMA; cholesterol; 1,2-Distearoyl-sn-glycero-3- 65 phosphocholine (DSPC); and polyethylene glycol (PEG) 2000-DMG.

96. The vaccine of paragraph 95, wherein the lipid nanoparticle further comprises trisodium citrate buffer, sucrose and water.

97. A respiratory syncytial virus (RSV) vaccine, comprising: at least one messenger ribonucleic acid (mRNA) polynucleotide having a 5' terminal cap 7mG(5')ppp(5')NlmpNp, a sequence identified by any one of SEO ID NO: 57-80 and a 3' polyA tail, formulated in a lipid nanoparticle comprising DLin-MC3-DMA, cholesterol, 1,2-Distearoyl-sn-glycero-3phosphocholine (DSPC), and polyethylene glycol (PEG) 2000-DMG, wherein the uracil nucleotides of the sequence identified by any one of SEQ ID NO: 57-80 are modified to include N1-methyl pseudouridine at the 5-position of the uracil nucleotide.

This disclosure is not limited in its application to the details of construction and the arrangement of components set forth in the following description or illustrated in the drawings. The disclosure is capable of other embodiments 20 and of being practiced or of being carried out in various ways. Also, the phraseology and terminology used herein is for the purpose of description and should not be regarded as limiting. The use of "including," "comprising," or "having," "containing," "involving," and variations thereof herein, is meant to encompass the items listed thereafter and equivalents thereof as well as additional items.

EXAMPLES

Example 1: Manufacture of Polynucleotides

According to the present disclosure, the manufacture of polynucleotides and/or parts or regions thereof may be accomplished utilizing the methods taught in International Publication WO2014/152027, entitled "Manufacturing Methods for Production of RNA Transcripts," the contents of which is incorporated herein by reference in its entirety.

Purification methods may include those taught in International Publication WO2014/152030 and International Publication WO2014/152031, each of which is incorporated herein by reference in its entirety.

Detection and characterization methods of the polynucleotides may be performed as taught in International Publication WO2014/144039, which is incorporated herein by reference in its entirety.

Characterization of the polynucleotides of the disclosure may be accomplished using polynucleotide mapping, reverse transcriptase sequencing, charge distribution analysis, detection of RNA impurities, or any combination of two or more of the foregoing. "Characterizing" comprises determining the RNA transcript sequence, determining the purity of the RNA transcript, or determining the charge heterogeneity of the RNA transcript, for example. Such methods are taught in, for example, International Publication WO2014/ 144711 and International Publication WO2014/144767, the content of each of which is incorporated herein by reference in its entirety.

Example 2: Chimeric Polynucleotide Synthesis

According to the present disclosure, two regions or parts of a chimeric polynucleotide may be joined or ligated using triphosphate chemistry. A first region or part of 100 nucleotides or less is chemically synthesized with a 5' monophosphate and terminal 3'desOH or blocked OH, for example. If the region is longer than 80 nucleotides, it may be synthesized as two strands for ligation.

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If the first region or part is synthesized as a non-positionally modified region or part using in vitro transcription (IVT), conversion the 5'monophosphate with subsequent capping of the 3' terminus may follow.

Monophosphate protecting groups may be selected from 5 any of those known in the art.

The second region or part of the chimeric polynucleotide may be synthesized using either chemical synthesis or IVT methods. IVT methods may include an RNA polymerase that can utilize a primer with a modified cap. Alternatively, a cap of up to 130 nucleotides may be chemically synthesized and coupled to the IVT region or part.

For ligation methods, ligation with DNA T4 ligase, followed by treatment with DNase should readily avoid con-15 catenation.

The entire chimeric polynucleotide need not be manufactured with a phosphate-sugar backbone. If one of the regions or parts encodes a polypeptide, then such region or part may comprise a phosphate-sugar backbone.

Ligation is then performed using any known click chemistry, orthoclick chemistry, solulink, or other bioconjugate chemistries known to those in the art.

Synthetic Route

The chimeric polynucleotide may be made using a series ²⁵ of starting segments. Such segments include:

(a) a capped and protected 5' segment comprising a normal 3'OH (SEG. 1)

(b) a 5' triphosphate segment, which may include the coding region of a polypeptide and a normal 3'OH (SEG. 2) ³⁰

(c) a 5' monophosphate segment for the 3' end of the chimeric polynucleotide (e.g., the tail) comprising cordycepin or no 3'OH (SEG. 3)

After synthesis (chemical or IVT), segment 3 (SEG. 3) may be treated with cordycepin and then with pyrophos- ³⁵ phatase to create the 5' monophosphate.

Segment 2 (SEG. 2) may then be ligated to SEG. 3 using RNA ligase. The ligated polynucleotide is then purified and treated with pyrophosphatase to cleave the diphosphate.

The treated SEG.2-SEG. 3 construct may then be purified 40 and SEG. 1 is ligated to the 5' terminus. A further purification step of the chimeric polynucleotide may be performed.

Where the chimeric polynucleotide encodes a polypeptide, the ligated or joined segments may be represented as: 5'UTR (SEG. 1), open reading frame or ORF (SEG. 2) and 45 3'UTR+PolyA (SEG. 3).

The yields of each step may be as much as 90-95%.

Example 3: PCR for cDNA Production

PCR procedures for the preparation of cDNA may be performed using $2\times$ KAPA HIFITM HotStart ReadyMix by Kapa Biosystems (Woburn, Mass.). This system includes $2\times$ KAPA ReadyMix 12.5 µl; Forward Primer (10 µM) 0.75 µl; Reverse Primer (10 PM) 0.75 µl; Template cDNA 100 ng; 55 and dH₂O diluted to 25.0 µl. The reaction conditions may be at 95° C. for 5 min. The reaction may be performed for 25 cycles of 98° C. for 20 sec, then 58° C. for 15 sec, then 72° C. for 45 sec, then 72° C. for 5 min, then 4° C. to termination. 60

The reaction may be cleaned up using Invitrogen's PURELINKTM PCR Micro Kit (Carlsbad, Calif.) per manufacturer's instructions (up to 5 μ g). Larger reactions may require a cleanup using a product with a larger capacity. Following the cleanup, the cDNA may be quantified using 65 the NANODROPTM and analyzed by agarose gel electrophoresis to confirm that the cDNA is the expected size. The

cDNA may then be submitted for sequencing analysis before proceeding to the in vitro transcription reaction.

Example 4: In Vitro Transcription (IVT)

The in vitro transcription reaction generates RNA polynucleotides. Such polynucleotides may comprise a region or part of the polynucleotides of the disclosure, including chemically modified RNA (e.g., mRNA) polynucleotides. The chemically modified RNA polynucleotides can be uniformly modified polynucleotides. The in vitro transcription reaction utilizes a custom mix of nucleotide triphosphates (NTPs). The NTPs may comprise chemically modified NTPs, or a mix of natural and chemically modified NTPs, or natural NTPs.

A typical in vitro transcription reaction includes the following:

| 1) | Template cDNA | 1.0 µg |
|----|--|---------------------------|
| 2) | 10x transcription buffer | 2.0 μl |
| | (400 mM Tris-HCl pH 8.0, 190 mM | |
| | MgCl ₂ , 50 mM DTT, 10 mM Spermidine) | |
| 3) | Custom NTPs (25 mM each) | 0.2 μl |
| 4) | RNase Inhibitor | 20 U |
| 5) | T7 RNA polymerase | 3000 U |
| 6) | dH ₂ 0 | up to $20.0 \ \mu$ l. and |
| 7) | Incubation at 37° C. for 3 hr-5 hrs. | |

The crude IVT mix may be stored at 4° C. overnight for cleanup the next day. 1 U of RNase-free DNase may then be used to digest the original template. After 15 minutes of incubation at 37° C., the mRNA may be purified using Ambion's MEGACLEARTM Kit (Austin, Tex.) following the manufacturer's instructions. This kit can purify up to 500 μ g of RNA. Following the cleanup, the RNA polynucleotide may be quantified using the NanoDrop and analyzed by agarose gel electrophoresis to confirm the RNA polynucle-otide is the proper size and that no degradation of the RNA has occurred.

Example 5: Enzymatic Capping

Capping of a RNA polynucleotide is performed as follows where the mixture includes: IVT RNA 60 μ g-180 μ g and dH₂O up to 72 μ l. The mixture is incubated at 65° C. for 5 minutes to denature RNA, and then is transferred immediately to ice.

The protocol then involves the mixing of $10\times$ Capping Buffer (0.5 M Tris-HCl (pH 8.0), 60 mM KCl, 12.5 mM MgCl₂) (10.0 µl); 20 mM GTP (5.0 µl); 20 mM S-Adenosyl Methionine (2.5 µl); RNase Inhibitor (100 U); 2'-O-Methyltransferase (400U); Vaccinia capping enzyme (Guanylyl transferase) (40 U); dH₂O (Up to 28 µl); and incubation at 37° C. for 30 minutes for 60 µg RNA or up to 2 hours for 180 µg of RNA.

The RNA polynucleotide may then be purified using Ambion's MEGACLEAR[™] Kit (Austin, Tex.) following
⁵⁵ the manufacturer's instructions. Following the cleanup, the RNA may be quantified using the NANODROP[™] (ThermoFisher, Waltham, Mass.) and analyzed by agarose gel electrophoresis to confirm the RNA polynucleotide is the proper size and that no degradation of the RNA has
⁶⁰ occurred. The RNA polynucleotide product may also be sequenced by running a reverse-transcription-PCR to generate the cDNA for sequencing.

Example 6: PolyA Tailing Reaction

Without a poly-T in the cDNA, a poly-A tailing reaction must be performed before cleaning the final product. This is

done by mixing capped IVT RNA (100 µl); RNase Inhibitor (20 U); 10x Tailing Buffer (0.5 M Tris-HCl (pH 8.0), 2.5 M NaCl, 100 mM MgCl₂) (12.0 µl); 20 mM ATP (6.0 µl); Poly-A Polymerase (20 U); dH₂O up to 123.5 µl and incubation at 37° C. for 30 min. If the poly-A tail is already 5 in the transcript, then the tailing reaction may be skipped and proceed directly to cleanup with Ambion's MEGA-CLEAR™ kit (Austin, Tex.) (up to 500 µg). Poly-A Polymerase may be a recombinant enzyme expressed in yeast.

It should be understood that the processivity or integrity of the polyA tailing reaction may not always result in an exact size polyA tail. Hence, polyA tails of approximately between 40-200 nucleotides, e.g., about 40, 50, 60, 70, 80, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 15 104, 105, 106, 107, 108, 109, 110, 150-165, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164 or 165 are within the scope of the present disclosure.

Example 7: Natural 5' Caps and 5' Cap Analogues

5'-capping of polynucleotides may be completed concomitantly during the in vitro-transcription reaction using the following chemical RNA cap analogs to generate the 5'-guanosine cap structure according to manufacturer pro- 25 tocols: 3'-O-Me-m7G(5')ppp(5') G [the ARCA cap];G(5') ppp(5')A; G(5')ppp(5')G; m7G(5')ppp(5')A; m7G(5')ppp (5')G (New England BioLabs, Ipswich, Mass.). 5'-capping of modified RNA may be completed post-transcriptionally using a Vaccinia Virus Capping Enzyme to generate the 30 "Cap 0" structure: m7G(5')ppp(5')G (New England Bio-Labs, Ipswich, Mass.). Cap 1 structure may be generated using both Vaccinia Virus Capping Enzyme and a 2'-O methyl-transferase to generate: m7G(5')ppp(5')G-2'-O-35 methyl. Cap 2 structure may be generated from the Cap 1 structure followed by the 2'-O-methylation of the 5'-antepenultimate nucleotide using a 2'-O methyl-transferase. Cap 3 structure may be generated from the Cap 2 structure followed by the 2'-O-methylation of the 5'-preantepenulti- $_{40}$ mate nucleotide using a 2'-0 methyl-transferase. Enzymes are preferably derived from a recombinant source.

When transfected into mammalian cells, the modified mRNAs have a stability of between 12-18 hours or more than 18 hours, e.g., 24, 36, 48, 60, 72 or greater than 72 45 hours

Example 8: Capping Assays

Protein Expression Assay

Polynucleotides (e.g., mRNA) encoding a polypeptide, containing any of the caps taught herein, can be transfected into cells at equal concentrations. The amount of protein secreted into the culture medium can be assayed by ELISA at 6, 12, 24 and/or 36 hours post-transfection. Synthetic 55 polynucleotides that secrete higher levels of protein into the medium correspond to a synthetic polynucleotide with a higher translationally-competent cap structure. Purity Analysis Synthesis

RNA (e.g., mRNA) polynucleotides encoding a polypep- 60 tide, containing any of the caps taught herein can be compared for purity using denaturing Agarose-Urea gel electrophoresis or HPLC analysis. RNA polynucleotides with a single, consolidated band by electrophoresis correspond to the higher purity product compared to polynucleotides with 65 multiple bands or streaking bands. Chemically modified RNA polynucleotides with a single HPLC peak also corre-

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spond to a higher purity product. The capping reaction with a higher efficiency provides a more pure polynucleotide population.

Cytokine Analysis

RNA (e.g., mRNA) polynucleotides encoding a polypeptide, containing any of the caps taught herein can be transfected into cells at multiple concentrations. The amount of pro-inflammatory cytokines, such as TNF-alpha and IFNbeta, secreted into the culture medium can be assayed by ELISA at 6, 12, 24 and/or 36 hours post-transfection. RNA polynucleotides resulting in the secretion of higher levels of pro-inflammatory cytokines into the medium correspond to a polynucleotides containing an immune-activating cap structure.

Capping Reaction Efficiency

RNA (e.g., mRNA) polynucleotides encoding a polypeptide, containing any of the caps taught herein can be analyzed for capping reaction efficiency by LC-MS after nucle-20 ase treatment. Nuclease treatment of capped polynucleotides yield a mixture of free nucleotides and the capped 5'-5triphosphate cap structure detectable by LC-MS. The amount of capped product on the LC-MS spectra can be expressed as a percent of total polynucleotide from the reaction and correspond to capping reaction efficiency. The cap structure with a higher capping reaction efficiency has a higher amount of capped product by LC-MS.

> Example 9: Agarose Gel Electrophoresis of Modified RNA or RT PCR Products

Individual RNA polynucleotides (200-400 ng in a 20 µl volume) or reverse transcribed PCR products (200-400 ng) may be loaded into a well on a non-denaturing 1.2% Agarose E-Gel (Invitrogen, Carlsbad, Calif.) and run for 12-15 minutes, according to the manufacturer protocol.

> Example 10: Nanodrop Modified RNA Quantification and UV Spectral Data

Chemically modified RNA polynucleotides in TE buffer (1 µl) are used for Nanodrop UV absorbance readings to quantitate the yield of each polynucleotide from an chemical synthesis or in vitro transcription reaction.

Example 11: Formulation of Modified mRNA Using Lipidoids

RNA (e.g., mRNA) polynucleotides may be formulated 50 for in vitro experiments by mixing the polynucleotides with the lipidoid at a set ratio prior to addition to cells. In vivo formulation may require the addition of extra ingredients to facilitate circulation throughout the body. To test the ability of these lipidoids to form particles suitable for in vivo work, a standard formulation process used for siRNA-lipidoid formulations may be used as a starting point. After formation of the particle, polynucleotide is added and allowed to integrate with the complex. The encapsulation efficiency is determined using a standard dye exclusion assays.

Example 12: Immunogenicity Study

The instant study is designed to test the immunogenicity in mice of candidate hMPV vaccines comprising a mRNA polynucleotide encoding Fusion (F) glycoprotein, major surface glycoprotein G, or a combination thereof, obtained from hMPV.

Mice are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) with candidate vaccines. Candidate vaccines are chemically modified or unmodified. A total of four immunizations are given at 3-week intervals (i.e., at weeks 0, 3, 6, and 9), and sera are collected after each ⁵ immunization until weeks 33-51. Serum antibody titers against Fusion (F) glycoprotein or major surface glycoprotein (G) protein are determined by ELISA. Sera collected from each mouse during weeks 10-16 are pooled, and total IgG purified. Purified antibodies are used for immunoelectron microscopy, antibody-affinity testing, and in vitro protection assays.

Example 13: hMPV Rodent Challenge

The instant study is designed to test the efficacy in cotton rats of candidate hMPV vaccines against a lethal challenge using an hMPV vaccine comprising mRNA encoding Fusion (F) glycoprotein, major surface glycoprotein G, or a combination of both antigens obtained from hMPV. Cotton rats are challenged with a lethal dose of the hMPV.

Animals are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) at week 0 and week 3 with candidate hMPV vaccines with and without adjuvant. Can-25 didate vaccines are chemically modified or unmodified. The animals are then challenged with a lethal dose of hMPV on week 7 via IV, IM or ID. Endpoint is day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or ³⁰ paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios ³⁵ 50:10:1.5:38.5. The cationic lipid is DLin-KC2-DMA (50 mol %) or DLin-MC3-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DOMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example. 40

Example 14: Immunogenicity of hMPV mRNA Vaccine in BALB/c Mice

The instant study was designed to test the immunogenic- 45 ity in BALB/c mice of hMPV vaccines comprising an mRNA polynucleotide encoding the hMPV Fusion (F) glycoprotein. The mRNA polynucleotide encodes the fulllength fusion protein and comprises the wild-type nucleotide sequence obtained from the hMPV A2a strain. Mice were 50 divided into 3 groups (n=8 for each group) and immunized intramuscularly (IM) with PBS, a 10 µg dose of mRNA vaccines encoding hMPV fusion protein, or a 2 µg dose of mRNA vaccines encoding hMPV fusion protein. A total of two immunizations were given at 3-week intervals (i.e., at 55 weeks 0, and 3 weeks), and sera were collected after each immunization according to the schedule described in Table 1. Serum antibody titers against hMPV fusion glycoprotein were determined by ELISA and antibodies were detected in the sera collected on day 14 onward. Both vaccine doses 60 tested induced comparable levels of immune response in mice (FIGS. 2A-2C).

Additionally, mice sera were used for IgG isotyping (FIGS. **3A-3**C). Both hMPV fusion protein-specific IgG1 and IgG2a were detected in mice sera. hMPV fusion protein 65 mRNA vaccine also induced Th1 and Th2 cytokine responses, with a Th1 bias.

Sera from mice immunized with either $10 \mu g$ or $2 \mu g$ doses of the hMPV fusion protein mRNA vaccine contain neutralizing antibodies. The ability of these antibodies to neutralize hMPV B2 strain was also tested. The antibody-containing sera successfully neutralized the hMPV B2 virus (FIG. 4).

Example 15: T-Cell Stimulation

The instant study was designed to test T-cell stimulation in the splenocytes of mice immunized with mRNA vaccines encoding hMPV fusion protein, as described herein. Immunization of BALB/c mice was performed as described in Example 14. The splenocytes for each group were pooled and split into two parts. One part of splenocytes from each group of mice was stimulated with hMPV-free media, Con-¹⁵ canavalin A or a hMPV fusion protein peptide pool comprising 15-mers (15 amino acids long); while the other part of splenocytes from each group of mice was stimulated with hMPV-free media, Concanavalin A or inactivated hMPV virus. Secreted mouse cytokines were measured using the 20 Meso Scale Discovery (MSD) assay.

Cytokines specific to Th1 or Th2 responses were measured. For Th1 response, IFN- γ , IL2 and IL12 were detected from splenocytes stimulated with the hMPV fusion protein peptide pool at a level comparable to that of Concanavalin A (FIGS. **5A-5**C). For a Th2 response, the hMPV fusion protein peptide pool induced the secretion of detectable IL10, TNF- α , IL4 and IL, but not IL5, while Concanavalin A stimulated the secretion of all the above-mentioned Th2 cytokines (FIGS. **6A-6**E) at a much higher level.

In contrast, inactivated hMPV virus only induced the secretion of IL2 in the Th1 response comparable to that of Concanavalin A (FIGS. 7A-7C). For the Th2 response, the inactivated hMPV virus induced the secretion of detectable IL10, TNF- α , IL4 and IL6, but not IL5, while Concanavalin A stimulated the secretion of all the above-mentioned Th2 cytokines (FIGS. 8A-8E) at a much higher level.

Example 16: hMPV Rodent Challenge in Cotton Rats Immunized with mRNA Vaccine Encoding hMPV Fusion Protein

The instant study was designed to test the efficacy in cotton rats of hMPV vaccines against a lethal challenge. mRNA vaccines encoding hMPV fusion protein were used. The mRNA polynucleotide encodes a full-length fusion protein and comprises the wild-type nucleotide sequence obtained from the hMPV A2a strain.

Cotton rats were immunized intramuscularly (IM) at week 0 and week 3 with the mRNA vaccines encoding hMPV fusion protein with either 2 μ g or 10 μ g doses for each immunization. The animals were then challenged with a lethal dose of hMPV in week 7 post initial immunization via IV, IM or ID. The endpoint was day 13 post infection, death or euthanasia. Viral titers in the noses and lungs of the cotton rats were measured. The results (FIGS. 9A and 9B) show that a 10 μ g dose of mRNA vaccine protected the cotton mice 100% in the lung and drastically reduced the viral titer in the nose after challenge (~2 log reduction). Moreover, a 2 μ g dose of mRNA vaccine showed a 1 log reduction in lung viral titer in the cotton mice challenged.

Further, the histopathology of the lungs of the cotton mice immunized and challenged showed no pathology associated with vaccine-enhanced disease (FIG. **10**).

Example 17: Immunogenicity Study

The instant study is designed to test the immunogenicity in mice of candidate PIV3 vaccines comprising a mRNA

polynucleotide encoding hemagglutinin-neuraminidase or fusion protein (F or F0) obtained from PIV3.

Mice are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) with candidate vaccines. Candidate vaccines are chemically modified or unmodified. A ⁵ total of four immunizations are given at 3-week intervals (i.e., at weeks 0, 3, 6, and 9), and sera are collected after each immunization until weeks 33-51. Serum antibody titers against hemagglutinin-neuraminidase or fusion protein (F or F0) are determined by ELISA. Sera collected from each ¹⁰ mouse during weeks 10-16 are, optionally, pooled, and total IgGs are purified. Purified antibodies are used for immunoelectron microscopy, antibody-affinity testing, and in vitro protection assays.

Example 18: PIV3 Rodent Challenge

The instant study is designed to test the efficacy in cotton rats of candidate PIV3 vaccines against a lethal challenge 20 using a PIV3 vaccine comprising mRNA encoding hemagglutinin-neuraminidase or fusion protein (F or F0) obtained from PIV3. Cotton rats are challenged with a lethal dose of the PIV3.

Animals are immunized intravenously (IV), intramuscu- 25 larly (IM), or intradermally (ID) at week 0 and week 3 with candidate PIV3 vaccines with and without adjuvant. Candidate vaccines are chemically modified or unmodified. The animals are then challenged with a lethal dose of PIV3 on week 7 via IV, IM or ID. Endpoint is day 13 post infection, ³⁰ death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

In experiments where a lipid nanoparticle (LNP) formu-³⁵ lation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DLin-KC2-DMA (50 mol %) or DLin-MC3-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DOMG (1.5 40 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

Example 19: hMPV/PIV Cotton Rat Challenge

The instant study was designed to test the efficacy in cotton rats of candidate hMPV mRNA vaccines, PIV3 mRNA vaccines, or hMPV/PIV combination mRNA vaccines against a lethal challenge using PIV3 strain or hMPV/A2 strain. The study design is shown in Table 9.

Cotton rats of 10-12 weeks old were divided into 12 groups (n=5), and each group was vaccinated with mRNA vaccines indicated in Table 9. The PIV3 vaccine comprises mRNA encoding hemagglutinin-neuraminidase or fusion protein (F or F0) obtained from PIV3. The hMPV mRNA 55 vaccine encodes the full-length hMPV fusion protein. The hMPV/PIV combination mRNA vaccine is a mixture of the PIV3 vaccine and hMPV vaccine at a 1:1 ratio.

Cotton rats were immunized intramuscularly (IM) at week 0 and week 3 with candidate vaccines with the doses 60 indicated in Table 9. Cotton rats immunized with hMPV mRNA vaccines or hMPV/PIV combination mRNA vaccines were challenged with a lethal dose of hMPV/A2 strain on week 7 via IM. Cotton rats immunized with PIV mRNA vaccines or hMPV/PIV combination mRNA vaccines were 65 challenged with a lethal dose of PIV3 strain on week 7 via IM.

The endpoint was day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis were euthanized. Body temperature and weight were assessed and recorded daily.

Lung and nose hMPV/A2 (FIG. 12) or PIV3 (FIG. 13) viral titers were assessed. Lung histopathology of the immunized and challenged cotton rat immunized and challenged were assessed to determine pathology associated with vaccine enhance disease. Neutralization antibody titers in the serum of immunized cotton rats on day 0 and 42 post immunization were assessed (FIG. 11).

hMPV/A2 (FIG. 14) or PIV3 (FIG. 15) neutralizing antibody titers in the serum samples of the immunized ¹⁵ cotton rat 42 days post immunization were measured. All mRNA vaccines tested induced strong neutralizing antibodies cotton rats. Lung histopathology of the immunized cotton rats were also evaluated (FIG. 16). Low occurrence of alevolitis and interstitial pneumonia was observed, indicat-²⁰ ing no antibody-dependent enhancement (ADE) of hMPV or PIV associated diseases.

Example 20: Betacoronavirus Immunogenicity Study

The instant study is designed to test the immunogenicity in rabbits of candidate betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1 or a combination thereof) vaccines comprising a mRNA polynucleotide encoding the spike (S) protein, the S1 subunit (S1) of the spike protein, or the S2 subunit (S2) of the spike protein obtained from a betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1).

Rabbits are vaccinated on week 0 and 3 via intravenous (IV), intramuscular (IM), or intradermal (ID) routes. One group remains unvaccinated and one is administered inactivated betacoronavirus. Serum is collected from each rabbit on weeks 1, 3 (pre-dose) and 5. Individual bleeds are tested for anti-S1 or anti-S2 activity via a virus neutralization assay from all three time points, and pooled samples from week 5 only are tested by Western blot using inactivated betacoronavirus (e.g., inactivated MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1).

In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DLin-KC2-DMA (50 mol %) or DLin-MC3-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DOMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

Example 21: Betacoronavirus Challenge

The instant study is designed to test the efficacy in rabbits of candidate betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-HKU1 or a combination thereof) vaccines against a lethal challenge using a betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-HKU1 or a combination thereof) vaccine comprising mRNA encoding the spike (S) protein, the S1 subunit (S1) of the spike protein, or the S2 subunit (S2) of the spike protein obtained from betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1). Rabbits are challenged with a lethal dose (10xLD90; ~100 plaque-forming units; PFU) of betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1).

The animals used are 6-8 week old female rabbits in groups of 10. Rabbits are vaccinated on weeks 0 and 3 via an IM, ID or IV route of administration. Candidate vaccines are chemically modified or unmodified. Rabbit serum is tested for microneutralization (see Example 14). Rabbits are ¹⁰ then challenged with ~1 LD90 of betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1) on week 7 via an IN, IM, ID or IV route of administration. Endpoint is day 13 post infection, death or euthanasia. ¹⁵ Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

Example 22: Microneutralization Assay

Nine serial 2-fold dilutions (1:50-1:12,800) of rabbit serum are made in 50 µl virus growth medium (VGM) with trypsin in 96 well microtiter plates. Fifty microliters of virus 25 containing ~50 pfu of betacoronavirus (e.g., MERS-CoV, SARS-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1) is added to the serum dilutions and allowed to incubate for 60 minutes at room temperature (RT). Positive control wells of virus 30 without sera and negative control wells without virus or sera are included in triplicate on each plate. While the serumvirus mixtures incubate, a single cell suspension of Madin-Darby Canine-Kidney cells are prepared by trypsinizing (Gibco 0.5% bovine pancrease trypsin in EDTA) a confluent 35 monolayer and suspended cells are transferred to a 50 ml centrifuge tube, topped with sterile PBS and gently mixed. The cells are then pelleted at 200 g for 5 minutes, supernatant aspirated and cells resuspended in PBS. This procedure is repeated once and the cells are resuspended at a concen- 40 tration of 3×10^5 /ml in VGM with porcine trypsin. Then, 100 µl of cells are added to the serum-virus mixtures and the plates incubated at 35° C. in C02 for 5 days. The plates are fixed with 80% acetone in phosphate buffered saline (PBS) for 15 minutes at RT, air dried and then blocked for 30 45 minutes containing PBS with 0.5% gelatin and 2% FCS. An antibody to the S proteins, S1 protein or S2 protein is diluted in PBS with 0.5% gelatin/2% FCS/0.5% Tween 20 and incubated at RT for 2 hours. Wells are washed and horseradish peroxidase-conjugated goat anti-mouse IgG added, 50 followed by another 2 hour incubation. After washing, O-phenylenediamine dihydrochloride is added and the neutralization titer is defined as the titer of serum that reduced color development by 50% compared to the positive control wells.

Example 23: MERS CoV Vaccine Immunogenicity Study in Mice

The instant study was designed to test the immunogenic- 60 ity in mice of candidate MERS-CoV vaccines comprising a mRNA polynucleotide encoding the full-length Spike (S) protein, or the S2 subunit (S2) of the Spike protein obtained from MERS-CoV.

Mice were vaccinated with a 10 µg dose of MERS-CoV 65 mRNA vaccine encoding either the full-length MERS-CoV Spike (S) protein, or the S2 subunit (S2) of the Spike protein

on days 0 and 21. Sera were collected from each mice on days 0, 21, 42, and 56. Individual bleeds were tested for anti-S, anti-S2 activity via a virus neutralization assay from all four time points.

As shown in FIG. 17, the MERS-CoV vaccine encoding the full-length S protein induced strong immune response after the boost dose on day 21. Further, full-length S protein vaccine generated much higher neutralizing antibody titers as compared to S2 alone (FIG. 18).

Example 24: MERS CoV Vaccine Immunogenicity Study in New Zealand White Rabbits

The instant study was designed to test the immunogenic-15 ity of candidate MERS-CoV mRNA vaccines encoding the full-length Spike (S) protein. The New Zealand white rabbits used in this study weighed about 4-5 kg. The rabbits were divided into three groups (Group 1a, Group 1b, and Group 2, n=8). Rabbits in Group 1a were immunized intramuscu-²⁰ larly (IM) with one 20 µg dose of the MERS-CoV mRNA vaccine encoding the full-length Spike protein on day 0. Rabbits in Group 1b were immunized intramuscularly (IM) with one 20 µg dose of the MERS-CoV mRNA vaccine encoding the full-length Spike protein on day 0, and again on day 21 (booster dose). Group 2 received placebo (PBS). The immunized rabbits were then challenged and samples were collected 4 days after challenge. The viral loads in the lungs, bronchoalveolar lavage (Bal), nose, and throat of the rabbits were determined, e.g., via quantitative PCR. Replicating virus in the lung tissues of the rabbits were also detected. Lung histopathology were evaluated and the neutralizing antibody titers in serum samples of the rabbits were determined.

Two 20 μ g doses of MERS-CoV mRNA vaccine resulted in a 3 log reduction of viral load in the nose and led to complete protection in the throat of the New Zealand white rabbits (FIG. **19**A). Two 20 μ g doses of MERS-CoV mRNA vaccine also resulted in a 4 log reduction of viral load in the BAL of the New Zealand white rabbits (FIG. **19**B). One 20 μ g dose of MERS-CoV mRNA vaccine resulted in a 2 log reduction of viral load, while two 20 μ g doses of MERS-CoV mRNA vaccine resulted in an over 4 log reduction of viral load in the lungs of the New Zealand white rabbits (FIG. **19**C).

Quantitative PCR results show that two 20 µg doses of MERS-CoV mRNA vaccine reduced over 99% (2 log) of viruses in the lungs of New Zealand white rabbits (FIG. 20A). No replicating virus were detected in the lungs (FIG. 20B).

Further, as shown in FIG. 21, two 20 µg doses of MERS-CoV mRNA vaccine induced significant amount of neutralizing antibodies against MERS-CoV (ECso between 500-1000).

The MERS-CoV mRNA vaccine induced antibody titer is 55 3-5 fold better than any other vaccines tested in the same model.

Example 25: Immunogenicity Study

The instant study is designed to test the immunogenicity in mice of candidate MeV vaccines comprising a mRNA polynucleotide encoding MeV hemagglutinin (HA) protein, MeV Fusion (F) protein or a combination of both.

Mice are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) with candidate vaccines. Up to three immunizations are given at 3-week intervals (i.e., at weeks 0, 3, 6, and 9), and sera are collected after each

immunization until weeks 33-51. Serum antibody titers against MeV HA protein or MeV F protein are determined by ELISA.

Example 26: MeV Rodent Challenge

The instant study is designed to test the efficacy in transgenic mice of candidate MeV vaccines against a lethal challenge using a MeV vaccine comprising mRNA encoding MeV HA protein or MeV F protein. The transgenic mice 10 express human receptor CD46 or signaling lymphocyte activation molecule (SLAM) (also referred to as CD150). Humans are the only natural host for MeV infection, thus transgenic lines are required for this study. CD46 is a complement regulatory protein that protects host tissue from 15 complement deposition by binding to complement components C3b and C4b. Its expression on murine fibroblast and lymphoid cell lines renders these otherwise refractory cells permissive for MeV infection, and the expression of CD46 on primate cells parallels the clinical tropism of MeV 20 infection in humans and nonhuman primates (Rall G F et al. PNAS USA 1997; 94(9):4659-63). SLAM is a type 1 membrane glycoprotein belonging to the immunoglobulin super-

family. It is expressed on the surface of activated lymphocytes, macrophages, and dendritic cells and is thought to play an important role in lymphocyte signaling. SLAM is a receptor for both wild-type and vaccine MeV strains (Sellin C I et al. *J Virol.* 2006; 80(13):6420-29).

CD46 or SLAM/CD150 transgenic mice are challenged with a lethal dose of the MeV. Animals are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) at week 0 and week 3 with candidate MeV vaccines with and without adjuvant. The animals are then challenged with a lethal dose of MeV on week 7 via IV, IM or ID. Endpoint is day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DLin-KC2-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DOMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

TABLE 1

| | Animal | | 111111 | minia | 10 gennent y | studios t | leeding schedul | | | |
|---------|-------------------|---------------|-----------|-------|--------------|-----------|-----------------|--------|--------|-------------------------|
| | groups | | | | | | Day | | | |
| | (n = 8) | vaccine | -2 | 0 | 7 | 14 | 21 | 28 | 35 | 56 |
| Placebo | Group $1 (n = 8)$ | PBS) (IM) | Pre-Bleed | Prime | Bleeds | Bleeds | Bleeds/Boost | Bleeds | Bleeds | Harvest Spleens/Term |
| 10 µg | Group | | | | | | | | | inal Bleeds |
| Dose | 2(n = 8) | | | | | | | | | |
| 2 μg | Group | 2 µg | | | | | | | | |
| Dose | 3(n = 8) |) (IM) | | | | | | | | |

Total n = 24

40 Each of the sequences described herein encompasses a chemically modified sequence or an unmodified sequence which includes no nucleotide modifications.

| TABLE 2 | 2 |
|---------|---|
|---------|---|

| | | SEQ II |
|----------------------------|--|--------|
| Description | Sequence | NO: |
| gi 122891979 gb EF051124.1 | ATGAGCTGGAAGGTGGTGATTATCTTCAGCCTGCTGATTA | 1 |
| Human | CACCTCAACACGGCCTGAAGGAGAGCTACCTGGAAGAGA | |
| metapneumovirus | GCTGCTCCACCATCACCGAGGGCTACCTGAGCGTGCTGC | |
| isolate TN/92-4 | GGACCGGCTGGTACACCAACGTGTTCACCCTGGAGGTGG | |
| fusion protein gene, | GCGACGTGGAGAACCTGACCTGCAGCGACGGCCCTAGCC | |
| complete genome | TGATCAAGACCGAGCTGGACCTGACCAAGAGCGCTCTGA | |
| | GAGAGCTGAAGACCGTGTCCGCCGACCAGCTGGCCAGAG | |
| | AGGAACAGATCGAGAACCCTCGGCAGAGCAGATTCGTGC | |
| | TGGGCGCCATCGCTCTGGGAGTCGCCGCTGCCGCTGCAG | |
| | TGACAGCTGGAGTGGCCATTGCTAAGACCATCAGACTGG | |
| | AAAGCGAGGTGACAGCCATCAACAATGCCCTGAAGAAG | |
| | ACCAACGAGGCCGTGAGCACCCTGGGCAATGGAGTGAGA | |
| | GTGCTGGCCACAGCCGTGCGGGAGCTGAAGGACTTCGTG | |
| | AGCAAGAACCTGACCAGAGCCATCAACAAGAACAAGTG | |
| | CGACATCGATGACCTGAAGATGGCCGTGAGCTTCTCCCA | |
| | GTTCAACAGACGGTTCCTGAACGTGGTGAGACAGTTCTC | |
| | CGACAACGCTGGAATCACACCTGCCATTAGCCTGGACCT | |
| | GATGACCGACGCCGAGCTGGCTAGAGCCGTGCCCAACAT | |
| | GCCCACCAGCGCTGGCCAGATCAAGCTGATGCTGGAGAA | |
| | CAGAGCCATGGTGCGGAGAAAGGGCTTCGGCATCCTGAT | |
| | TGGGGTGTATGGAAGCTCCGTGATCTACATGGTGCAGCT | |
| | GCCCATCTTCGGCGTGATCGACACCCCTGCTGGATCGTG | |

TABLE 2-continued

| Description | Sequence | SEQ II NO: |
|------------------------------------|---|---------------|
| | AAGGCCGCTCCTAGCTGCTCCGAGAAGAAAGGAAACTAT | |
| | GCCTGTCTGCTGAGAGAGGACCAGGGCTGGTACTGCCAG | |
| | AACGCCGGAAGCACAGTGTACTATCCCAACGAGAAGGAC | |
| | TGCGAGACCAGAGGCGACCACGTGTTCTGCGACACCGCT | |
| | GCCGGAATCAACGTGGCCGAGCAGAGCAAGGAGTGCAA | |
| | CATCAACATCAGCACAACCAACTACCCCTGCAAGGTGAG CACCGGACGGCACCCCATCAGCATGGTGGCTCTGAGCCC | |
| | TCTGGGCGCTCTGGTGGCCTGCTATAAGGGCGTGTCCTGT | |
| | AGCATCGGCAGCAATCGGGTGGGCATCATCAAGCAGCTG | |
| | AACAAGGGATGCTCCTACATCACCAACCAGGACGCCGAC | |
| | ACCGTGACCATCGACAACACCGTGTACCAGCTGAGCAAG | |
| | GTGGAGGGCGAGCAGCACGTGATCAAGGGCAGACCCGT | |
| | GAGCTCCAGCTTCGACCCCATCAAGTTCCCTGAGGACCA GTTCAACGTGGCCCTGGACCAGGTGTTTGAGAACATCGA | |
| | GAACAGCCAGGCCCTGGTGGACCAGGTGTTTGAGAACATCGA | |
| | GTCCAGCGCTGAGAAGGGCAACACCGGCTTCATCATTGT | |
| | GATCATTCTGATCGCCGTGCTGGGCAGCTCCATGATCCTG | |
| | GTGAGCATCTTCATCATTATCAAGAAGACCAAGAAACCC | |
| | ACCGGAGCCCCTCCTGAGCTGAGCGGCGTGACCAACAAT | |
| | GGCTTCATTCCCCACAACTGA | |
| jb AY525843.1 : 3065-4684 Juman | ATGTCTTGGAAAGTGATGATCATCATTTCGTTACTCATAA CACCCCAGCACGGGCTAAAGGAGAGTTATTTGGAAGAAT | 2 |
| netapneumovirus | CATGTAGTACTATAACTGAGGGATACCTCAGTGTTTTAAG | |
| lsolate NL/1/99, | AACAGGCTGGTACACTAATGTCTTCACATTAGAAGTTGGT | |
| complete genome | GATGTTGAAAATCTTACATGTACTGATGGACCTAGCTTAA | |
| | TCAAAACAGAACTTGATCTAACAAAAAGTGCTTTAAGGG | |
| | AACTCAAAACAGTCTCTGCTGATCAGTTGGCGAGAGAGG | |
| | AGCAAATTGAAAATCCCAGACAATCAAGATTTGTCTTAG | |
| | GTGCGATAGCTCTCGGAGTTGCTACAGCAGCAGCAGTCA CAGCAGGCATTGCAATAGCCAAAACCATAAGGCTTGAGA | |
| | GTGAGGTGAATGCAATTAAAGGTGCTCTCAAACAAACTA | |
| | ATGAAGCAGTATCCACATTAGGGAATGGTGTGCGGGTCC | |
| | TAGCCACTGCAGTGAGAGAGCTAAAAGAATTTGTGAGCA | |
| | AAAACCTGACTAGTGCAATCAACAGGAACAAATGTGACA | |
| | TTGCTGATCTGAAGATGGCTGTCAGCTTCAGTCAATTCAA | |
| | CAGAAGATTTCTAAATGTTGTGCGGCAGTTTTCAGACAAT | |
| | GCAGGGATAACACCAGCAATATCATTGGACCTGATGACT GATGCTGAGTTGGCCAGAGCTGTATCATACATGCCAACA | |
| | TCTGCACGGCAGATAAAACTGATGTTGGAGAACCGCGCA | |
| | ATGGTAAGGAGAAAAGGATTTGGAATCCTGATAGGGGTC | |
| | TACGGAAGCTCTGTGATTTACATGGTTCAATTGCCGATCT | |
| | TTGGTGTCATAGATACACCTTGTTGGATCATCAAGGCAGC | |
| | TCCCTCTTGCTCAGAAAAAACGGGAATTATGCTTGCCTC | |
| | CTAAGAGAGGATCAAGGGTGGTATTGTAAAAATGCAGGA TCTACTGTTTACTACCCAAATGAAAAAGACTGCGAAACA | |
| | AGAGGTGATCATGTTTTTTGTGACACAGCAGCAGGGATC | |
| | AATGTTGCTGAGCAATCAAGAGAATGCAACATCAACATA | |
| | TCTACTACCAACTACCCATGCAAAGTCAGCACAGGAAGA | |
| | CACCCTATAAGCATGGTTGCACTATCACCTCTCGGTGCTT | |
| | TGGTGGCTTGCTATAAAGGGGTAAGCTGCTCGATTGGCA | |
| | | |
| | TGGAATCATCAAACAATTACCCAAAGGCTGCTCATACAT AACCAACCAGGATGCAGACACTGTAACAATTGACAATAC | |
| | CGTGTATCAACTAAGCAAAGTTGAAGGTGAACAGCATGT | |
| | AATAAAAGGGAGACCAGTTTCAAGCAGTTTTGATCCAAT | |
| | CAAGTTTCCTGAGGATCAGTTCAATGTTGCGCTTGATCAA | |
| | GTCTTCGAAAGCATTGAGAACAGTCAGGCACTAGTGGAC | |
| | CAGTCAAACAAAATTCTAAACAGTGCAGAAAAAGGAAA | |
| | CACTGGTTTCATTATCGTAGTAGTATTTTGGTTGCTGTTCTTG | |
| | GTCTAACCATGATTTCAGTGAGCATCATCATCATAATCAA GAAAACAAGGAAGCCCACAGGAGCACCTCCAGAGCTGA | |
| | ATGGTGTCACCAACGGCGGTTTCATACCACATAGTTA | |
| b KJ627414.1 : 3015-4634 | ATGTCTTGGAAAGTGATGATTATCATTTCGTTACTCATAA | 3 |
| luman | CACCTCAGCATGGACTAAAAGAAAGTTATTTAGAAGAAT | |
| netapneumovirus | CATGTAGTACTATAACTGAAGGATATCTCAGTGTTTTAAG | |
| strain hMPV/Homo | AACAGGTTGGTACACCAATGTCTTTACATTAGAAGTTGGT | |
| sapiens/PER/CFI0497/ 2010/B, | GATGTTGAAAATCTTACATGTACTGATGGACCTAGCTTAA TCAAAACAGAACTTGACCTAACCAAAAGTGCTTTAAGAG | |
| complete genome | AACTCAAAACAGTTTCTGCTGATCAGTTAGCGAGAGAAG | |
| | AACAAATTGAAAAATCCCAGACAATCAAGGTTTGTCCTAG | |
| | GTGCAATAGCTCTTGGAGTTGCCACAGCAGCAGCAGTCA | |
| | | |
| | CAGCAGGCATTGCAATAGCCAAAACTATAAGGCTTGAGA | |

TABLE 2-continued

| Description | Sequence | SEQ II NO: |
|----------------------------------|--|---------------|
| Jeacription | sequence | NO: |
| | ATGAGGCAGTATCAACACTAGGAAATGGAGTGCGGGTCC TAGCCACTGCAGTAAGAGAGCTGAAAGAATTTGTGAGCA | |
| | AAAACCTGACTAGTGCGATCAACAAGAACAAGTGTGAGCA | |
| | TTGCTGATTTGAAGATGGCTGTCAGCTTCAGTCAGTTCAA | |
| | CAGAAGATTCCTAAATGTTGTGCGGCAGTTTTCAGACAAT | |
| | GCAGGGATAACACCAGCAATATCATTGGACCTGATGAAT | |
| | GATGCTGAGCTGGCCAGAGCTGTATCATACATGCCAACA | |
| | TCTGCAGGACAGATAAAACTAATGTTAGAGAACCGTGCA ATGGTGAGGAGAAAAGGATTTGGAATCTTGATAGGGGTC | |
| | TACGGAAGCTCTGTGATTTACATGGTCCAGCTGCCGATCT | |
| | TTGGTGTCATAAATACACCTTGTTGGATAATCAAGGCAGC | |
| | TCCCTCTTGTTCAGAAAAAGATGGAAATTATGCTTGCCTC | |
| | CTAAGAGAGGATCAAGGGTGGTATTGTAAAAATGCAGGA | |
| | TCCACTGTTTACTACCCAAATGAAAAAGACTGCGAAACA AGAGGTGATCATGTTTTTTGTGACACAGCAGCAGGGATC | |
| | AATGTTGCTGAGCAATCAAGAGAATGCAACATCAACATCAACATCAACATCAACATCAACATA | |
| | TCTACCACCAACTACCCATGCAAAGTCAGCACAGGAAGA | |
| | CACCCTATCAGCATGGTTGCACTATCACCTCTCGGTGCTT | |
| | TGGTAGCTTGCTACAAAGGGGTTAGCTGCTCGACTGGCA | |
| | GTAATCAGGTTGGAATAATCAAACAACTACCTAAAGGCT | |
| | GCTCATACATAACTAACCAGGACGCAGACACTGTAACAA TTGACAACACTGTGTATCAACTAAGCAAAGTTGAGGGTG | |
| | AACAGCATGTAATAAAAGGGAGACCAGTTTCAAGCAGTT | |
| | TTGATCCAATCAGGTTTCCTGAGGATCAGTTCAATGTTGC | |
| | GCTTGATCAAGTCTTTGAAAGCATTGAAAACAGTCAAGC | |
| | ACTAGTGGACCAGTCAAACAAAATTCTGAACAGTGCAGA | |
| | AAAAGGAAACACTGGT TTCATTATTGTAATAATTTTGATTGCTGTTCTTGGGTTAAC | |
| | CATGATTTCAGTGAGCATCATCATCATCAAAAAAAAAC | |
| | AAGGAAGCCCACAGGGGCACCTCCGGAGCTGAATGGTGT | |
| | TACCAACGGCGGTTTCATACCGCATAGTTAG | |
| gb KJ723483.1 : 5586-7310 | ATGGAGTTGCCAATCCTCAAAACAAATGCAATTACCACA | 4 |
| Human | ATCCTTGCTGCAGTCACACTCTGTTTCGCTTCCAGTCAAA | |
| respiratory | ACATCACTGAAGAATTTTATCAATCAACATGCAGTGCAG | |
| syncytial virus | TTAGCAAAGGCTATCTTAGTGCTCTAAGAACTGGTTGGTA | |
| strain RSVA/Homo | TACTAGTGTTATAACTATAGAATTAAGTAATATCAAGGA | |
| sapiens/USA/841- | AAATAAGTGTAATGGAACAGATGCTAAGGTAAAATTGAT AAAACAAGAATTAGATAAATATAAAAATGCTGTAACAGA | |
| 215A-01/1984, complete genome | ATTGCAGTTGCTCATGCAAAGCACACCAGCAGCCAACAA | |
| somprete genome | TCGAGCCAGAAGAGAACTACCAAGGTTTATGAATTATAC | |
| | ACTCAATAATACCAAAAATACCAATGTAACATTAAGCAA | |
| | GAAAAGGAAAAGAAGATTTCTTGGCTTTTTGTTAGGTGTT | |
| | GGATCTGCAATCGCCAGTGGCATTGCTGTATCTAAGGTCC | |
| | | |
| | TACTATCCACAAACAAGGCTGTAGTCAGCTTATCAAATG GAGTTAGTGTCTTAACCAGCAAAGTGTTAGACCTCAAAA | |
| | ACTATATAGATAAACAGTTGTTACCTATTGTGAACAAGC | |
| | AAAGCTGCAGCATATCAAACATTGAAACTGTGATAGAGT | |
| | TCCAACAAAAGAACAACAGACTACTAGAGATTACCAGGG | |
| | AATTTAGTGTTAATGCAGGTGTAACTACACCTGTAAGCAC | |
| | TTATATGTTAACTAATAGTGAATTATTATCATTAATCAAT | |
| | GATATGCCTATAACAAATGATCAGAAAAAGTTAATGTCC AACAATGTTCAAATAGTTAGACAGCAAAGTTACTCTATC | |
| | ATGTCCATAATAAAGGAGGAAGTCTTAGCATATGTAGTA | |
| | CAATTACCACTATATGGTGTAATAGATACACCCTGTTGGA | |
| | AACTGCACACATCCCCTCTATGTACAACCAACACAAAGG | |
| | AAGGGTCCAACATCTGCTTAACAAGAACCGACAGAGGAT | |
| | GGTATTGTGACAATGCAGGATCAGTATCTTTCTTCCCACA | |
| | AGCTGAAACATGTAAAGTTCAATCGAATCGGGTATTTTGT | |
| | GACACAATGAACAGTTTAACATTACCAAGTGAAGTAAAT CTCTGCAACATTGACATATTCAACCCCAAATATGATTGCA | |
| | AAATTATGACTTCAAAAACAGATGTAAGCAGCTCCGTTA | |
| | TCACATCTCTAGGAGCCATTGTGTCATGCTATGGCAAAAC | |
| | TAAATGTACAGCATCCAATAAAAATCGTGGGATCATAAA | |
| | GACATTTTCTAACGGGTGTGATTATGTATCAAATAAGGG | |
| | | |
| | AATAAGCAAGAAGGCAAAAGTCTCTATGTAAAAGGTGAA | |
| | CCAATAATAAATTTCTATGACCCATTAGTGTTCCCCCTCTG ATGAATTTGATGCATCAATATCTCAAGTCAATGAGAAGA | |
| | | |
| | TTAACCAGAGCCTAGCATTTATTCGTAAATCCGATGAATT | |
| | TTAACCAGAGCCTAGCATTTATTCGTAAATCCGATGAATT ATTACATAATGTAAATGCTGGTAAATCCACCACAAATAT | |
| | | |

TABLE 2-continued

| | | SEQ I |
|--------------------------------------|--|-------|
| Description | Sequence | NO: |
| | GTGGTATAAATAATATTGCATTTAGTAACTGA | |
| | hMPV mRNA Sequences | |
| gi 122891979 gb EF051124.1 Human | AUGAGCUGGAAGGUGGUGAUUAUCUUCAGCCUGCUGAU UACACCUCAACACGGCCUGAAGGAGAGCUACCUGGAAG | 57 |
| netapneumo virus | AGAGCUGCUCCACCAUCACCGAGGGCUACCUGAGCGUG | |
| isolate TN/92-4 | CUGCGGACCGGCUGGUACACCAACGUGUUCACCCUGGA | |
| fusion protein gene, | GGUGGGCGACGUGGAGAACCUGACCUGCAGCGACGGCC | |
| complete genome | CUAGCCUGAUCAAGACCGAGCUGGACCUGACCAAGAGC GCUCUGAGAGAGCUGAAGACCGUGUCCGCCGACCAGCU | |
| | GCCCAGAGAGAGCCGAGACCGGGCAGAGCCGGCGGCAGAGCA | |
| | GAUUCGUGCUGGGCGCCAUCGCUCUGGGAGUCGCCGCU | |
| | GCCGCUGCAGUGACAGCUGGAGUGGCCAUUGCUAAGAC | |
| | CAUCAGACUGGAAAGCGAGGUGACAGCCAUCAACAAUG CCCUGAAGAAGACCAACGAGGCCGUGAGCACCCUGGGC | |
| | AAUGGAGUGAGAGUGCUGGCCACACCGUGAGCACCCUGGGC | |
| | GAAGGACUUCGUGAGCAAGAACCUGACCAGAGCCAUCA | |
| | ACAAGAACAAGUGCGACAUCGAUGACCUGAAGAUGGCC | |
| | GUGAGCUUCUCCCAGUUCAACAGACGGUUCCUGAACGU | |
| | GGUGAGACAGUUCUCCGACAACGCUGGAAUCACACCUG CCAUUAGCCUGGACCUGAUGACCGACGCCGAGCUGGCU | |
| | AGAGCCGUGCCCAACAUGCCCACCAGCGCUGGCCAGAU | |
| | CAAGCUGAUGCUGGAGAACAGAGCCAUGGUGCGGAGAA | |
| | AGGGCUUCGGCAUCCUGAUUGGGGUGUAUGGAAGCUCC | |
| | GUGAUCUACAUGGUGCAGCUGCCCAUCUUCGGCGUGAU | |
| | CGACACACCCUGCUGGAUCGUGAAGGCCGCUCCUAGCU GCUCCGAGAAGAAAGGAAACUAUGCCUGUCUGCUGAGA | |
| | GAGGACCAGGGCUGGUACUGCCAGAACGCCGGAAGCAC | |
| | AGUGUACUAUCCCAACGAGAAGGACUGCGAGACCAGAG | |
| | GCGACCACGUGUUCUGCGACACCGCUGCCGGAAUCAAC | |
| | GUGGCCGAGCAGAGCAAGGAGUGCAACAUCAACAUCAG CACAACCAACUACCCCUGCAAGGUGAGCACCGGACGGC | |
| | ACCCCAUCAGCAUGGUGGCUCUGAGCCCUCUGGGCGCU | |
| | CUGGUGGCCUGCUAUAAGGGCGUGUCCUGUAGCAUCGG | |
| | CAGCAAUCGGGUGGGCAUCAUCAAGCAGCUGAACAAGG | |
| | GAUGCUCCUACAUCACCAACCAGGACGCCGACACCGUG ACCAUCGACAACACCGUGUACCAGCUGAGCAAGGUGGA | |
| | GGGCGAGCAGCACCGUGAUCAAGGGCAGACCCGUGAGCU | |
| | CCAGCUUCGACCCCAUCAAGUUCCCUGAGGACCAGUUC | |
| | AACGUGGCCCUGGACCAGGUGUUUGAGAACAUCGAGAA | |
| | | |
| | CCAGCGCUGAGAAGGGCAACACCGGCUUCAUCAUUGUG AUCAUUCUGAUCGCCGUGCUGGGCAGCUCCAUGAUCCU | |
| | GGUGAGCAUCUUCAUCAUUAUCAAGAAGACCAAGAAAC | |
| | CCACCGGAGCCCCUCCUGAGCUGAGCGGCGUGACCAAC AAUGGCUUCAUUCCCCACAACUGA | |
| | | |
| b AY525843.1 : 3065-4684 Juman | AUGUCUUGGAAAGUGAUGAUCAUCAUUUCGUUACUCAU AACACCCCAGCACGGGCUAAAGGAGAGUUAUUUGGAAG | 58 |
| etapneumovirus | AAUCAUGUAGUACUAUAACUGAGGGAUACCUCAGUGUU | |
| solate NL/1/99, | UUAAGAACAGGCUGGUACACUAAUGUCUUCACAUUAGA | |
| omplete genome | AGUUGGUGAUGUUGAAAAUCUUACAUGUACUGAUGGA CCUAGCUUAAUCAAAACAGAACUUGAUCUAACAAAAAG | |
| | UGCUUUAAGGGAACUCAAAACAGUCUCUGCUGAUCAGU | |
| | UGGCGAGAGAGGAGCAAAUUGAAAAUCCCAGACAAUCA | |
| | AGAUUUGUCUUAGGUGCGAUAGCUCUCGGAGUUGCUAC | |
| | AGCAGCAGCAGUCACAGCAGGCAUUGCAAUAGCCAAAA | |
| | CCAUAAGGCUUGAGAGUGAGGUGAAUGCAAUUAAAGG UGCUCUCAAACAAACUAAUGAAGCAGUAUCCACAUUAG | |
| | GGAAUGGUGUGCGGGUCCUAGCCACUGCAGUGAGAGAG | |
| | CUAAAAGAAUUUGUGAGCAAAAACCUGACUAGUGCAAU | |
| | CAACAGGAACAAAUGUGACAUUGCUGAUCUGAAGAUGG | |
| | CUGUCAGCUUCAGUCAAUUCAACAGAAGAUUUCUAAAU GUUGUGCGGCAGUUUUCAGACAAUGCAGGGAUAACACC | |
| | AGCAAUAUCAUUGGACCUGAUGACUGAUGCUGAGUUGG | |
| | CCAGAGCUGUAUCAUACAUGCCAACAUCUGCAGGGCAG | |
| | AUAAAACUGAUGUUGGAGAACCGCGCAAUGGUAAGGAG | |
| | AAAAGGAUUUGGAAUCCUGAUAGGGGUCUACGGAAGCU CUGUGAUUUACAUGGUUCAAUUGCCGAUCUUUGGUGUC | |
| | CUGUGAUUUACAUGUUCAAUUGUUGAUUUUGGUGUC | |
| | | |
| | AUAGAUACACCUUGUUGGAUCAUCAAGGCAGCUCCCUC UUGCUCAGAAAAAAACGGGAAUUAUGCUUGCCUCCUAA | |
| | AUAGAUACACCUUGUUGGAUCAUCAAGGCAGCUCCCUC | |

TABLE 2-continued

| Deservite | Service en | SEQ ID |
|-------------------------------------|--|-------------|
| Description | Sequence | NO : |
| | AAUGUUGCUGAGCAAUCAAGAGAAUGCAACAUCAACAU AUCUACUACCAACUACCCAUGCAAAGUCAGCACAGGAA | |
| | GACACCCUAUAAGCAUGGUUGCACUAUCACCUCUCGGU | |
| | GCUUUGGUGGCUUGCUAUAAAGGGGUAAGCUGCUCGAU | |
| | UGGCAGCAAUUGGGU | |
| | UGGAAUCAUCAAACAAUUACCCAAAGGCUGCUCAUACA | |
| | UAACCAACCAGGAUGCAGACACUGUAACAAUUGACAAU | |
| | ACCGUGUAUCAACUAAGCAAAGUUGAAGGUGAACAGCA | |
| | UGUAAUAAAAGGGAGACCAGUUUCAAGCAGUUUUGAUC | |
| | CAAUCAAGUUUCCUGAGGAUCAGUUCAAUGUUGCGCUU | |
| | GAUCAAGUCUUCGAAAGCAUUGAGAACAGUCAGGCACU | |
| | AGUGGACCAGUCAAACAAAAUUCUAAACAGUGCAGAAA | |
| | AAGGAAACACUGGUUUCAUUAUCGUAGUAAUUUUGGU UGCUGUUCUUGGUCUAACCAUGAUUUCAGUGAGCAUCA | |
| | UCAUCAUAAUCAAGAAAACAAGGAAGCCCACAGGAGCA | |
| | CCUCCAGAGCUGAAUGGUGUCACCAACGGCGGUUUCAU | |
| | ACCACAUAGUUAG | |
| gb KJ627414.1 : 3015-4634 | AUGUCUUGGAAAGUGAUGAUUAUCAUUUCGUUACUCAU | 59 |
| Juman | AACACCUCAGCAUGGACUAAAAGAAAGUUAUUUAGAAG | |
| netapneumovirus | AAUCAUGUAGUACUAUAACUGAAGGAUAUCUCAGUGUU | |
| strain hMPV/Homo | UUAAGAACAGGUUGGUACACCAAUGUCUUUACAUUAGA | |
| sapiens/PER/CFI0497/ | AGUUGGUGAUGUUGAAAAUCUUACAUGUACUGAUGGA | |
| 2010/B, | CCUAGCUUAAUCAAAACAGAACUUGACCUAACCAAAAG | |
| complete genome | UGCUUUAAGAGAACUCAAAACAGUUUCUGCUGAUCAGU | |
| | UAGCGAGAGAAGAACAAAUUGAAAAUCCCAGACAAUCA | |
| | AGGUUUGUCCUAGGUGCAAUAGCUCUUGGAGUUGCCAC | |
| | AGCAGCAGCAGUCACAGCAGGCAUUGCAAUAGCCAAAA CUAUAAGGCUUGAGAGUGAAGUGA | |
| | UGCUCUCAAAACAACCAAUGAGGGAGGGAGUGCAAUCAAAGG | |
| | GAAAUGGAGUGCGGGUCCUAGCCACUGCAGUAAGAGAG | |
| | CUGAAAGAAUUUGUGAGCAAAAACCUGACUAGUGCGAU | |
| | CAACAAGAACAAGUGUGACAUUGCUGAUUUGAAGAUGG | |
| | CUGUCAGCUUCAGUCAGUUCAACAGAAGAUUCCUAAAU | |
| | GUUGUGCGGCAGUUUUCAGACAAUGCAGGGAUAACACC | |
| | AGCAAUAUCAUUGGACCUGAUGAAUGAUGCUGAGCUGG | |
| | CCAGAGCUGUAUCAUACAUGCCAACAUCUGCAGGACAG | |
| | AUAAAACUAAUGUUAGAGAACCGUGCAAUGGUGAGGA | |
| | GAAAAGGAUUUGGAAUCUUGAUAGGGGUCUACGGAAG | |
| | CUCUGUGAUUUACAUGGUCCAGCUGCCGAUCUUUGGUG UCAUAAAUACACCUUGUUGGAUAAUCAAGGCAGCUCCC | |
| | UCUUGUUCAGAAAAAGAUGGAAAAUUAUGCUUGCCUCCU | |
| | AAGAGAGGAUCAAGGGUGGUAUUGUAAAAAUGCAGGA | |
| | UCCACUGUUUACUACCCAAAUGAAAAAGACUGCGAAAC | |
| | AAGAGGUGAUCAUGUUUUUUGUGACACAGCAGCAGGGA | |
| | UCAAUGUUGCUGAGCAAUCAAGAGAAUGCAACAUCAAC | |
| | AUAUCUACCACCAACUACCCAUGCAAAGUCAGCACAGG | |
| | AAGACACCCUAUCAGCAUGGUUGCACUAUCACCUCUCG | |
| | GUGCUUUGGUAGCUUGCUACAAAGGGGUUAGCUGCUCG | |
| | ACUGGCAGUAAUCAGGUUGGAAUAAUCAAACAACUACC | |
| | UAAAGGCUGCUCAUACAUAACUAACCAGGACGCAGACA | |
| | CUGUAACAAUUGACAACACUGUGUAUCAACUAAGCAAA | |
| | GUUGAGGGUGAACAGCAUGUAAUAAAAGGGAGACCAG UUUCAAGCAGUUUUGAUCCAAUCAGGUUUCCUGAGGAU | |
| | CAGUUCAAUGUUGCGCUUGAUCCAAUCAGGUUUCCUGAGGAU | |
| | UGAAAACAGUCAAGCACUAGUGGACCAGUCAAACAAA | |
| | UUCUGAACAGUGCAGAAAAAGGAAACACUGGU | |
| | UUCAUUAUUGUAAUAAUUUUGAUUGCUGUUCUUGGGU | |
| | UAACCAUGAUUUCAGUGAGCAUCAUCAUCAUAAUCAAA | |
| | AAAACAAGGAAGCCCACAGGGGCACCUCCGGAGCUGAA | |
| | UGGUGUUACCAACGGCGGUUUCAUACCGCAUAGUUAG | |
| b KJ723483.1 : 5586-7310 | AUGGAGUUGCCAAUCCUCAAAACAAAUGCAAUUACCAC | 60 |
| luman | AAUCCUUGCUGCAGUCACACUCUGUUUCGCUUCCAGUC | |
| respiratory | AAAACAUCACUGAAGAAUUUUUAUCAAUCAACAUGCAGU | |
| syncytial virus strain RSVA/Homo | GCAGUUAGCAAAGGCUAUCUUAGUGCUCUAAGAACUGG UUGGUAUACUAGUGUUAUAACUAUAGAAUUAAGUAAU | |
| sapiens/USA/841- | AUCAAGGAAAAUAAGUGUAAACUAUAGAAUUAAGUAAU | |
| 215A-01/1984, | UAAAAUUGAUAAAACAAGAAUUAGAUAAAUAUAAAAA | |
| complete genome | UGCUGUAACAGAAUUGCAGUUGCUCAUGCAAAGCACAC | |
| | CAGCAGCCAACAAUCGAGCCAGAAGAGAACUACCAAGG | |
| | UUUAUGAAUUAUACACUCAAUAAUACCAAAAAUACCAA | |
| | UGUAACAUUAAGCAAGAAAAGGAAAAGAAGAUUUCUU | |
| | GGCUUUUUGUUAGGUGUUGGAUCUGCAAUCGCCAGUGG | |
| | CALIFICATION AND CALCOLLACE CONTRACT ACCOUNTS | |

CAUUGCUGUAUCUAAGGUCCUGCACCUAGAAGGGGAAG

TABLE 2-continued

| SEQ ID NO: | Sequence | Description |
|---------------|---|-------------|
| | UGAACAAAAUCAAAAGUGCUCUACUAUCCACAAACAAG | |
| | GCUGUAGUCAGCUUAUCAAAUGGAGUUAGUGUCUUAAC | |
| | CAGCAAAGUGUUAGACCUCAAAAACUAUAUAGAUAAAC | |
| | AGUUGUUACCUAUUGUGAACAAGCAAAGCUGCAGCAUA | |
| | UCAAACAUUGAAACUGUGAUAGAGUUCCAACAAAAGAA | |
| | CAACAGACUACUAGAGAUUACCAGGGAAUUUAGUGUUA | |
| | AUGCAGGUGUAACUACACCUGUAAGCACUUAUAUGUUA | |
| | ACUAAUAGUGAAUUAUUAUCAUUAAUCAAUGAUAUGCC | |
| | UAUAACAAAUGAUCAGAAAAAGUUAAUGUCCAACAAUG | |
| | UUCAAAUAGUUAGACAGCAAAGUUACUCUAUCAUGUCC | |
| | AUAAUAAAGGAGGAAGUCUUAGCAUAUGUAGUACAAU | |
| | UACCACUAUAUGGUGUAAUAGAUACACCCUGUUGGAAA | |
| | CUGCACACAUCCCCUCUAUGUACAACCAACACAAAGGA | |
| | AGGGUCCAACAUCUGCUUAACAAGAACCGACAGAGGAU | |
| | GGUAUUGUGACAAUGCAGGAUCAGUAUCUUUCUUCCCA | |
| | CAAGCUGAAACAUGUAAAGUUCAAUCGAAUCGGGUAUU | |
| | UUGUGACACAAUGAACAGUUUAACAUUACCAAGUGAAG | |
| | UAAAUCUCUGCAACAUUGACAUAUUCAACCCCAAAUAU | |
| | GAUUGCAAAAUUAUGACUUCAAAAACAGAUGUAAGCAG | |
| | CUCCGUUAUCACAUCUCUAGGAGCCAUUGUGUCAUGCU | |
| | AUGGCAAAACUAAAUGUACAGCAUCCAAUAAAAAUCGU | |
| | GGGAUCAUAAAGACAUUUUCUAACGGGUGUGAUUAUG | |
| | UAUCAAAUAAGGGGGUGGAUACUGUGUCUGUAGGUAA | |
| | UACAUUAUAUUAUGUAAAUAAGCAAGAAGGCAAAAGU | |
| | CUCUAUGUAAAAGGUGAACCAAUAAUAAAUUUCUAUGA | |
| | CCCAUUAGUGUUCCCCUCUGAUGAAUUUGAUGCAUCAA | |
| | UAUCUCAAGUCAAUGAGAAGAUUAACCAGAGCCUAGCA | |
| | UUUAUUCGUAAAUCCGAUGAAUUAUUACAUAAUGUAA | |
| | AUGCUGGUAAAUCCACCACAAAUAUCAUGAUAACUACU | |
| | AUGEUGGUARAUCEACEACAMAUAUGUUAUGUUAUCAUUAA | |
| | UUGCAGUUGGACUGCUCCUAUACUGCAAGGCCAGAAGC | |
| | | |
| | | |
| | ACACCAGUCACACUAAGUAAGGAUCAACUGAGUGGUAU AAAUAAUAUUGCAUUUAGUAACUGA | |

| TABLE | 3 |
|-------|---|
|-------|---|

| | hMPV Amino Acid Sequences | |
|----------------------------|--|---------------|
| Description | Sequence | SEQ II NO: |
| gi 122891979 gb EF051124.1 | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGW | 5 |
| Human | YTNVFTLEVGDVENLTCSDGPSLIKTELDLTKSALRELKTVS | |
| metapneumovirus | ADQLAREEQIENPRQSRFVLGAIALGVAAAAAVTAGVAIAK | |
| isolate TN/92-4 | TIRLESEVTAINNALKKTNEAVSTLGNGVRVLATAVRELKD | |
| fusion protein gene, | FVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS | |
| complete cds | DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRA | |
| | MVRRKGFGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPS | |
| | CSEKKGNYACLLREDQGWYCQNAGSTVYYPNEKDCETRG | |
| | DHVFCDTAAGINVAEQSKECNINISTTNYPCKVSTGRHPISM | |
| | VALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD | |
| | ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQF | |
| | NVALDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAV | |
| | LGSSMILVSIFIIIKKTKKPTGAPPELSGVTNNGFIPHN | |
| gb AY525843.1 : 3065-4684 | MSWKVMIIISLLITPQHGLKESYLEESCSTITEGYLSVLRTGW | 6 |
| Human | YTNVFTLEVGDVENLTCTDGPSLIKTELDLTKSALRELKTVS | |
| metapneumovirus | ADQLAREEQIENPRQSRFVLGAIALGVATAAAVTAGIAIAKT | |
| isolate NL/1/99, | IRLESEVNAIKGALKQTNEAVSTLGNGVRVLATAVRELKEF | |
| complete cds | VSKNLTSAINRNKCDIADLKMAVSFSQFNRRFLNVVRQFSD | |
| - | NAGI TPAI SLDLMTDAELARAVSYMPTSAGQI KLMLENRAM | |
| | VRRKGFGILIGVYGSSVIYMVQLPIFGVIDTPCWIIKAAPSCS | |
| | EKNGNYACLLREDQGWYCKNAGSTVYYPNEKDCETRGDH | |
| | VFCDTAAGINVAEQSRECNINISTTNYPCKVSTGRHPISMVA | |
| | LSPLGALVACYKGVSCSIGSNWVGIIKQLPKGCSYITNQDAD | |
| | TVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFNV | |
| | ALDQVFESIENSQALVDQSNKILNSAEKGNTGFIIVVILVAVL | |
| | GLTMISVSIIIIIKKTRKPTGAPPELNGVTNGGFIPHS | |
| gb KJ627414.1 : 3015-4634 | MSWKVMIIISLLITPQHGLKESYLEESCSTITEGYLSVLRTGW | 7 |
| Human | YTNVFTLEVGDVENLTCTDGPSLIKTELDLTKSALRELKTVS | |
| metapneumovirus | ADQLAREEQIENPROSRFVLGAIALGVATAAAVTAGIAIAKT | |

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| TABLE | 3-continued |
|-------|-------------|
| | |

| hMPV Amino Acid Sequences | | |
|---------------------------|---|---------------|
| Description | Sequence | SEQ II NO: |
| strain hMPV/Homo | IRLESEVNAIKGALKTTNEAVSTLGNGVRVLATAVRELKEF | |
| sapiens/PER/CFI0497/ | VSKNLTSAINKNKCDIADLKMAVSFSQFNRRFLNVVRQFSD | |
| 2010/B, | NAGITPAISLDLMNDAELARAVSYMPTSAGQIKLMLENRAM | |
| complete cds | VRRKGFGILIGVYGSSVIYMVQLPIFGVINTPCWIIKAAPSCS | |
| | EKDGNYACLLREDQGWYCKNAGSTVYYPNEKDCETRGDH | |
| | VFCDTAAGINVAEQSRECNINISTTNYPCKVSTGRHPISMVA | |
| | LSPLGALVACYKGVSCSTGSNQVGIIKQLPKGCSYITNQDAD | |
| | TVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIRFPEDQFNV | |
| | ALDQVFESIENSQALVDQSNKILNSAEKGNTGFIIVIILIAVLG | |
| | LTMISVSIIIIIKKTRKPTGAPPELNGVTNGGFIPHS | |
| gb KJ723483.1 : 5586-7310 | MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKG | 8 |
| Human | YLSALRTGWYTSVITIELSNIKENKCNGTDAKVKLIKQELDK | |
| respiratory | YKNAVTELQLLMQSTPAANNRARRELPRFMNYTLNNTKNT | |
| syncytial virus | NVTLSKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKI | |
| strain RSVA/Homo | KSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQLLPIVN | |
| sapiens/USA/841- | KOSCSISNIETVIEFOOKNNRLLEITREFSVNAGVTTPVSTYM | |
| 215A-01/1984. | LTNSELLSLINDMPITNDOKKLMSNNVOIVROOSYSIMSIIKE | |
| complete cds | EVLAYVVOLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTR | |
| | TDRGWYCDNAGSVSFFPOAETCKVOSNRVFCDTMNSLTLP | |
| | SEVNLCNIDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGK | |
| | TKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVN | |
| | KQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSL | |
| | AFIRKSDELLHNVNAGKSTTNIMITTIIIVIIVILLSLIAVGLLL | |
| | | |
| | YCKARSTPVTLSKDQLSGINNIAFSN | |

TABLE 4

| hMPV NCBI Accession Numbers (Amino Acid Sequences) | | |
|---|--------------------|--|
| Virus | GenBank Accession | |
| F [Human metapneumovirus] [Human metapneumovirus] | AEK26895.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53565.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53566.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53569.1 | |
| fusion protein [Human metapneumovirus] | AEZ52347.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53574.1 | |
| fusion glycoprotein [Human metapneumovirus] | AHV79473.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53570.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53567.1 | |
| fusion protein [Human metapneumovirus] | AAS22125.1 | |
| fusion glycoprotein [Human metapneumovirus] | AHV79795.1 | |
| fusion glycoprotein [Human metapneumovirus] | AHV79455.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53568.1 | |
| fusion protein [Human metapneumovirus] | AAS22109.1 | |
| fusion glycoprotein [Human metapneumovirus] | AGU68417.1 | |
| fusion glycoprotein [Human metapneumovirus] | AGJ74228.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53575.1 | |
| fusion protein [Human metapneumovirus] | AAU25820.1 | |
| fusion glycoprotein [Human metapneumovirus] | AGU68377.1 | |
| fusion glycoprotein [Human metapneumovirus] | AGU68371.1 | |
| fusion glycoprotein [Human metapneumovirus] | AGJ74087.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53560.1 | |
| fusion glycoprotein [Human metapneumovirus] | AHV79858.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53577.1 | |
| fusion protein [Human metapneumovirus] | AAS22085.1 | |
| fusion protein [Human metapneumovirus] | AEZ52348.1 | |
| fusion glycoprotein [Human metapneumovirus] | AGJ74044.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53563.1 | |
| fusion glycoprotein precursor [Human metapneumovirus] | YP_012608.1 | |
| fusion glycoprotein [Human metapneumovirus] | AGJ74053.1 | |
| fusion protein [Human metapneumovirus] | BAM37562.1 | |
| fusion glycoprotein [Human metapneumovirus] | ACJ53561.1 | |
| fusion glycoprotein [Human metapneumovirus] | AGU68387.1 | |
| fusion [Human metapneumovirus] | AGL74060.1 | |
| fusion glycoprotein precursor [Human metapneumovirus] | AAV88364.1 | |
| fusion protein [Human metapneumovirus] | AAN52910.1 | |
| fusion protein [Human metapneumovirus] | AAN52915.1 | |
| fusion protein [Human metapneumovirus] | BAM37564.1 | |
| fusion glycoprotein precursor [Human metapneumovirus] | BAH59618.1 | |
| fusion protein [Human metapneumovirus] | AAQ90144.1 | |
| italea protein filunian metaphetinovirub] | 7 E 1 X 2 V 1 TT 1 | |

TABLE 4-continued

| | d Sequences) |
|---|--------------------------|
| Virus | GenBank Accession |
| fusion glycoprotein [Human metapneumovirus] | AHV79446.1 |
| fusion protein [Human metapneumovirus] | AEL87260.1 |
| fusion glycoprotein [Human metapneumovirus] | AHV79867.1 ABO66027.2 |
| fusion protein [Human metapneumovirus] fusion glycoprotein [Human metapneumovirus] | AGQ00027.2 ACJ53621.1 |
| fusion protein [Human metapneumovirus] | AAN52911.1 |
| fusion glycoprotein [Human metapneumovirus] | AHV79536.1 |
| fusion glycoprotein [Human metapneumovirus] | AGU68411.1 |
| fusion protein [Human metapneumovirus] | AEZ52346.1 |
| fusion protein [Human metapneumovirus] | AAN52913.1 |
| fusion protein [Human metapneumovirus] | AAN52908.1 |
| fusion glycoprotein [Human metapneumovirus] | ACJ53553.1 |
| fusion glycoprotein [Human metapneumovirus] fusion protein [Human metapneumovirus] | AIY25727.1 ABM67072.1 |
| fusion protein [Human metapheumovirus] | AEZ52361.1 |
| fusion protein [Human metapneumovirus] | AAS22093.1 |
| fusion glycoprotein [Human metapneumovirus] | AGH27049.1 |
| fusion protein [Human metapneumovirus] | AAK62968.2 |
| fusion glycoprotein [Human metapneumovirus] | ACJ53556.1 |
| fusion glycoprotein [Human metapneumovirus] | ACJ53620.1 |
| fusion protein [Human metapneumovirus] | ABQ58820.1 |
| F [Human metapneumovirus] [Human metapneumovirus] | AEK26886.1 |
| fusion glycoprotein [Human metapneumovirus] | ACJ53619.1 |
| fusion glycoprotein [Human metapneumovirus] | ACJ53555.1 |
| fusion [Human metapneumovirus] fusion protein [Human metapneumovirus] | AGL74057.1 ABD27850.1 |
| fusion protein [Human metapheumovirus] | AEZ52349.1 |
| fusion protein [Human metapneumovirus] | ABD27848.1 |
| fusion protein [Human metapneumovirus] | ABD27846.1 |
| fusion protein [Human metapneumovirus] | ABQ66021.1 |
| fusion protein [Human metapneumovirus] | AFM57710.1 |
| fusion protein [Human metapneumovirus] | AFM57709.1 |
| fusion protein [Human metapneumovirus] | ABH05968.1 |
| fusion protein [Human metapneumovirus] | AEZ52350.1 |
| fusion protein [Human metapneumovirus] | AFM57712.1 |
| fusion protein [Human metapneumovirus] fusion protein [Human metapneumovirus] | AEZ52364.1 AAN52912.1 |
| fusion protein [Human metapneumovirus] | AEZ52363.1 |
| fusion [Human metapneumovirus] | AGL74059.1 |
| fusion glycoprotein [Human metapneumovirus] | ACJ53583.1 |
| fusion protein [Human metapneumovirus] | AEZ52356.1 |
| fusion protein [Human metapneumovirus] | AEZ52353.1 |
| fusion glycoprotein [Human metapneumovirus] | ACJ53581.1 |
| fusion glycoprotein [Human metapneumovirus] | ACJ53578.1 |
| fusion protein [Human metapneumovirus] | AAS22117.1 BAN75965.1 |
| fusion protein [Human metapneumovirus] fusion protein [Human metapneumovirus] | AGF92105.1 |
| fusion protein [Human metapneumovirus] | AAS22077.1 |
| fusion protein [Human metapheumovirus] | AAN52909.1 |
| fusion glycoprotein [Human metapneumovirus] | ACJ53586.1 |
| fusion protein [Human metapneumovirus] | AAQ90145.1 |
| fusion glycoprotein [Human metapneumovirus] | AGT75042.1 |
| fusion [Human metapneumovirus] | AGL74058.1 |
| fusion protein [Human metapneumovirus] | AEL87263.1 |
| fusion glycoprotein [Human metapneumovirus] | AGH27057.1 |
| fusion glycoprotein [Human metapneumovirus] | AHV79491.1 |
| F [Human metapneumovirus] [Human metapneumovirus] | AEK26906.1 |
| fusion glycoprotein [Human metapneumovirus] fusion protein [Human metapneumovirus] | ACJ53580.1 AEZ52354.1 |
| fusion protein [Human metapheumovirus] | AAN52914.1 |
| G [Human metapneumovirus] [Human metapneumovirus] | AEK26901.1 |
| glycoprotein [Human metapneumovirus] | AFI56738.1 |
| lycoprotein [Human metapneumovirus] | AFI56739.1 |
| glycoprotein [Human metapneumovirus] | AFI56745.1 |
| G protein [Human metapneumovirus] | AAQ62718.1 |
| G protein [Human metapneumovirus] | AAQ62719.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGH27104.1 |
| G protein [Human metapneumovirus] | AAQ62729.1 |
| G protein [Human metapneumovirus] | AAQ62728.1 |
| glycoprotein [Human metapneumovirus] | AFI56753.1 |
| glycoprotein [Human metapneumovirus] glycoprotein [Human metapneumovirus] | AFI56746.1 AFI56750.1 |
| glycoprotein [Human metapneumovirus] glycoprotein [Human metapneumovirus] | AFI56750.1 AFI56747.1 |
| G protein [Human metapneumovirus] | AAQ62721.1 |
| glycoprotein [Human metapneumovirus] | AAT46573.1 |
| glycoprotein [Human metapneumovirus] | AFI56748.1 |

TABLE 4-continued

| hMPV NCBI Accession Numbers (Amino Acid | GenBank Accession |
|--|--------------------------|
| | |
| glycoprotein [Human metapneumovirus] glycoprotein [Human metapneumovirus] | AFI56736.1 AFI56749.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGH27131.1 |
| attachment glycoprotein G [Human metapneumovirus] | AHV79558.1 |
| glycoprotein [Human metapneumovirus] | AFI56740.1 |
| glycoprotein [Human metapneumovirus] | AFI56741.1 AFI56744.1 |
| glycoprotein [Human metapneumovirus] attachment glycoprotein G [Human metapneumovirus] | AHV79790.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGH27122.1 |
| attachment glycoprotein G [Human metapneumovirus] | AHV79763.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGZ48849.1 |
| glycoprotein [Human metapneumovirus] attachment glycoprotein G [Human metapneumovirus] | AFI56743.1 AHV79450.1 |
| glycoprotein [Human metapneumovirus] | AFI56751.1 |
| attachment glycoprotein [Human metapneumovirus] | AAS48482.1 |
| attachment glycoprotein G [Human metapneumovirus] | AHV79889.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43050.1 |
| glycoprotein [Human metapneumovirus] | AFI56754.1 |
| attachment glycoprotein G [Human metapneumovirus] glycoprotein [Human metapneumovirus] | AHV79601.1 AFI56752.1 |
| attachment glycoprotein G [Human metapneumovirus] | AHV79871.1 |
| G protein [Human metapneumovirus] | AEZ68099.1 |
| attachment glycoprotein G [Human metapneumovirus] | AHV79817.1 |
| attachment glycoprotein G [Human metapneumovirus] | AHV79943.1 |
| attachment glycoprotein G [Human metapneumovirus] | BAN75968.1 AGW43045.1 |
| attachment surface glycoprotein [Human metapneumovirus] attachment glycoprotein G [Human metapneumovirus] | AGW43045.1 AHV79628.1 |
| attachment glycoprotein [Human metapneumovirus] | AFK49783.1 |
| G protein [Human metapneumovirus] | AAQ62723.1 |
| attachment glycoprotein [Human metapneumovirus] | ABD27839.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43046.1 |
| G protein [Human metapneumovirus] | AAQ62717.1 AFI56742.1 |
| glycoprotein [Human metapneumovirus] attachment protein [Human metapneumovirus] | ABQ44522.1 |
| glycoprotein [Human metapneumovirus] | AFI56735.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43065.1 |
| G protein [Human metapneumovirus] | AAQ62724.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43075.1 |
| attachment surface glycoprotein [Human metapneumovirus] glycoprotein [Human metapneumovirus] | AGW43062.1 AAT46579.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43064.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43054.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43042.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43078.1 |
| attachment surface glycoprotein [Human metapneumovirus] G protein [Human metapneumovirus] | AGW43067.1 AAQ62722.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43063.1 |
| glycoprotein [Human metapneumovirus] | AAT46571.1 |
| glycoprotein [Human metapneumovirus] | AAT46578.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGJ74232.1 |
| glycoprotein [Human metapneumovirus] | AAT46580.1 |
| glycoprotein [Human metapneumovirus] attachment surface glycoprotein [Human metapneumovirus] | AAT46574.1 AGW43061.1 |
| attachment glycoprotein [Human metapneumovirus] | AFK49791.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43047.1 |
| glycoprotein [Human metapneumovirus] | ABC26386.1 |
| attachment glycoprotein [Human metapneumovirus] | AAS48466.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43048.1 |
| attachment glycoprotein G [Human metapneumovirus] attachment surface glycoprotein [Human metapneumovirus] | AGH27140.1 AGW43049.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGJ74082.1 |
| attachment glycoprotein G [Human metapneumovirus] | AHV79442.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGJ74091.1 |
| attachment glycoprotein G [Human metapneumovirus] | AHV79477.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43056.1 |
| attachment protein [Human metapneumovirus] attachment glycoprotein G [Human metapneumovirus] | ABQ44523.1 BAH59622.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43070.1 |
| glycoprotein [Human metapneumovirus] | AAT46585.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGU68409.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGJ74223.1 |
| attachment glycoprotein [Human metapneumovirus] | AAS22129.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGJ74048.1 |
| G protein [Human metanasumovinue] | |
| G protein [Human metapneumovirus] glycoprotein [Human metapneumovirus] | AAQ62725.1 ABC26384.1 |

TABLE 4-continued

| hMPV NCBI Accession Numbers (Amino Acid | Sequences) |
|--|--------------------------|
| Virus | GenBank Accession |
| attachment glycoprotein G [Human metapneumovirus] | YP_012612.1 |
| attachment surface glycoprotein [Human metapneumovirus] | AGW43071.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGJ74162.1 |
| attachment glycoprotein G [Human metapneumovirus] | AGH27095.1 |
| attachment glycoprotein G [Human metapneumovirus] | AHV79531.1 |
| G protein [Human metapneumovirus] attachment glycoprotein [Human metapneumovirus] | AAQ62726.1 AAS48465.1 |
| attachment givcoprotein [runnan metaphetiniovirus] | AGW43058.1 |
| P [Human metapneumovirus] [Human metapneumovirus] | AEK26894.1 |
| phosphoprotein [Human metapneumovirus] | AHV79631.1 |
| phosphoprotein [Human metapneumovirus] | AHV79901.1 |
| phosphoprotein [Human metapneumovirus] | AHV79570.1 |
| phosphoprotein [Human metapneumovirus] | AGJ74076.1 |
| phosphoprotein [Human metapneumovirus] | AA\$22123.1 |
| phosphoprotein [Human metapneumovirus] | ABB16895.1 |
| phosphoprotein [Human metapneumovirus] | AHV79579.1 |
| phosphoprotein [Human metapneumovirus] | AGJ74244.1 |
| phosphoprotein [Human metapneumovirus] | AHV79856.1 |
| phosphoprotein [Human metapneumovirus] | ACJ70113.1 |
| phosphoprotein [Human metapneumovirus] | AGZ48843.1 |
| phosphoprotein [Human metapneumovirus] | AHV79498.1 |
| phosphoprotein [Human metapneumovirus] | AHV79480.1 |
| phosphoprotein [Human metapneumovirus] | ABQ43382.1 AAS22107.1 |
| phosphoprotein [Human metapneumovirus] phosphoprotein [Human metapneumovirus] | ABB16898.1 |
| phosphoprotein [Human metapheumovirus] | AGH27134.1 |
| phosphoprotein [Human metapheumovirus] | ABB16899.1 |
| phosphoprotein [Human metapneumovirus] | AGH27098.1 |
| phosphoprotein [Human metapneumovirus] | AAN52866.1 |
| phosphoprotein [Human metapneumovirus] | AAS22083.1 |
| phosphoprotein [Human metapneumovirus] | YP_012606.1 |
| phosphoprotein [Human metapneumovirus] | AHV79973.1 |
| phosphoprotein [Human metapneumovirus] | AHV79462.1 |
| phosphoprotein [Human metapneumovirus] | AGJ74042.1 |
| phosphoprotein [Human metapneumovirus] | AAV88362.1 |
| P [Human metapneumovirus] [Human metapneumovirus] | AIL23591.1 |
| phosphoprotein [Human metapneumovirus] | AHV79453.1 |
| phosphoprotein [Human metapneumovirus] | AGJ74261.1 |
| phosphoprotein [Human metapneumovirus] | AGH27116.1 |
| phosphoprotein [Human metapneumovirus] | ABB16444.1 |
| phosphoprotein [Human metapneumovirus] | ABB16445.1 |
| phosphoprotein [Human metapneumovirus] | AHV79507.1 |
| phosphoprotein [Human metapneumovirus] | BAH59616.1 |
| phosphoprotein [Human metapneumovirus] | ABB16443.1 ABO43388.1 |
| phosphoprotein [Human metapneumovirus] phosphoprotein [Human metapneumovirus] | ABQ43389.1 ABQ43389.1 |
| phosphoprotein [Human metapheumovirus] | ABQ43395.1 ABQ43395.1 |
| phosphoprotein [Human metapheunovirus] | ABO43385.1 |
| phosphoprotein [Human metapneumovirus] | AAP84042.1 |
| phosphoprotein [Human metaphounovirus] | AAN52868.1 |
| phosphoprotein [Human metapneumovirus] | AAP84041.1 |
| phosphoprotein [Human metapneumovirus] | AGH27080.1 |
| phosphoprotein [Human metapneumovirus] | ABQ43387.1 |
| phosphoprotein [Human metapneumovirus] | AAS22099.1 |
| phosphoprotein [Human metapneumovirus] | ABB16896.1 |
| phosphoprotein [Human metapneumovirus] | AGJ74094.1 |
| phosphoprotein [Human metapneumovirus] | AEZ68089.1 |
| phosphoprotein [Human metapneumovirus] | ABK97002.1 |
| phosphoprotein [Human metapneumovirus] | AAP13486.1 |
| phosphoprotein [Human metapneumovirus] | AHV79444.1 |
| phosphoprotein [Human metapneumovirus] | AHV79865.1 |
| phosphoprotein [Human metapneumovirus] | AGJ74226.1 |
| phosphoprotein [Human metapneumovirus] | ABQ43383.1 |
| phosphoprotein [Human metapneumovirus] | AAN52863.1 |
| phosphoprotein [Human metapneumovirus] | AHV79775.1 |
| phosphoprotein [Human metapneumovirus] | AEZ68094.1 |
| phosphoprotein [Human metapneumovirus] | AHV79883.1 |
| phosphoprotein [Human metapneumovirus] | AEZ68092.1 |
| phosphoprotein [Human metapneumovirus] | ABQ43390.1 |
| phosphoprotein [Human metapneumovirus] | ABQ43386.1 |
| phosphoprotein [Human metapneumovirus] | ABQ43391.1 ACS16062.1 |
| phosphoprotein [Human metapneumovirus] | |
| phosphoprotein [Human metapneumovirus] | AEZ68090.1 |
| phosphoprotein [Human metapneumovirus] | AAK62967.1 |
| phosphoprotein [Human metapneumovirus] | AEZ68093.1 |
| phosphoprotein [Human metapneumovirus] | AEZ68088.1 |

TABLE 4-continued

| Virus | GenBank Accession |
|---|--------------------------|
| phosphoprotein [Human metapneumovirus] | ABQ43392.1 |
| hosphoprotein [Human metapneumovirus] | ABQ43393.1 |
| hosphoprotein [Human metapneumovirus] | ABQ43384.1 |
| hosphoprotein [Human metapneumovirus] hosphoprotein [Human metapneumovirus] | ABQ43394.1 ABK96999.1 |
| hosphoprotein [Human metapneumovirus] | AHV79489.1 |
| hosphoprotein [Human metapneumovirus] | AGJ74235.1 |
| hosphoprotein [Human metapneumovirus] | AAS22075.1 |
| hosphoprotein [Human metapneumovirus] | AAS22115.1 |
| hosphoprotein [Human metapneumovirus] | AII17601.1 |
| hosphoprotein [Human metapneumovirus] | ABK97000.1 |
| hosphoprotein [Human metapneumovirus] | AHV79561.1 |
| hosphoprotein [Human metapneumovirus] hosphoprotein [Human metapneumovirus] | AGT75040.1 AAN52864.1 |
| hosphoprotein [Human metapneumovirus] | ABK97001.1 |
| phosphoprotein [Human metapneumovirus] | AGT74979.1 |
| bhosphoprotein [Human metapneumovirus] | AHV79955.1 |
| hosphoprotein [Human metapneumovirus] | AGH27055.1 |
| hosphoprotein [Human metapneumovirus] | AAV88361.1 |
| hosphoprotein [Human metapneumovirus] | ABQ43397.1 |
| hosphoprotein [Human metapneumovirus] | AGJ74173.1 |
| [Human metapneumovirus] [Human metapneumovirus] | AEK26904.1 |
| hosphoprotein [Human metapneumovirus] | ACJ70104.1 |
| phosphoprotein [Human metapneumovirus] phosphoprotein [Human metapneumovirus] | ABK97003.1 AGT74955.1 |
| phosphoprotein [Human metapneumovirus] | AG174955.1 AAN52856.1 |
| phosphoprotein [Human metapheumovirus] | AAN52862.1 |
| bhosphoprotein [Human metapneumovirus] | AGJ74138.1 |
| bhosphoprotein [Human metapneumovirus] | AHV79613.1 |
| hosphoprotein [Human metapneumovirus] | AGJ74060.1 |
| hosphoprotein [Human metapneumovirus] | AAQ67684.1 |
| hosphoprotein [Human metapneumovirus] | AEA02278.1 |
| I [Human metapneumovirus] [Human metapneumovirus] | AEK26899.1 |
| nucleoprotein [Human metapneumovirus] | ACS16061.1 AAS88425.1 |
| nucleoprotein [Human metapneumovirus] nucleoprotein [Human metapneumovirus] | YP_012605.1 |
| nucleoprotein [Human metapheumovirus] | AHV79882.1 |
| nucleoprotein [Human metapheumovirus] | AHV79774.1 |
| nucleocapsid protein [Human metapneumovirus] | AAN52886.1 |
| ucleoprotein [Human metapneumovirus] | AAS22082.1 |
| ucleoprotein [Human metapneumovirus] | AHV79864.1 |
| ucleoprotein [Human metapneumovirus] | AHV79828.1 |
| ucleoprotein [Human metapneumovirus] | AGJ74084.1 |
| nucleocapsid protein [Human metapneumovirus] | AAN52888.1 |
| J [Human metapneumovirus] [Human metapneumovirus] ucleoprotein [Human metapneumovirus] | AIL23590.1 AAK62966.1 |
| ucleoprotein [Human metapneumovirus] | AHV79972.1 |
| ucleoprotein [Human metapneumovirus] | AHV79470.1 |
| ucleoprotein [Human metapheumovirus] | AHV79452.1 |
| ucleoprotein [Human metapneumovirus] | AGJ74243.1 |
| ucleoprotein [Human metapneumovirus] | AHV79533.1 |
| ucleoprotein [Human metapneumovirus] | AGJ74181.1 |
| ucleoprotein [Human metapneumovirus] | AHV79497.1 |
| ucleoprotein [Human metapneumovirus] | AHV79702.1 |
| ucleoprotein [Human metapneumovirus] | AHV79648.1 |
| ucleoprotein [Human metapneumovirus] | AHV79435.1 |
| utative nucleoprotein [Human metapneumovirus] nucleocapsid protein [Human metapneumovirus] | AGJ74260.1 AAN52887.1 |
| ucleoprotein [Human metapneumovirus] | AGU68386.1 |
| nucleocapsid protein [Human metapheumovirus] | AAN52899.1 |
| ucleoprotein [Human metapneumovirus] | AAR17673.1 |
| ucleocapsid protein [Human metapneumovirus] | AAN52898.1 |
| ucleoprotein [Human metapneumovirus] | AEA02277.1 |
| ucleoprotein [Human metapneumovirus] | AHV79612.1 |
| ucleoprotein [Human metapneumovirus] | AGU68416.1 |
| ucleoprotein [Human metapneumovirus] | AGU68408.1 |
| ucleoprotein [Human metapneumovirus] | AGU68370.1 |
| nucleoprotein [Human metapneumovirus] | AAQ67683.1 |
| ucleoprotein [Human metapneumovirus] | AGJ74137.1 |
| uucleoprotein [Human metapneumovirus] uucleocapsid protein [Human metapneumovirus] | AGU68344.1 ABK96997.1 |
| ucleoprotein [Human metapneumovirus] | AGU68413.1 |
| ucleocapsid protein [Human metapneumovirus] | AAN52891.1 |
| ucleoprotein [Human metapneumovirus] | AGU68360.1 |
| nucleoprotein [Human metapneumovirus] | AGU68353.1 |
| ucleocapsid protein [Human metapneumovirus] | ABK96996.1 |

TABLE 4-continued

| Virus | GenBank Accession |
|--|--------------------------|
| nucleoprotein [Human metapneumovirus] | AAR17666.1 |
| N [Human metapneumovirus] [Human metapneumovirus] | AEK26903.1 |
| nucleoprotein [Human metapneumovirus] | AGT75039.1 |
| nucleoprotein [Human metapneumovirus] | AGU68410.1 |
| nucleoprotein [Human metapneumovirus] | AAS22074.1 |
| nucleoprotein [Human metapneumovirus] | AHV79560.1 |
| nucleoprotein [Human metapneumovirus] | AGT74978.1 |
| nucleoprotein [Human metapneumovirus] | AGJ74128.1 |
| nucleoprotein [Human metapneumovirus] | AAR17663.1 |
| nucleoprotein [Human metapneumovirus] | AAR17662.1 |
| nucleoprotein [Human metapneumovirus] | AAR17664.1 |
| nucleoprotein [Human metapneumovirus] | AAR17657.1 |
| nucleoprotein [Human metapneumovirus] | AAR17659.1 |
| nucleoprotein [Human metapneumovirus] | AAR17661.1 |
| nucleoprotein [Human metapneumovirus] | AGU68352.1 |
| nucleoprotein [Human metapneumovirus] | AGU68373.1 |
| nucleoprotein [Human metapneumovirus] | AGU68376.1 |
| nucleoprotein [Human metapneumovirus] | AGU68342.1 |
| nucleoprotein [Human metapneumovirus] | AGU68365.1 |
| nucleoprotein [Human metapneumovirus] | AGU68363.1 |
| nucleoprotein [Human metapneumovirus] | AGU68398.1 |
| nucleoprotein [Human metapneumovirus] | AGU68348.1 |
| nucleoprotein [Human metapneumovirus] | AGU68354.1 |
| nucleoprotein [Human metapneumovirus] | AGU68391.1 |
| nucleoprotein [Human metapneumovirus] | AGU68389.1 AGU68399.1 |
| nucleoprotein [Human metapneumovirus] nucleoprotein [Human metapneumovirus] | AGU68337.1 |
| nucleoprotein [Human metapheumovirus] | AGC08557.1 AAR17660.1 |
| nucleoprotein [Human metapneumovirus] | AAR17667.1 |
| nucleoprotein [Human metapneumovirus] | AGU68402.1 |
| nucleoprotein [Avian metapneumovirus type C] | CDN30025.1 |
| nucleoprotein [Avian metapneumovirus] | AGZ87947.1 |
| Nucleoprotein [Avian metapneumovirus type C] | CAL25113.1 |
| nucleocapsid protein [Avian metapneumovirus] | ABO42286.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38430.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK54155.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38426.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38425.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38424.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAF05909.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38435.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38428.1 |
| nucleoprotein [Human metapneumovirus] | AAR17669.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38429.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38427.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38423.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38434.1 |
| nucleoprotein [Human metapneumovirus] | AGU68338.1 |
| nucleoprotein [Avian metapneumovirus] | YP_443837.1 |
| nucleoprotein [Human metapneumovirus] | AGU68384.1 |
| nucleocapsid protein [Avian metapneumovirus] | AAK38431.1 |
| nucleoprotein [Human metapneumovirus] | AGU68405.1 |
| nucleoprotein [Human metapneumovirus] | AGU68382.1 |
| nucleoprotein [Human metapneumovirus] | AGU68395.1 |
| nucleocapsid [Human metapneumovirus] | AAL35389.3 |
| nucleoprotein [Human metapneumovirus] | AEZ68064.1 |

TABLE 5

| PI | V3 Nucleic Acid Sequences | |
|---|---|---------------|
| Description | Sequence | SEQ ID NO: |
| >gb KJ672601.1 : 4990-6609 Human parainfluenza virus 3 strain HPIV3/Homo sapiens/PER/FLA4815/ 2008[fusion glycoprotein F0] | ATGCCAATTTCAATACTGTTAATTATTACAACCATGATC ATGCCATCACACTGCCAAATAGACATCACAAAACTACA GCATGTAGGTGTATTGGTCAACAGTCCCAAAGGGATGA AGATATCACAAAACTTCGAAACAAGATATCTAATCCTGA GTCTCATACCAAAAATAGAAGATTCTAACTCTTGTGGTG ACCAACAGATCAAGCAATACAAGAGGTTATTGGATGAA CTGATCATCCTTTATATGATGGACTAAGATTACAGAAA GATGGATAGTGACTAACTAAGAATCCAATGAAACAC TGATCCCAGAACAGAA | 9 |

TABLE 5-continued

| | 3 Nucleic Acid Sequences | anc |
|---|--|---------------|
| Description | Sequence | SEQ ID NO: |
| Description | AACTATTGCTCTAGGAGTAGCAACCTCAGCACAAATTAC AGCAGCAGTTGCTCTGGTTGAAGCCAAGCAGCAGGACAGA CAGACATTGAAAAACTCAGGAAGCAAGCAGCAGGACAATCAGGGACACA AATAAAGCAGTGCAGT | NU: |
| gi 612507167 gb AHX22430.1 hemagglutinin- neuraminidase [Human parainfluenza virus 3] | CAAAATGATAAGCCGTATGTATTAACAAACAAG ATGGAATACTGGAAGCACACCAACCACGGAAAGGATGC TGGTAATGAGCTGGAGAGCACCCACCACGGAAAGGATGC ACAAGCTCACCAACAAGATAACATATATATTGTGGACG ATAACCCTGGTGTTATTATCAATAGTCTTCATCATAGTG CTAACTAATTCCATCAAAAGTGAAAAGGCCGCGGAATC ATGCTACAAGACCAAAATGAAAAGGCCTCTTACCAATGC AGAAAAGATCCAAGTGGCATCGGATAATACTAATGATC TAATACAGTCAGGAGTGAATACAAGGCTTCTTACAATTC AGAATACGGTCATGGCATCGGATAATACTATGATGAT CAATTACAGTCAGGAGTGTATAAATGAATCAATGGACA AACAATATCGGATCTTAGGAAATCAATTGATGAAATTA CAATTAGAAATGGATGTTAGGAATTAATGATGA ATAACACATGATGTGGGTATAAAAACCTTTAAATCCAGAT GATTTCTGGAGATGGCGCTCTGGTCTTCCACCTTGAGA ATAACACATGATGTGGGGTATAAAACCTTTAATCCAGAT GATTTCTGGAGATGCGCACCGGCATGGCAAGAA ATAACCCATGATGTGGGGTATAAAACCTTTAATCCAGAT GATTTCTGGAGATGCGCGCTCTGGTCTCCACCTTGATG AAAACTCCAAAATAAGAATAATGACCGGGACAAGGAA ATCATGCCAACAACGACGTTGTGATGGGGCATAGGAA ATCATATCAAGTATTACCGAGGTTGCCAGGACTTAAGGAA ATCATATCAAGTATTACGGAGTATAAGGGATAATAGGGAA ATCATATCAAGTATTACGGAGTATATAGGGATAATAGGGA ATCATATCAAGTATTACGGAGTATATAGGAGTAATAAGG CCCAAAGTTGGTACCTGAGTTTAAGGACTAAGTCTCCA CCCAAAAGTTGATGACTGGATATTAGCACCGTCTCCA CCCAAAGTTGGTACCTGAGTTTAAGGACTAATACGGACTATGC GCCAAAGTTGATGACAGAGACTAGATAATGCCACAGG GCTCAAACCAACAGAACTTGGATATAGCACCACGG GCTCAAACCAACAGGACTTGAATATGCCACACGA GGGTAAGGAGGATGGTCACGAAAAATAAATTATAA GTTTGGACCACCAACAGGGATTATACCACCGGGACAAGAA GAGACTGTAATCAAGACACCGAAAATAAATTGCC CCCAAAGGGTCTGGAAACACACGAA GAGACTGAACCAACTGGGTCCTGAGGAAAACACAGA GCTGAACCAACTGGGTCCTGAAGGAAAAACACAGA GCTGAACCAAACTGGGACTCAATAAATGGGAATAA CATTACTGAACCAACTGGGGTCCAGAAGAACCACAG GCTGAACCAAACTGGGATCACACAAAAAGGAATAA CTTCTACTAGGACACAAGAGACTCACAAAAATGGAAAT CTTCTACTAGGACACAGAGATTAACCAATGGAGATAA CATAGGACAAAAATTACTGGGGCTCAGAAGAAAACAAGA GCATAGGACACAAAATTACCGGAGTCACAAAAAAGGACAT GCATAAGGACAACAAGACTCACACAAGAAAAAAGGACT CAAGGGAAACCAACAGGACTACCACAAAAAAAGGACT GCATAAGGGACATCCACACAGGAAACAAAAAAGGACT GCATAAGGGACATCCACACAGGAAAAAAAGGACT GCATAAGGGACATCCACACAGGAACAAAAACGACT GCATAGGGACATCCACACACGAAACCACGAAA GGGTAAACGACGGCGCATAACCACACAAAAAACCACTCACCACAAAAAACAACCACT | 10 |

TABLE 5-continued

| Description | Sequence | SEQ ID NO: |
|-----------------------------|---|---------------|
| | GCTGGGTACACAACAACAAGCTGCATTACACACTATAA CAAAGGGTATTGTTTTCATATAGTAGAAATAAATCATAA AAGCTTAAACACATTTCAACCCATGTTGTTCAAAACAGA GATTCCAAAAAGCTGCAGT | |
| HPIV3_HN_Codon Optimized | ATGGAATACTGGAAGCACCACCACCACGGCAAGGACGC CGGCAACGAGCTGGAAACCAGCACACCACGACGACGAC ACAAGCTGACCAACAAGAGCACAACGCACACACGACG CTGACCCATAGCATCAACAACGAGTTCATCATCGTG CTGACCAATAGCATCAAGGCGACAACACCAACGAC CCGACGAGACCCAGGCGTGAACACCAACGACCACCAACGAC CTGATCCAGGACGTCACGACACCACGACCACCACCAC CAGAGACACCAGGGCGTGAACACCAGGACGTCATCAGCCCCGCAGACACCACGACACCACGAC CAGCATCAGCGACCTGCGGAACTACATCCACCACCACCAC CAGCACTCCGGAACGACCACGAACGTCCAGGCCTGACCAC CACCATCCGGAACGACCACGGAAGTCCATCAGCCCCCGA GAATCAACCCACGACGTGGGCATCAAGCCCCTGAACCCC GACGATTTCTGGCGGGTGTACAAGCGGCCTGGCCCGG ACTGCTGGCCATGCCTAACCACGATGCTGGCCCGG GACCCCCCAGGCTCGCTAACCACGGACGTGATCATCAG GCACGCCCCGGCGTCACCACGGTGATCCACGCCTG CACCAGCAACCTGATCAACCGCCGGGCATCATCACC GTGAACTCCGGCCTGGTGCCCGACCTGAACCATCGGCCTG CAGCCACCTTCAACGATCGGCCTGAACCATCGGCC CAGCCACCCTCGCGTGACCAACGAACGAAGAAGACCG CAGCCCCCCCAAGGTGGACGACGACGACCACGGACT CAGCCACCCTCGCGCGCCCGACCTGAACCACGACGGC CAGCCCCCCCAAGGTGGACGACGACGACCACGGCATCG CAGCCCCCCCAAGGTGGACGACGACGACCACGGCG CAGCCCCCCCAAGGTGGCGCGACCACGGCGTGACCAGCGCG CAGCCCCCCCAAGGTGGACGACGACGACCACGGCCTG CAGCCCCCCCAAGGTGGCCGACCACGGCGTCAAGAACAA CAACATCAGCTTCGACGACCACCCGGCTGCAAGAACAA CAACATCAGCTTCGACGACCCCCGGCTGCAAGAACAA CAACATCAGCTTCGACCACCCGGCTGCAAGAACCACCCC TTCTGTGGGCCCGGCGCAGAACCACCCCCGGTCACGACAACAA CAACATCAGCATCGGCCGCGCACAACCCCCCGGCTGGAACATC CTCCCGGGCATCGGCCACACCCCGGCTGCAAGAACCACC CCCAGAGAGCTGCAACACCCCCCGGCTGCAAGAACACC CCCAGAGAGCTGCAACACCCCCCGGCTGCAAGAACCACC TTCTGGGGCCCGGCCAGAACCCCCCAGCCCTGG GACAACTCCGCCAGAACGCCCACACGCCCTGG GACAACTCCGGCCAGAACGCCCCCCGGGCACACCCCCTGG GACAACTCCGCCCGGCCTACACCGGCACACCCCCGGGAACAAC CCCGGGCCGCGCACAACGCCCACACGCCCCCGGACACACACACACACACACACCCCCC | 11 |
| HPIV3_F_Codon Optimized | ATGCCCATCAGCATCCTGCTGATCATCACCACAATGATC ATGGCCAGCCACTGCCAGATCGACATCACCAAGCTGCA GCACGTGGGCGTGCTCGTGAACAGCCCCAAGGGCATGA AGATCAGCCAGAACTTCGAGACAGCCACCAGCTGCTGGACAG GCCTGATCCCCAAGATCGAGGACAGCAACAGCTGCGGC GACCAGCAGATCAAGCAGTACAAGCGGCTGCTGGACAG ACTGATCATCCCCCTGTACGACGGCAGCAGGAACAA CCGACCCCCGGACCGACGAGAGACAACGAGGACAG GCACAATCGCCCTGGGAGTGGCACAAGCGACGAGAACA CCGACCCCCGGACCGAGAGAGTCGTCGGGCGCGAGATT ACAGCGCCTGTGGCCCTGGTGGAAGCAACGAGGCCAG AATCGGCCTGTGGCCTGGTGGAAGCCAAGCGAGGCCAG AAGCGTCATCGAGAAGCGAGGCCACAAGCGAGGCCAG AAGCGGCCTGTGGCCCTGGTGGAAGCCAAGCGAGGCCAG AAGCGACATCGAGAAGCCGAGGCCAGGCC | 12 |

TABLE 5-continued

| | 3 Nucleic Acid Sequences | |
|---|---|---------------|
| Description | Sequence | SEQ ID NO: |
| | TGGTACATCCCTCTGCCCAGCCACATTATGACCAAGGGC GCCTTTCTGGGCGGAGCCGACGTGAAAGAGTGCATCGA GGCCTTCAGCAGCTACATCTGCCCCAGCGACCCTGGCT CGTGCTGAACCACGGATGGAAAGCTGCCTGGGCGCCA ACATCAGCCAGTGCCCCAGAACCACCGTGACCGCGCA ATCGTGCCCAGATACGCCTCCGGAATGGCGGCGTGGT GCCAACTGCATCACCACCACCGTGTACCTGCAACGGCATC GGCAACCGGATCAACCACCACCGTGTACCTGCGACGCGCAC ACGGCATGCTTCAATACCACCAACAGAGGGCATCCA ACGGCATGCTTCAATACCACCAACAGAGGGCACCCTG GCCTTCTACACCCCCGACGACTATCACCCTGAACAACTCC GTGGCTCTGGACCCCCCGACGAGGCACCCTG GCCTTCTGGCCCCGACGACATCTCCATCGAGCTGAAC AAGGCCAAGAGCGACCTGGAAGAGCCCCAGGGCATC GGCACCGGAGCAACCAGAAGAGTGGAACCCATGGGCATCA AAGGCCAAGAGCGACCACCACCATCATCGGCAGCT GGCACCAGAGCAGCACCACCATCATCGGCAGCT GGCACCAGAGCAGCACCACCATCATCGGCAGCT GGCACCAGAGCAGCACCACCATCATCGTGATCATCAC TATCGCCATTAAGTACTACCGGATCCAGAAACGGAACC CAGGTGGCCCAGAATGACAAGCCCACACACTGCGAACGAA | |
| | PIV3 mRNA Sequences | |
| >gb KJ672601.1 : 4990-6609 Human parainfluenza virus 3 strain HPIV3/Homo sapiens/PER/FL44815/ 2008[fusion glycoprotein F0] | AUGCCAAUUUCAAUACUGUUAAUUAUUACAACCAUGA UCAUGCAUUCAAUACUGCCAAUAGACAUCACAAACU ACAGCAUGUAGGUGUAUUGUCAACAGUCCCAAAGGG AUGAAGAUAUCACAAAACUUCGAAACAAGUUUCUAACUC UUGUGUGACCAACAGAUCAAGAAUAUCAAGGUUA UUGGUGUGACCAACAGAUCAAGCAAUACAAGAGUUCUAACUC UUGUGUGACCAACAGAUCAUCAAGCAAUACAAGAGUUCUUA GAUUACAGAAGGAUGUGAUUAUUCAUACUACUAGUAUCCAAGAAUC CAAUGAAAACACUGAUCCCUUUUAUAUGAUGACUAACAAG GAUUACAGAAGGAUGUGAUUAUUCUUCUAGGAGUAGCAA CCUCAGCACAAUUACAGCAGCAGUUGCUUGGUUGA AGCCAACCAGCAAGAUCCAGCAGUUGCUUGGUUGA AGCCAACCAGGCAAGAUCCAACAUUGAAAAACUCAAG GAAGCAAUCAGGGACACAUUGAUAUGCUCUGGUUGA AUCAGUCCAGGAUUAUGCUCACAAGAAUUCCAAG GAAGCAAUCAGGGACACAAUAAAAGCAGUGCCA UUCAGAGCUCUGUAGGAUAUUGAUAGUACCAAUUAA AUCAGUCCAGGAUUAUGUUCAACAAAGAAAUCGUGCCA UCCAGACUCGGAGACUAGGUUGUGAAGCAACAUUAA AUCAGUCCAGGAUUAUGUUGAACAAAGAAAUCGUGCCA UCCAAUUCGGGACUAGGUUGUGAAGCAAGCAGCAGGACAUUC AGUUGCGAGACUAGGUUGUGAAGCAAGCACAUCAA GAAAAGGAAUAAAUUUCACAGGUAUUACUCAGAAUU AACAAAUAUAUUUGGUGAUAACAAGGUACUUACUACAAC AGUUGCACAAAUAUCACAGGAAUUACUCAGAAUU AACAAAUUAAUUUGGUGAUACAAGGUACUUCAAACAUCAAC AGUUGACAAAUAAUCACAGGAAUUUAACACACUCCAAC AGUUGACAAAUAAUCACAGAAAUAUCUACAACAUCAAC AGUUGACAAAUAAUCACAGAAUAUCUACUACUACAAC AGUUGACAAAUAACCUCCAAGUCCCUUU AUUGACCAACUGCUGAACACUCAAAUCUACAAGAA GAAUCAAUAAAGGUGAGAGUUCAAAUCUACAAGGAAUGGU AUUCCUCUUCCCAGCCUUCAAAUCUACAAGAAGAG AUUCCAUAUCAAGAAUUAUCCAAAAUCUACAAGAAGAA GCAUUCAGACUGCUGAACACUCAAAUUCUACAAGGA AUUCCUAGUUCUAGGAGACGUUCUAUCAAG AAACAUAUCCCAAUGUCCAAGUACUACAAGGAAUGGU AUAUCCCAAUUGCCAAGUACAUCUAAAGGAAUGGU AUAUCCCAAUUGCAAUGUACAACAUCUACAAGGAAUGGU AUAUCCCAAUUGCAAUGUACAACACUCAAUGAACACACAAUCAA GAAUUCUAAACCAUGAAUGAACCAACACACACUCAAGGA AACAUAUUCCUAGGUAAUGAAUCAACCAACACACAUCAA GAGUUCCAAAUUGUUCAACAACCAACACUAGGA AUCAAAAUUGUAUAACAACUACAACACUACAAGAA GAGUUCCAAAUUGUUGAAUCAACCAACACACACACACACA | 61 |
| gi 612507167 gb AHX22430.1 hemagglutinin- neuraminidase Human parainfluenza virus 3] | AUGGAAUACUGGAAGCACACCAACCACGGAAAGGAUG CUGGUAAUGAGCUGGAGACAUCCACAGCCACUCAUGG CAACAAGCUCACCAACAAGAUAACAUAUAUAUUGUGG ACGAUAACCCUGGUGUUAUUAUCAAUAGUCUUCAUCA UAGUGCUAACUAAUUCCAUCAAAAGUGAAAAGGCCCG GAAGUCAUUGCUACAAGACAUAAAUAAUGAGUUUAUG GAAGUUACAGAAAAGAUCCAAGUGGCAUCGGAUAAUA CUAAUGAUCUAAUACAGUCAGGAGUGAAUACAAGGCU | 62 |

TABLE 5-continued

| | | SEQ II |
|---------------|---|--------|
| escription | Sequence | NO: |
| | UCUUACAAUUCAGAGUCAUGUCCAGAAUUAUAUACCA | |
| | AUAUCAUUGACACAACAAAUAUCGGAUCUUAGGAAAU | |
| | UCAUUAGUGAAAUUACAAUUAGAAAUGAUAAUCAAGA AGUGCCACCACAAAGAAUAACACAUGAUGUGGGUAUA | |
| | AAACCUUUAAAUCCAGAUGAUUUCUGGAGAUGCACGU | |
| | CUGGUCUUCCAUCUUUGAUGAAAACUCCAAAAAUAAG | |
| | AUUAAUGCCGGGACCAGGAUUAUUAGCUAUGCCAACG | |
| | ACUGUUGAUGGCUGUGUCAGAACCCCGUCCUUAGUGA | |
| | UAAAUGAUCUGAUUUAUGCUUACACCUCAAAUCUAAU UACUCGAGGUUGCCAGGAUAUAGGGAAAUCAUAUCAA | |
| | GUAUUACAGAUAGGGAUAAUAACUGUAAACUCAGACU | |
| | UGGUACCUGACUUAAAUCCUAGGAUCUCUCAUACCUU | |
| | CAACAUAAAUGACAAUAGAAAGUCAUGUUCUCUAGCA | |
| | CUCCUAAAUACAGAUGUAUAUCAACUGUGUUCAACCC | |
| | CAAAAGUUGAUGAAAGAUCAGAUUAUGCAUCAUCAGG | |
| | CAUAGAAGAUAUUGUACUUGAUAUUGUCAAUUAUGAU GGCUCAAUCUCGACAACAAGAUUUAAGAAUAAUAAUA | |
| | UAAGUUUUGAUCAACCAUAUGCGGCAUUAUACCCAUC | |
| | UGUUGGACCAGGGAUAUACUACAAAGGCAAAAUAAUA | |
| | UUUCUCGGGUAUGGAGGUCUUGAACAUCCAAUAAAUG | |
| | AGAAUGCAAUCUGCAACACAACUGGGUGUCCUGGGAA | |
| | AACACAGAGAGACUGUAAUCAAGCAUCUCAUAGUCCA | |
| | UGGUUUUCAGAUAGAAGGAUGGUCAACUCUAUAAUUG UUGUUGACAAGGGCUUGAACUCAGUUCCAAAAUUGAA | |
| | GGUAUGGACGAUAUCUAUGAGACAAAAUUACUGGGGG | |
| | UCAGAAGGAAGAUUACUUCUACUAGGUAACAAGAUCU | |
| | ACAUAUACACAAGAUCUACAAGUUGGCACAGCAAGUU | |
| | ACAAUUAGGAAUAAUUGACAUUACUGACUACAGUGAU | |
| | AUAAGGAUAAAAUGGACAUGGCAUAAUGUGCUAUCAA | |
| | GACCAGGAAACAAUGAAUGUCCAUGGGGACAUUCAUG UCCGGAUGGAUGUAUAACGGGAGUAUAUACCGAUGCA | |
| | UAUCCACUCAAUCCCACAGGAAGCAUUGUAUCAUCUG | |
| | UCAUAUUGGACUCACAAAAAUCGAGAGUCAACCCAGU | |
| | CAUAACUUACUCAACAGCAACCGAAAGGGUAAACGAG | |
| | CUGGCUAUCCGAAACAAAACACUCUCAGCUGGGUACA | |
| | CAACAACAAGCUGCAUUACACACUAUAACAAAGGGUA | |
| | UUGUUUUCAUAUAGUAGAAAUAAAUCAUAAAAGCUUA | |
| | AACACAUUUCAACCCAUGUUGUUCAAAACAGAGAUUC CAAAAAGCUGCAGU | |
| PIV3 HN Codon | AUGGAAUACUGGAAGCACACCAACCACGGCAAGGACG | 63 |
| timized | CCGGCAACGAGCUGGAAACCAGCACAGCCACACGCGC | 0.5 |
| - | AACAAGCUGACCAACAAGAUCACCUACAUCCUGUGGA | |
| | CCAUCACCCUGGUGCUGCUGAGCAUCGUGUUCAUCAUC | |
| | GUGCUGACCAAUAGCAUCAAGAGCGAGAAGGCCAGAG | |
| | AGAGCCUGCUGCAGGACAUCAACAACGAGUUCAUGGA | |
| | AGUGACCGAGAAGAUCCAGGUGGCCAGCGACAACACC AACGACCUGAUCCAGAGCGGCGUGAACACCCGGCUGCU | |
| | GACCAUCCAGAGCCACGUGCAGAACUACAUCCCCAUCA | |
| | GCCUGACCCAGCAGAUCAGCGACCUGCGGAAGUUCAUC | |
| | AGCGAGAUCACCAUCCGGAACGACAACCAGGAAGUGC | |
| | CCCCCCAGAGAAUCACCCACGACGUGGGCAUCAAGCCC | |
| | CUGAACCCCGACGAUUUCUGGCGGUGUACAAGCGGCC | |
| | UGCCCAGCCUGAUGAAGACCCCCCAAGAUCCGGCUGAUG CCUGGCCCUGGACUGCCGCCAUGCCUACCACAGUGGA | |
| | CCUGGCCCUGGACUGCUGGCCAUGCCUACCACAGUGGA UGGCUGUGUGCGGACCCCCAGCCUCGUGAUCAACGAUC | |
| | UGAUCUACGCCUACACCAGCAUCUGAUCAACCGGGGC | |
| | UGCCAGGAUAUCGGCAAGAGCUACCAGGUGCUGCAGA | |
| | | |
| | UCGGCAUCAUCACCGUGAACUCCGACCUGGUGCCCGAC | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACACC | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACACC GACGUGUACCAGCUGUGCAGCACCCCCAAGGUGGACG | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACACC GACGUGUACCAGCUGUGCAGCACCCCCAAGGUGGACG AGAGAAGCGACUACGCCAGCAGCGGCAUCGAGGAUAU | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAAGAGCUGCAGCCUGGCUCUGCUGAACACCC GACGUGUACCAGCUGUGCAGCACCCCAAGGUGGACG AGAGAAGCGACUACGCCAGCAGCGGCAUCGAGGAUAU CGUGCUGGACAUCGUGAACUACGACGGCAGCAUCAGC | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACACC GACGUGUACCAGCUGUGCAGCACCCCCAAGGUGGACG AGAGAAGCGACUACGCCAGCAGCGGCAUCGAGGAUAU | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGCUCCUGCUGAACACC GACGUGUACCAGCUGUGCAGCACCCCCAGGUGGACG AGAGAAGCGACUACGCCAGCAGCGGCAUCGAGGAUAU CGUGCUGGACAUCGUGAACUACGACGCGCAGCAUCAGC ACCACCCGGUUCAAGAACAACAACAUCAGCUUCGACCA | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACACC GACGUGUACCAGCUGUGCAGCACCCCCAAGGUGGACG AGAGAAGCGACUACGCCAGCAGCGCAUCGAGGAUAU CGUGCUGGACAUCGUGAACUACGACGGCAGCAUCAGC ACCACCCGGUUCAAGAACAACAACAUCAGCUUCGACCA GCCCUACGCCGCCUGUACCCUUCUGUGGGCCCUGGCA | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACACCC GACGUGUACCAGCUGUGCAGCACCCCAAGGUGGACG AGAGAAGCGACUACGCCAGCAGCGGCAUCGAGGAUAU CGUGCUGGACAUCGUGAACUACGACGGCGAGCAUCAGC ACCACCCGGUUCAAGAACAACAACAUCAGCUUCGACCA GCCCUACGCCGCCUGUAACUACCUUCGUGGGCCCUGGCA UCUACUACAAGGGCAAGAUCAUCUUCCUGGGCUACGG CGGCCUGGAACACCACAUCAACGACAUCGAC | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGCUUCCUGCUGAACACC GACGUGUACCAGCUGUGCAGCACCCCCCAGGUGGACG AGAGAAGCGACUACGCCAGCAGCGGCAUCGAGGAUAU CGUGCUGGACAUCGUGAACUACGACGCGCGCAUCGAGC ACCACCCGGUUCAAGAACAACAACAUCAGCUUCGACCA GCCCUGAGCGCCCUGGACCUUCUUCCUGGGCCCCUGGCA UCUACUACAAGGGCAAGAUCAUCUUCCUGGGCUACGG CGGCCUGGAACACCCCAUCAACGAGAACGCCAUCUGCA ACACCACCGGCUGCCUGGCAAGAACCGCAGG | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACAUC GACGUGUACCAGCUGUGCAGCACCCCCAAGGUGGACG AGAGAAGCGACUACGCCAGCAGCGCAUCGAGGAUAU CGUGCUGGACAUCGUGAACUACGACGGCGAGCAUCAGC ACCACCCGGUUCAAGAACAACAACAUCAGCUUCGACCA GCCCUACGCCGCCUUGUACCUUCUGUGGGCCCUGGCA UCUACUACAAGGGCAAGAUCAUCUUCCUGGGCUACGG CGGCCUGGAACACCCAUCAACGAGAACGCCAUCUGCA ACACCACCGGCUGCCCUGGCAAGAGACGCCAUCUGC AAUCAGGCCAGCCACGCCCUGGUCAGCGACCGCAG AAUCAGGCCAGCCACGCCCUGGUCAGCGACCGCAG AAUCAGCCACGCCUGAUCAUCGUGGUCGACAAGGGCCUG | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACAUC GACGUGUACCAGCUGUGCAGCACCCCCAAGGUGGACG AGAGAAGCGACUACGCCAGCAGCGCAUCGAGGAUAU CGUGCUGGACAUCGUGAACUACGACGGCAGCAUCAGC ACCACCCGGUUCAAGAACAACAACAUCAGCUUCGACCA GCCCUACGCCGCCUUGUACCUUUCUUGUGGGCCCUGGCA UCUACUACAAGGGCAAGAUCAUCUUCCUGGGCUACGG CGGCCUGGAACACCCCUUCAACGAGAACGCCAUCUGCA ACACCACCGGCUGCCCUGGCAAGACCCAGGAGACUCGC AAUCAGCCACCCCAUCACCAGGACCACGCAG AAUCAGCCACCCACACCCCUGGUUCAGCGACCGCAG AAUCAGCCACCCAACACCUGGUUCAGCGACCGCAG AAUGGUCAACUCUAUCAUCGUGGUGACCAAUCAGCA | |
| | CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACAUC GACGUGUACCAGCUGUGCAGCACCCCCAAGGUGGACG AGAGAAGCGACUACGCCAGCAGCGCAUCGAGGAUAU CGUGCUGGACAUCGUGAACUACGACGGCGAGCAUCAGC ACCACCCGGUUCAAGAACAACAACAUCAGCUUCGACCA GCCCUACGCCGCCUUGUACCUUCUGUGGGCCCUGGCA UCUACUACAAGGGCAAGAUCAUCUUCCUGGGCUACGG CGGCCUGGAACACCCAUCAACGAGAACGCCAUCUGCA ACACCACCGGCUGCCCUGGCAAGAGACGCCAUCUGC AAUCAGGCCAGCCACGCCCUGGUCAGCGACCGCAG AAUCAGGCCAGCCACGCCCUGGUCAGCGACCGCAG AAUCAGCCACGCCUGAUCAUCGUGGUCGACAAGGGCCUG | |

TABLE 5-continued

| - | |
|--|--|
| ACAUCACCGACUACAGGACAUCCGAUCAAGUGGACC UGGCACAACGUGCUGAGCAGACCCGGCAACAAUGAGU GCCCUUGGGGCCACAGCUGCCCCGAUGGAUGUAUCACC GGCGUGUACACCGACGCUACCCCGGAGAUCUACCGG CUCCAUCGUGUCCAGCGUGAUCCUGGACAGCCAGAAA AGCAGAGUGAACCACGGCCAUCAGAACACAGCC CGAGAGGGAGUGAACGAACUGGCCAUCAGAACC CUGAGCGCCGGCUACACCACCACAAGCUGCAUCACACA | |
| CUACAACAAGGGCUACUGCUUCCACAUCGUGGAAAUC AACCACAAGUCCCUGAACACCUUCCAGCCCAUGCUGUU CAAGACCGAGAUCCCCAAGAGCUGCUCC | |
| AUGCCCAUCAGCAUCCUGCUGAUCAUCACCACAAUGAU CAUGGCCAGCAUGCCAGAUCGACAUCACCAAGCUGC AGCACGUGGGCUGUGUGUGAACAGCCCCAAGGCUU GAAGAUCAGCCAGAACUUCGAGACACCCUACCUGAUC UUGAGCCUGAUCCCCAAGAUCGAGACACGCUACCUGAUC GCGCCGACUGAUCAUCCCCCUGUACGACGCCUGCU GGACAGACUGAUCAUCCCCCUGUACGACGCCUGCUG GGCAGAAGACCUGAUCAUCCCCUGUACGACGCCUGCGC UGCAGAAGACCUGAUCGUGACCAACAGGAUUCUUCGGCG GCGUGAUCGGCACAAUCGCCUGGAGAGUUCUUCGGCG GCGUGAUCGGCACAAUCGACAUCGAGAGGUGCACAAG CGCCCAGAUUCAGCCCUUGUGCAGAGCGUGCAGA AGCAGGCCAGAAUCGACAUCGAGAGCUGCAGAGCGU UCCAGCGUGGGCAAUCUGAUCGUGCCGUGUGGAAGGCC AGCCGGCUGGCCAUCUGAUCGUGCCGUGUGGAAGCUG GGCUGGGCCUGCACAACAGCGUGCAGAGCUGCAG UCCAGCGUGGGCAUCUGAUCGUGCGCUGUAU CGCCCGGCUGGCCUGUGAACAAGAGUGCCGCUCUAU CGCCCGGCUGGCCUGUGAACGACGCUGCAGGCUGCACAA CAUCUUCGGCGACAACAUCGGCAGCCUGCAGCUGCAGAU GGCAUUGACCGAGAUCUGCGCCGCUGUACCGCA CCAACAUCACCGGAGAUCGACCGCAGCUGCAGCA CAUCUUCGGCGACAACAUCGGCAGCCUGCAGGAAAAG GGCAUUAAGUGCACGGGAUCGCCAGCAU CAACAUCACCGAGAUCUUCACCACCAGCACCGUGAU AAGUACGACAUCUUCGACGCUGCUGUCACCGA GACUGCUGAACACCCCAGAUCUACCGCAGCUU CUCCUACAACAUCCAGAAGCGGCUGCCCUGUGACCA CAACUCACCCUGCAGGUGUGACCGCACUA CAGCAUCACCCUGCAGGUGCGCCUGACCACACU CUCCUACACACCCCAGAUCUACAGAGGGCCUUCUCGGC GACUGCUGAACACCCCAGAUCUACAGAGCA CCACGCCUGAACACCCCGCAGUGGUCCACCA GACUGCUGAACACCCCAGAUCUACAGAGCCA CCACGCUGACACCCCGGACCCUGGCCUUCUGGCC AGUUCCACACCACGUGACCUCGACCUUCUGGCC AGUACCCCACAUUAUGACCACAGGCGCUUUCUGGCC AGUACCCCCCCCCC | 64 |
| | GGCGUGUACACCGACGCUACCCCUGAAUCCUACAGAA AGCAGAQUGAACCCCGUGAUCACGACAGCACGACAA AGCAGAQUGAACGCCCGUGAUCACGACAGCACCGCC CUGAGCGCCGGCUACACCACCACAGCCUGCAUCAAACAAGACC CUACAACAAGGCCCGUACACCACCACAAGCUGCAUCAACAA CUACAACAAGGCCUGAACACCUUCCACACACAAGCU CAAGACCGAGAUCCCCUGAUCAUCACCACACAAGAU CAAGACCGAGAUCCCCGAGAUCGACAUCACCACAAGGU GACGCUGGGCGUGCUGUGAUCAUCACCACAAGCUG CUGAGCCUGGCCAGAUCGGCAUCACCACAAGCUG CUGAGCCUGGCCGGCUGUGAUCAUCACCACAAGCUG CGGCGGCCAGAACUUCGAGACAGCAUCACCAAGCUG CUGAGCCUGAUCCCCCAGAUCGAGACAGCAACCAGCU CGGCGGACCAGCAGAUCGAGACAGCAACAGCU CGGGCGACCAGCAGAUCGAGGACAGCAACAGCU CGGGCGACCAGCAGAUCGAGGACAGCAACAGCU CGGGCGACCAGCAGAUCGAGGACGACAACCAGCU GGGACAACUGAUCAUCCCCCUGUGAGCAGCAACGACAA CGAGAACACCGACCCCCGGGACCGAGAGUUCUUCGGGG GCGUGAUCGGCACAAUCGCCCUGGGGGUGGCCACAAG CGCCCAGAUUACAGCCCUUGUGGCCCUGGUGAAGCCA AGCAGGCCAGAAGCGACAUCGAGAGAGUACCAA GGCCAGAUUACAGCCCUUGGAGCGAGAGCCAAG CGCCCGGCUGGCCACAAUCGAGAGAGUGCCACAAG CGCCCGGCUGGCCACACAGGCCUGGUGGAAGCCA AGCAGGCCAGAACGACAACAGGCGUGCAG UCCAGGCUAGGCACAUCGAGAGAGCGCAAGGCC GGCUUGGCCGGACACCAACAGGCGUGGCCACAAG CGCCUGGGCACACCAACAGGCCUGCGGCGGCG GGCUUGGGCCGGACACCGCGGCGGCCGCCUCUUU CGCCCGGCUGGCUGUGAACGCGGCCGCCUCUUU CGCCCGGCUGGCUGGAGAUCUGCGCGCCUCUUU CGCCCGGCUGGCUGGCGCGGCGGCGCAGCCAA CAUCUUCGCGGACAACAGCACUGCGGCGCGCCCUCUUU CGCCCGGCUGGCUGGCGGCGGCGCGCCGCCUGGAGU GGCAUUGACGCGCGAGAUCUGCGCGCGCCGCCGCAGACGA CAUCUCCGGGACAACCAGCCUGCUGCAGCCAA CAUCUUCGCGCAAAUCGGCGGCUGCCCGAGACGA CCAACAUCACCGAGAUCUGACCCACGGCGUGCCCAAGCCA CCAACAUCACCGAGAUCGCGCGCGCCUGGAGACAACACCA CACGACCACCCUGCAAGUGGCGCGCCCCUGGCGCCGCCUUCUGGC GAACAGCUGGAAGACCCAGGACUGAGCCCACACCA GCUACAUCUGCCCAGAACCGCGAGUGGCACACUCGCC CACGACGCGUGAACACCCAGGACCUGGACCCCUCCGCU CCCCACAACACCCCGGACCUGGCCUUCAGCC AGUACCACCCCCGGACCUCCGACAUCCGCCCU CCCACAACACCCCGGACCUCGACAUCCGCCC AGUACCACCACCACCACGGCAUCCGCCCU CCCACAACACCCCGGACCUCGACAUCCGCCCU CCCCCACAACACCCCGGAUCCCCGGCAUCAGCCCU CCCCCACAACCACCCGGCAUCCGCGCUUCGGCCCU UCUACACCCCCGACAUCCCCGACAUCCGCCU CCCCCACAACACCCGGAUCCCCGGCCUUCGGCCCU CUCACCCCCGACGACUCCGACUCCGACCUCGGCCUUCGCCCU CUCACCCCCGACGACCUCCGACUCCGACCUCGGCCUU CCCCCACAAGCCCCGACAUCCCCGACCUCGGCCUU |

TABLE 6

| | PIV3 Amino Acid Sequences | |
|---|--|---------------|
| Description | Sequence | SEQ ID NO: |
| >gi 612507166 gb AHX22429.1 fusion glycoprotein | MPISILLIITTMIMASHCQIDITKLQHVGVLVNSPKGMKISQ NFETRYLILSLIPKIEDSNSCGDQQIKQYKRLLDRLIIPLYDG LRLQKDVIVTNQESNENTDPRTERFFGGVIGTIALGVATSA | 13 |
| FO [Human] parainfluenza virus 3] | QITAAVALVEAKQARSDIEKLKEAIRDTNKAVQSVQSSVG NLIVAIKSVQDYVNKEIVPSIARLGCEAAGLQLGIALTQHYS ELTNIFGDNIGSLQEKGIKLQGIASLYRTNITEIFTTSTVDKY | |
| -1 | DIYDLLFTESIKVRVIDVDLNDYSITLQVRLPLLTRLLNTQIY | |

| TABLE 6-continued |
|-------------------|
|-------------------|

| | PIV3 Amino Acid Sequences | |
|---|---|---------------|
| Description | Sequence | SEQ II NO: |
| gi 612507167 gb AHX22430.1 hemagglutinin- neuraminidase [Human parainfluenza virus 3] | KVDSISYNIQNREWYIPLPSHIMTKGAFLGGADVKECIEAFS SYICPSDPGFVLNHEMESCLSGNISQCPRTTVTSDIVPRYAF VNGGVVANCITTTCTCNGIGNRINQPPDQGVKIITHKECNTI GINGMLFNTNKEGTLAFYTPDDITLNNSVALDPIDISIELNK AKSDLEESKEWIRRSNQKLDSIGSWHQSSTTIIVILIMMIILFI INITIITIAIKYYRIQKRNRVDQNDKPYVLTNK MEYWKHTNHGKDAGNELETSTATHGNKLTNKITYILWTIT LVLLSIVFIIVLTNSIKSEKARESLLQDINNEFMEVTEKIQVA SDNTNDLIQSGVNTRLLTIQSHVQNYIPISLTQQISDLRKFIS EITIRNDNQEVPPQRITHDVGIKPLNPDDFWRCTSGLPSLMK TPKIRLMPGPGLLAMPTTVDGCVRTPSLVINDLIYAYTSNLI TRGCQDIGKSYQVLQIGIITVNSDLVPDLNPRISHTPNINDN | 14 |
| | RKSCSLALLNTDVYQLCSTPKVDERSDYASSGIEDIVLDIV NYDGSISTTRFKNNNISFDQPYAALYPSVGPGIYYKGKIIPL GYGGLEHPINENAICNTTGCPGKVTQRCNQASHSPWFSDR RMVNSIIVVDKGLNSVPKLKVMTISMRQNYWGSEGRLLLL GNKIYIYTRSTSWHSKLQLGIIDITDYSDIRIKWTWHNVLSR PGNNECPWGHSCPDGCITGVYTDAYPLNPTGSIVSSVILDS QKSRVNPVITYSTATERVNELAIRNKTLSAGYTTTSCITHY NKGYCFHIVEINHKSLNTFQPMLFKTEIPKSCS | |

TABLE 7

| PIV3 NCBI Accession Numbers (Nucleic Acid and Amino Acid Sequences) | | | | |
|---|-------------------|--|--|--|
| Description | GenBank Accession | | | |
| Fusion glycoprotein F0 [Human parainfluenza virus 3] | KJ672601.11: | | | |
| HPIV3/Homo sapiens/PER/FLA4815/2008 | 4990-6609 | | | |
| | AHX22429 | | | |
| | (Fusion protein) | | | |
| hemagglutinin-neuraminidase [Human parainfluenza virus 3] | KJ672601.1 : | | | |
| HPIV3/Homo sapiens/PER/FLA4815/2008 | 6724-8442 | | | |
| | AHX22430 | | | |
| | (HN protein) | | | |
| Recombinant PIV3/PIV1 virus fusion glycoprotein (F) | AF016281 | | | |
| and hemagglutinin (HN) genes, complete cds; and RNA | AAC23947 | | | |
| dependent RNA polymerase (L) gene, partial eds. | (hemagglutinin) | | | |
| Recombinant PIV3/PIV1 virus fusion glycoprotein (F) | AF016281 | | | |
| and hemagglutinin (HN) genes, complete cds; and RNA | AAC23947 | | | |
| lependent RNA polymerase (L) gene, partial cds. | (fusion protein) | | | |
| nemagglutinin-neuraminidase [Human parainfluenza virus 3] | BAO32044.1 | | | |
| nemagglutinin-neuraminidase [Human parainfluenza virus 3] | BAO32051.1 | | | |
| C protein [Human parainfluenza virus 3] | NP_599251.1 | | | |
| C protein [Human parainfluenza virus 3] | ABZ85670.1 | | | |
| C protein [Human parainfluenza virus 3] | AGT75164.1 | | | |
| C protein [Human parainfluenza virus 3] | AAB48686.1 | | | |
| C protein [Human parainfluenza virus 3] | AHX22115.1 | | | |
| C protein [Human parainfluenza virus 3] | AGW51066.1 | | | |
| C protein [Human parainfluenza virus 3] | AGW51162.1 | | | |
| C protein [Human parainfluenza virus 3] | AGT75252.1 | | | |
| C protein [Human parainfluenza virus 3] | AGT75188.1 | | | |
| C protein [Human parainfluenza virus 3] | AGW51218.1 | | | |
| C protein [Human parainfluenza virus 3] | AGW51074.1 | | | |
| C protein [Human parainfluenza virus 3] | AGT75323.1 | | | |
| C protein [Human parainfluenza virus 3] | AGT75307.1 | | | |
| C protein [Human parainfluenza virus 3] | AHX22131.1 | | | |
| C protein [Human parainfluenza virus 3] | AGW51243.1 | | | |
| C protein [Human parainfluenza virus 3] | AGT75180.1 | | | |
| C protein [Human parainfluenza virus 3] | AGT75212.1 | | | |
| C protein [Human parainfluenza virus 3] | AGW51186.1 | | | |
| C protein [Human parainfluenza virus 3] | AHX22075.1 | | | |
| C protein [Human parainfluenza virus 3] | AHX22163.1 | | | |
| C protein [Human parainfluenza virus 3] | AGT75196.1 | | | |
| C protein [Human parainfluenza virus 3] | AHX22491.1 | | | |
| C protein [Human parainfluenza virus 3] | AHX22139.1 | | | |
| C protein [Human parainfluenza virus 3] | AGW51138.1 | | | |
| C protein [Human parainfluenza virus 3] | AGW51114.1 | | | |
| C protein [Human parainfluenza virus 3] | AGT75220.1 | | | |
| C protein [Human parainfluenza virus 3] | AHX22251.1 | | | |
| RecName: Full = Protein C; AltName: Full = VP18 protein | P06165.1 | | | |

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TABLE 7-continued

| Description | GenBank Accession |
|---|--------------------------|
| C protein [Human parainfluenza virus 3] | AHX22187.1 |
| C protein [Human parainfluenza virus 3] | AGT75228.1 |
| C protein [Human parainfluenza virus 3] | AHX22179.1 |
| C protein [Human parainfluenza virus 3] C protein [Human parainfluenza virus 3] | AHX22427.1 AGW51210.1 |
| nonstructural protein C [Human parainfluenza virus 3] | BAA00922.1 |
| C protein [Human parainfluenza virus 3] | AHX22315.1 |
| C protein [Human parainfluenza virus 3] | AGW51259.1 |
| C protein [Human parainfluenza virus 3] | AHX22435.1 |
| C protein [Human parainfluenza virus 3] | AHX22123.1 |
| C protein [Human parainfluenza virus 3] | AHX22299.1 |
| C protein [Human parainfluenza virus 3] | AGW51267.1 CAA28430.1 |
| unnamed protein product [Human parainfluenza virus 3] C protein [Human parainfluenza virus 3] | AGW51178.1 |
| C protein [Human parainfluenza virus 3] | AHX22411.1 |
| RecName: Full = Protein C | P06164.1 |
| phosphoprotein [Human parainfluenza virus 3] | NP_067149.1 |
| phosphoprotein [Human parainfluenza virus 3] | AAB48685.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22498.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22490.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGT75259.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51137.1 AGW51145.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AGW51145.1 AGT75298.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51113.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGT75203.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGT75163.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22506.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51129.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22194.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGT75211.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22258.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AGW51121.1 AGT75282.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22146.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22138.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22322.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22370.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22098.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22130.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22418.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AHX22114.1 AHX22410.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGT75306.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22170.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22266.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22090.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGT75195.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22226.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22178.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AHX22122.1 AHX22186.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22066.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22522.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51225.1 |
| phosphoprotein [Human parainfluenza virus 3] | BAN29032.1 |
| phosphoprotein [Human parainfluenza virus 3] | ABZ85669.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22426.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22058.1 |
| phosphoprotein [Simian Agent 10] | ADR00400.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AHX22250.1 AHX22434.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22454.1 AHX22298.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22442.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22074.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51153.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51241.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22210.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51105.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGT75251.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22362.1 AHX22474.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AGW51217.1 |
| phosphoprotein [Human parainfluenza virus 3] | AIG60038.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22378.1 |
| | |

TABLE 7-continued

| Description | GenBank Accession |
|---|---------------------------|
| phosphoprotein [Human parainfluenza virus 3] | AGT75187.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51233.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22482.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AGW51161.1 AHX22306.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22162.1 |
| phosphoprotein [Human parainfluenza virus 3] | ACJ70087.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22466.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22346.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51089.1 AGW51073.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AGW51075.1 AGW51185.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51065.1 |
| phosphoprotein [Human parainfluenza virus 3] | ABY47603.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51049.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22330.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AGW51250.1 AGT75227.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51282.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51209.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51193.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGT75322.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGT75219.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AGW51258.1 AGW51041.1 |
| phosphoprotein [Human parainfluenza virus 3] | ACD99698.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51266.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGT75179.1 |
| phosphoprotein [Human parainfluenza virus 3] | AHX22282.1 |
| phosphoprotein [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] | AGW51169.1 AGW51274.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW51274.1 AGW51201.1 |
| phosphoprotein [Human parainfluenza virus 3] | AGW5120111 AGW51177.1 |
| RecName: Full = Phosphoprotein; Short = Protein P | P06162.1 |
| P protein [Human parainfluenza virus 3] | AAA66818.1 |
| phosphoprotein [Human parainfluenza virus 3] | AAA46866.1 |
| phosphoprotein [Human parainfluenza virus 3] polymerase-associated nucleocapsid phosphoprotein | BAA00031.1 RRNZP5 |
| (version 2) - parainfluenza virus type 3 | |
| [Human parainfluenza virus 3] | |
| phosphoprotein [Human parainfluenza virus 3] | AGT75171.1 |
| phosphoprotein [Human parainfluenza virus 3] | BAA00921.1 NP_599250.1 |
| D protein [Human parainfluenza virus 3] D protein [Human parainfluenza virus 3] | AHX22377.1 |
| D protein [Human parainfluenza virus 3] | AHX22121.1 |
| D protein [Human parainfluenza virus 3] | AGT75297.1 |
| D protein [Human parainfluenza virus 3] | AGW51136.1 |
| D protein [Human parainfluenza virus 3] | AGW51242.1 |
| D protein [Human parainfluenza virus 3] D protein [Human parainfluenza virus 3] | AGW51112.1 AHX22497.1 |
| D protein [Human parainfluenza virus 3] | AHX22145.1 |
| D protein [Human parainfluenza virus 3] | AGT75202.1 |
| D protein [Human parainfluenza virus 3] | AHX22385.1 |
| D protein [Human parainfluenza virus 3] | AGW51216.1 |
| D protein [Human parainfluenza virus 3] | AGT75281.1 |
| D protein [Human parainfluenza virus 3] D protein [Human parainfluenza virus 3] | AGT75194.1 AHX22521.1 |
| D protein [Human parainfluenza virus 3] | AGW51120.1 |
| D protein [Human parainfluenza virus 3] | AGT75313.1 |
| D protein [Human parainfluenza virus 3] | AHX22249.1 |
| D protein [Human parainfluenza virus 3] | AHX22097.1 |
| D protein [Human parainfluenza virus 3] | AGW51144.1 |
| D protein [Human parainfluenza virus 3] | AHX22089.1 AHX22225.1 |
| D protein [Human parainfluenza virus 3] D protein [Human parainfluenza virus 3] | AHX22223.1 AHX22137.1 |
| D protein [Human parainfluenza virus 3] | AHX22065.1 |
| D protein [Human parainfluenza virus 3] | AGW51224.1 |
| D protein [Human parainfluenza virus 3] | AGT75210.1 |
| D protein [Human parainfluenza virus 3] | AHX22393.1 |
| D protein [Human parainfluenza virus 3] | AGT75258.1 |
| D protein [Human parainfluenza virus 3] D protein [Human parainfluenza virus 3] | AHX22345.1 AGT75250.1 |
| D protein [Human parainfluenza virus 3] | AHX22113.1 |
| D protein [Human parainfluenza virus 3] | AGW51232.1 |
| D protein [Human parainfluenza virus 3] | AHX22057.1 |
| D protein [Human parainfluenza virus 3] | AHX22209.1 |

TABLE 7-continued

| Description | GenBank Accession |
|---|--------------------------|
| D protein [Human parainfluenza virus 3] | AGW51056.1 |
| D protein [Human parainfluenza virus 3] | AHX22161.1 |
| D protein [Simian Agent 10] | ADR00402.1 |
| D protein [Human parainfluenza virus 3] | AHX22361.1 |
| D protein [Human parainfluenza virus 3] | AGW51281.1 |
| D protein [Human parainfluenza virus 3] | AGW51184.1 |
| D protein [Human parainfluenza virus 3] | AGW51160.1 |
| D protein [Human parainfluenza virus 3] | AHX22465.1 |
| D protein [Human parainfluenza virus 3] | AHX22329.1 |
| D protein [Human parainfluenza virus 3] | AGW51064.1 |
| D protein [Human parainfluenza virus 3] | AGW51040.1 |
| D protein [Human parainfluenza virus 3] | AGT75226.1 |
| D protein [Human parainfluenza virus 3] | AG175220.1 AHX22425.1 |
| | |
| D protein [Human parainfluenza virus 3] | AHX22305.1 |
| D protein [Human parainfluenza virus 3] | AGW51249.1 |
| D protein [Human parainfluenza virus 3] | AHX22481.1 |
| D protein [Human parainfluenza virus 3] | AHX22281.1 |
| D protein [Human parainfluenza virus 3] | AGW51048.1 |
| D protein [Human parainfluenza virus 3] | AHX22297.1 |
| D protein [Human parainfluenza virus 3] | AGW51088.1 |
| D protein [Human parainfluenza virus 3] | AGT75305.1 |
| D protein [Human parainfluenza virus 3] | AHX22185.1 |
| D protein [Human parainfluenza virus 3] | AGW51104.1 |
| D protein [Human parainfluenza virus 3] | AHX22081.1 |
| D protein [Human parainfluenza virus 3] | AGW51192.1 |
| D protein [Human parainfluenza virus 3] | AHX22489.1 |
| D protein [Human parainfluenza virus 3] | AHX22441.1 |
| D protein [Human parainfluenza virus 3] | AHX22409.1 |
| D protein [Human parainfluenza virus 3] | AHX22369.1 |
| D protein [Human parainfluenza virus 3] | AHX22303.1 AHX22321.1 |
| D protein [Human parainfluenza virus 3] | AHX22073.1 |
| | |
| D protein [Human parainfluenza virus 3] | AGW51152.1 |
| D protein [Human parainfluenza virus 3] | AGW51072.1 |
| D protein [Human parainfluenza virus 3] | AGT75321.1 |
| D protein [Human parainfluenza virus 3] | AHX22257.1 |
| D protein [Human parainfluenza virus 3] | AHX22129.1 |
| D protein [Human parainfluenza virus 3] | AHX22417.1 |
| D protein [Human parainfluenza virus 3] | AGT75218.1 |
| D protein [Human parainfluenza virus 3] | AHX22265.1 |
| D protein [Human parainfluenza virus 3] | AGT75178.1 |
| D protein [Human parainfluenza virus 3] | AHX22433.1 |
| D protein [Human parainfluenza virus 3] | AGW51273.1 |
| D protein [Human parainfluenza virus 3] | AGW51208.1 |
| D protein [Human parainfluenza virus 3] | AGT75170.1 |
| D protein [Human parainfluenza virus 3] | AGT75162.1 |
| D protein [Human parainfluenza virus 3] | AGW51257.1 |
| D protein [Human parainfluenza virus 3] | AGW51257.1 AGW51200.1 |
| | |
| D protein [Human parainfluenza virus 3] | AGW51176.1 |
| D protein [Human parainfluenza virus 3] | AGT75186.1 |
| D protein [Human parainfluenza virus 3] | AGW51265.1 |
| D protein [Human parainfluenza virus 3] | AGW51168.1 |

TABLE 8

TABLE 8-continued

| | Signal Peptides | | 50 | 30 | | |
|---|--------------------------|---------------|----|----------------------|-----|--|
| Description | Sequence | SEQ ID NO: | | Descript | ion | |
| HuIgG _k signal peptide | METPAQLLFLLLLWLPDTTG | 15 | 55 | Japanese encephal | | |
| IgE heavy chain epsilon-1 signal peptide | MDWTWILFLVAAATRVHS | 16 | | signal s | | |
| Japanese encephalitis PRM signal sequence | MLGSNSGQRVVFTILLLLVAPAYS | 17 | 60 | | hM | |
| VSVq protein | MKCLLYLAFLFIGVNCA | 18 | | Group | n | |
| signal sequence | | | 65 | 1 | 5 | |

_____ 50 _____

| | | Signal Peptides | |
|---|---|-----------------|---------------|
| | Description | Sequence | SEQ ID NO: |
| | Japanese encephalitis JEV signal sequence | MWLVSLAIVTACAGA | 19 |
| | | | |
|) | | TABLE 9 | |

| - | hMPV/PIV Cotton Rat Challenge Study Design | | | | | |
|---|--|---|-------------------|-----------|-------|-----------|
| _ | Group | n | Test Article | [conc]/µg | Route | Challenge |
| | 1 | | Placebo | n/a | IM | hMPV/A2 |
| | 2 | 5 | hMPV vaccine mRNA | 30 | IM | hMPV/A2 |

TABLE 9-continued

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 $[conc]/\mu g$ Route Challenge

PIV3

PIV3

PIV3

| _ | | | | innaea | | | | | | nunaça | | |
|---|-------|----|-----------------------------------|------------|--------|-----------|-----|-------|-------------------------|-----------------|--------|----------|
| _ | | hl | MPV/PIV Cotton Rat Chall | enge Study | Design | | - | | hMPV/PIV Cotton Rat Cha | illenge Study I | Design | |
| _ | Group | n | Test Article | [conc]/µg | Route | Challenge | . 5 | Group | n Test Article | [conc]/µg | Route | (|
| | 3 | 5 | hMPV vaccine mRNA | 15 | IM | hMPV/A2 | | 10 | 5 PIV3 vaccine mRNA | 10 | IM | <u> </u> |
| | 4 | 5 | hMPV vaccine mRNA | 10 | IM | hMPV/A2 | | | 5 hMPV/PIV3 vaccine | 30 | IM | |
| | 5 | 5 | hMPV/PIV3 vaccine mRNA (15/15) | 30 | IM | hMPV/A2 | | 11 | mRNA (15/15) | 30 | 1111 | 1 |
| | 6 | 5 | FI-hMPV | n/a | IM | hMPV/A2 | | 12 | 5 FI-PIV3 | n/a | IM | J |
| | 7 | 5 | Placebo | n/a | IM | PIV3 | 10 | | | | | |
| | 8 | 5 | PIV3 vaccine mRNA | 30 | IM | PIV3 | r. | | 60 | | | |
| | 9 | 5 | PIV3 vaccine mRNA | 15 | IM | PIV3 | | | | | | _ |
| | | | | | | | | | | | | |

| TABLE 1 | 0 |
|---------|---|
|---------|---|

| Strain | Nucleic Acid Sequence | SEQ I NO: |
|-----------------------------|--|--------------|
| gb KJ156934.1 : 21405-25466 | ATGATACACTCAGTGTTTCTACTGATGTTCTTGTTAACACC | 20 |
| Middle | TACAGAAAGTTACGTTGATGTAGGGCCAGATTCTGTTAAG | |
| East respiratory | TCTGCTTGTATTGAGGTTGATATACAACAGACCTTCTTTGA | |
| syndrome | TAAAACTTGGCCTAGGCCAATTGATGTTTCTAAGGCTGAC | |
| oronavirus | GGTATTATATACCCTCAAGGCCGTACATATTCTAACATAA | |
| isolate | CTATCACTTATCAAGGTCTTTTTCCCTATCAGGGAGACCAT | |
| Riyadh 14 2013, | GGTGATATGTATGTTTACTCTGCAGGACATGCTACAGGCA | |
| pike protein | CAACTCCACAAAAGTTGTTTGTAGCTAACTATTCTCAGGA | |
| (nucleotide) | CGTCAAACAGTTTGCTAATGGGTTTGTCGTCCGTATAGGA | |
| | GCAGCTGCCAATTCCACTGGCACTGTTATTATTAGCCCATC | |
| | TACCAGCGCTACTATACGAAAAATTTACCCTGCTTTTATGC | |
| | TGGGTTCTTCAGTTGGTAATTTCTCAGATGGTAAAATGGG | |
| | CCGCTTCTTCAATCATACTCTAGTTCTTTTGCCCGATGGAT | |
| | GTGGCACTTTACTTAGAGCTTTTTATTGTATTCTAGAGCCT | |
| | CGCTCTGGAAATCATTGTCCTGCTGGCAATTCCTATACTTC | |
| | TTTTGCCACTTATCACACTCCTGCAACAGATTGTTCTGATG | |
| | GCAATTACAATCGTAATGCCAGTCTGAACTCTTTTAAGGA | |
| | GTATTTTAATTTACGTAACTGCACCTTTATGTACACTTATA | |
| | ACATTACCGAAGATGAGATTTTAGAGTGGTTTGGCATTAC | |
| | ACAAACTGCTCAAGGTGTTCACCTCTTCTCATCTCGGTATG | |
| | TTGATTTGTACGGCGGCAATATGTTTCAATTTGCCACCTTG | |
| | CCTGTTTATGATACTATTAAGTATTATTCTATCATTCCTCA | |
| | CAGTATTCGTTCTATCCAAAGTGATAGAAAAGCTTGGGCT | |
| | GCCTTCTACGTATATAAACTTCAACCGTTAACTTTCCTGTT | |
| | GGATTTTTCTGTTGATGGTTATATACGCAGAGCTATAGACT | |
| | GTGGTTTTAATGATTTGTCACAACTCCACTGCTCATATGAA | |
| | TCCTTCGATGTTGAATCTGGAGTTTATTCAGTTTCGTCTTT | |
| | CGAAGCAAAACCTTCTGGCTCAGTTGTGGAACAGGCTGAA | |
| | GGTGTTGAATGTGATTTTTCACCTCTTCTGTCTGGCACACC | |
| | TCCTCAGGTTTATAATTTCAAGCGTTTGGTTTTTACCAATT | |
| | GCAATTATAATCTTACCAAATTGCTTTCACTTTTTTCTGTG AATGATTTTACTTGTAGTCAAATATCTCCAGCAGCAATTGC | |
| | TAGCAACTGTTATTCTTCACTGATTTTGGATTATTTTTCAT | |
| | ACCCACTTAGTATGAAATCCGATCTCAGTGTTAGTTCTGCT | |
| | GGTCCAATATCCCAGTTTAATTATAAACAGTCCTTTTCTAA | |
| | TCCCACATGTTTGATCTTAGCGACTGTTCCTCATAACCTTA | |
| | CTACTATTACTAAGCCTCTTAAGTACAGCTATATTAACAA | |
| | GTGCTCTCGTCTTCTTTCTGATGATCGTACTGAAGTACCTC | |
| | AGTTAGTGAACGCTAATCAATACTCACCCTGTGTATCCATT | |
| | GTCCCATCCACTGTGTGGGGAAGACGGTGATTATTATAGGA | |
| | AACAACTATCTCCACTTGAAGGTGGTGGCTGGCTTGTTGC | |
| | TAGTGGCTCAACTGTTGCCATGACTGAGCAATTACAGATG | |
| | GGCTTTGGTATTACAGTTCAATATGGTACAGACACCAATA | |
| | GTGTTTGCCCCAAGCTTGAATTTGCTAATGACACAAAAAT | |
| | TGCCTCTCAATTAGGCAATTGCGTGGAATATTCCCTCTATG | |
| | GTGTTTCGGGCCGTGGTGTTTTTCAGAATTGCACAGCTGTA | |
| | GGTGTTCGACAGCAGCGCCTTTGTTTATGATGCGTACCAGA | |
| | ATTTAGTTGGCTATTATTCTGATGATGGCAACTACTACTGT | |
| | CTGCGTGCTTGTGTTGTGTTGTGTTCCTGTCTGTCATCTATGA | |
| | TAAAGAAACTAAAACCCACGCTACTCTATTTGGTAGTGTT | |
| | | |
| | GCATGTGAACACATTTCTTCTACCATGTCTCAATACTCCCG | |
| | TTCTACGCGATCAATGCTTAAACGGCGAGATTCTACATAT | |
| | GGCCCCCTTCAGACACCTGTTGGTTGTGTGTCCTAGGACTTGT | |
| | TAATTCCTCTTTGTTCGTAGAGGACTGCAAGTTGCCTCTCG | |
| | GTCAATCTCTCTGTGCTCTTCCTGACACCCTAGTACTCTC | |
| | ACACCTCGCAGTGTGCGCTCTGTGCCAGGTGAAATGCGCT | |
| | TGGCATCCATTGCTTTTAATCATCCCATTCAGGTTGATCAA | |
| | CTTAATAGTAGTTATTTTAAATTAAGTATACCCACTAATTT | |

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TABLE 10-continued

| B | etacoronavirus Nucleic Acid Sequence | |
|-------------------------------------|--|---------------|
| Strain | Nucleic Acid Sequence | SEQ II NO: |
| | TTCCTTTGGTGTGACTCAGGAGTACATTCAGACAACCATTC | |
| | AGAAAGTTACTGTTGATTGTAAACAGTACGTTTGCAATGG | |
| | TTTCCAGAAGTGTGAGCAATTACTGCGCGAGTATGGCCAG | |
| | TTTTGTTCCAAAATAAACCAGGCTCTCCATGGTGCCAATTT | |
| | ACGCCAGGATGATTCTGTACGTAATTTGTTTGCGAGCGTG | |
| | AAAAGCTCTCAATCATCTCCTATCATACCAGGTTTTGGAG GTGACTTTAATTTGACACTTCTAGAACCTGTTTCTATATCT | |
| | ACTGGCAGTCGTAGTGCACGTAGTGCTATTGAGGATTTGC | |
| | TATTTGACAAAGTCACTATAGCTGATCCTGGTTATATGCA | |
| | AGGTTACGATGATTGTATGCAGCAAGGTCCAGCATCAGCT | |
| | CGTGATCTTATTTGTGCTCAATATGTGGCTGGTTATAAAGT | |
| | ATTACCTCCTCTTATGGATGTTAATATGGAAGCCGCGTATA | |
| | CTTCATCTTTGCTTGGCAGCATAGCAGGTGTTGGCTGGACT | |
| | GCTGGCTTATCCTCCTTTGCTGCTATTCCATTTGCACAGAG TATVTTTTATATCCTCCTTTGCTGCTATTCCATTTGCACAGAG | |
| | TATYTTTTATAGGTTAAACGGTGTTGGCATTACTCAACAG GTTCTTTCAGAGAACCAAAAGCTTATTGCCAATAAGTTTA | |
| | ATCAGGCTCTGGGAGCTATGCAAACAGGCTTCACTACAAC | |
| | TAATGAAGCTTTTCCGGAAGGTTCAGGATGCTGTGAACAAC | |
| | AATGCACAGGCTCTATCCAAATTAGCTAGCGAGCTATCTA | |
| | ATACTTTTGGTGCTATTTCCGCCTCTATTGGAGACATCATA | |
| | CAACGTCTTGATGTTCTCGAACAGGACGCCCAAATAGACA | |
| | GACTTATTAATGGCCGTTTGACAACACTAAATGCTTTTGTT | |
| | GCACAGCAGCTTGTTCGTTCCGAATCAGCTGCTCTTTCCGC | |
| | TCAATTGGCTAAAGATAAAGTCAATGAGTGTGTCAAGGCA CAATCCAAGCGTTCTGGATTTTGCGGTCAAGGCACACATA | |
| | TAGTGTCCTTTGTTGTAAATGCCCCTAATGGCCTTACTTT | |
| | ATGCATGTTGGTTATTACCCTAGCAACCACATTGAGGTTGT | |
| | TTCTGCTTATGGTCTTTGCGATGCAGCTAACCCTACTAATT | |
| | GTATAGCCCCTGTTAATGGCTACTTTATTAAAACTAATAAC | |
| | ACTAGGATTGTTGATGAGTGGTCATATACTGGCTCGTCCTT | |
| | CTATGCACCTGAGCCCATCACCTCTCTTAATACTAAGTATG | |
| | TTGCACCACAGGTGACATACCAAAACATTTCTACTAACCT | |
| | CCCTCCTCCTCTCTCGGCAATTCCACCGGGATTGACTTCC AAGATGAGTTGGATGAGTTTTTCAAAAATGTTAGCACCAG | |
| | TATACCTAATTTTGGTTCTCTAACACAGATTAATACTACACAA | |
| | TACTCGATCTTACCTACGAGATGTTGTCTCTTCAACAAGTT | |
| | GTTAAAGCCCTTAATGAGTCTTACATAGACCTTAAAGAGC | |
| | TTGGCAATTATACTTATTACAACAAATGGCCGTGGTACAT | |
| | TTGGCTTGGTTTCATTGCTGGGCTTGTTGCCTTAGCTCTAT | |
| | GCGTCTTCTTCATACTGTGCTGCACTGGTTGTGGCACAAAC | |
| | TGTATGGGAAAACTTAAGTGTAATCGTTGTTGTGATAGAT | |
| | ACGAGGAATACGACCTCGAGCCGCATAAGGTTCATGTTCA CTAA | |
| IERS S FL | ATGATACACTCAGTGTTTCTACTGATGTTCTTGTTAACACC | 21 |
| PIKE | TACAGAAAGTTACGTTGATGTAGGGCCAGATTCTGTTAAG | |
| CEMC/2012 | TCTGCTTGTATTGAGGTTGATATACAACAGACTTTCTTTGA | |
| XBaI change(T to)) (nucleotide) | TAAAACTTGGCCTAGGCCAATTGATGTTTCTAAGGCTGAC GGTATTATATACCCTCAAGGCCGTACATATTCTAACATAA | |
| // (Indefeotine) | CTATCACTTATCAAGGTCTTTTTCCCTATCAGGGAGACCAT | |
| | GGTGATATGTATGTTTACTCTGCAGGACATGCTACAGGCA | |
| | CAACTCCACAAAAGTTGTTTGTAGCTAACTATTCTCAGGA | |
| | CGTCAAACAGTTTGCTAATGGGTTTGTCGTCCGTATAGGA | |
| | GCAGCTGCCAATTCCACTGGCACTGTTATTATTAGCCCATC | |
| | TACCAGCGCTACTATACGAAAAATTTACCCTGCTTTTATGC | |
| | TGGGTTCTTCAGTTGGTAATTTCTCAGATGGTAAAATGGG | |
| | CCGCTTCTTCAATCATACTCTAGTTCTTTTGCCCCGATGGAT GTGGCACTTTACTTAGAGCTTTTTATTGTATTCTGGAGCCT | |
| | CGCTCTGGAAATCATTGTCCTGCTGGCAATTCCTATACTTC | |
| | TTTTGCCACTTATCACACTCCTGCAACAGATTGTTCTGATG | |
| | GCAATTACAATCGTAATGCCAGTCTGAACTCTTTTAAGGA | |
| | GTATTTTAATTTACGTAACTGCACCTTTATGTACACTTATA | |
| | ACATTACCGAAGATGAGATTTTAGAGTGGTTTGGCATTAC | |
| | ACAAACTGCTCAAGGTGTTCACCTCTTCTCATCTCGGTATG | |
| | TTGATTTGTACGGCGGCAATATGTTTCAATTTGCCACCTTG | |
| | CCTGTTTATGATACTATTAAGTATTATTCTATCATTCCTCA CAGTATTCGTTCTATCCAAAGTGATAGAAAAGCTTGGGCT | |
| | GCCTTCTACGTTCTATCCAAAGTGATAGAAAAGCTTGGGCT GCCTTCTACGTATATAAACTTCAACCGTTAACTTTCCTGTT | |
| | GGATTTTTCTGTTGATGGTTATATACGCAGAGCTATAGACT | |
| | GTGGTTTTAATGATTTGTCACAACTCCACTGCTCATATGAA | |
| | TCCTTCGATGTTGAATCTGGAGTTTATTCAGTTTCGTCTTT | |
| | CGAAGCAAAACCTTCTGGCTCAGTTGTGGAACAGGCTGAA | |
| | GGTGTTGAATGTGATTTTTCACCTCTTCTGTCTGGCACACC | |
| | TCCTCAGGTTTATAATTTCAAGCGTTTGGTTTTTACCAATT | |
| | | |

GCAATTATAATCTTACCAAATTGCTTTCACTTTTTCTGTG

TABLE 10-continued

| Betacoro | navirus Nucleic Acid Sequence | |
|-------------------------------|---|--------------|
| Strain | Nucleic Acid Sequence | SEQ I NO: |
| | AATGATTTTACTTGTAGTCAAATATCTCCAGCAGCAATTGC | |
| | TAGCAACTGTTATTCTTCACTGATTTTGGATTACTTTTCAT | |
| | ACCCACTTAGTATGAAATCCGATCTCAGTGTTAGTTCTGCT | |
| | GGTCCAATATCCCAGTTTAATTATAAACAGTCCTTTTCTAA | |
| | TCCCACATGTTTGATTTTAGCGACTGTTCCTCATAACCTTA CTACTATTACTAAGCCTCTTAAGTACAGCTATATTAACAA | |
| | GTGCTCTCGTCTTCTTTCTGATGATCGTACTGAAGTACCAG | |
| | AGTTAGTGAACGCTAATCAATACTCACCCTGTGTATCCATT | |
| | GTCCCATCCACTGTGTGGGAAGACGGTGATTATTATAGGA | |
| | AACAACTATCTCCACTTGAAGGTGGTGGCTGGCTTGTTGC | |
| | TAGTGGCTCAACTGTTGCCATGACTGAGCAATTACAGATG | |
| | GGCTTTGGTATTACAGTTCAATATGGTACAGACACCAATA | |
| | GTGTTTGCCCCAAGCTTGAATTTGCTAATGACACAAAAAT | |
| | TGCCTCTCAATTAGGCAATTGCGTGGAATATTCCCTCTATG | |
| | GTGTTTCGGGCCGTGGTGTTTTTCAGAATTGCACAGCTGTA | |
| | GGTGTTCGACAGCAGCGCTTTGTTTATGATGCGTACCAGA ATTTAGTTGGCTATTATTCTGATGATGGCAACTACTACTGT | |
| | TTGCGTGCTTGTGTTAGTGTTCCTGTTTCTGTCATCTACTAGT | |
| | AAAGAAACTAAAACCCACGCTACTCTATTTGGTAGTGTTG | |
| | CATGTGAACACATTTCTTCTACCATGTCTCAATACTCCCGT | |
| | TCTACGCGATCAATGCTTAAACGGCGAGATTCTACATATG | |
| | GCCCCCTTCAGACACCTGTTGGTTGTGTCCTAGGACTTGTT | |
| | AATTCCTCTTTGTTCGTAGAGGACTGCAAGTTGCCTCTTGG | |
| | TCAATCTCTCTGTGCTCTTCCTGACACCCCTAGTACTCTCA | |
| | CACCTCGCAGTGTGCGCTCTGTTCCAGGTGAAATGCGCTT | |
| | GGCATCCATTGCTTTTAATCATCCTATTCAGGTTGATCAAC | |
| | TTAATAGTAGTTATTTTAAATTAAGTATACCCACTAATTTT TCCTTTGGTGTGACTCAGGAGTACATTCAGACAACCATTC | |
| | AGAAAGTTACTGTTGATTGTAAACAGTACGTTTGCAATGG | |
| | TTTCCAGAAGTGTGAGCAATTACTGCGCGAGTATGGCCAG | |
| | TTTTGTTCCAAAATAAACCAGGCTCTCCATGGTGCCAATTT | |
| | ACGCCAGGATGATTCTGTACGTAATTTGTTTGCGAGCGTG | |
| | AAAAGCTCTCAATCATCTCCTATCATACCAGGTTTTGGAG | |
| | GTGACTTTAATTTGACACTTCTGGAACCTGTTTCTATATCT | |
| | ACTGGCAGTCGTAGTGCACGTAGTGCTATTGAGGATTTGC | |
| | TATTTGACAAAGTCACTATAGCTGATCCTGGTTATATGCA | |
| | AGGTTACGATGATTGCATGCAGCAAGGTCCAGCATCAGCT CGTGATCTTATTTGTGCTCAATATGTGGCTGGTTACAAAGT | |
| | ATTACCTCCTCTTATGGATGTTAATATGGGAAGCCGCGTATA | |
| | CTTCATCTTTGCTTGGCAGCATAGCAGGTGTTGGCTGGACT | |
| | GCTGGCTTATCCTCCTTTGCTGCTATTCCATTTGCACAGAG | |
| | TATCTTTTATAGGTTAAACGGTGTTGGCATTACTCAACAGG | |
| | TTCTTTCAGAGAACCAAAAGCTTATTGCCAATAAGTTTAA | |
| | TCAGGCTCTGGGAGCTATGCAAACAGGCTTCACTACAACT | |
| | AATGAAGCTTTTCAGAAGGTTCAGGATGCTGTGAACAACA | |
| | ATGCACAGGCTCTATCCAAATTAGCTAGCGAGCTATCTAA | |
| | TACTTTTGGTGCTATTTCCGCCTCTATTGGAGACATCATAC AACGTCTTGATGTTCTCGAACAGGACGCCCAAATAGACAG | |
| | ACGTCTTGATGTTCTCGAACAGGACGCCCAAATAGACAG ACTTATTAATGGCCGTTTGACAACACTAAATGCTTTTGTTG | |
| | CACAGCAGCTTGTTCGTTCCGAATCAGCTGCTCTTTCCGCT | |
| | CAATTGGCTAAAGATAAAGTCAATGAGTGTGTCAAGGCAC | |
| | AATCCAAGCGTTCTGGATTTTGCGGTCAAGGCACACATAT | |
| | AGTGTCCTTTGTTGTAAATGCCCCTAATGGCCTTTACTTCA | |
| | TGCATGTTGGTTATTACCCTAGCAACCACATTGAGGTTGTT | |
| | TCTGCTTATGGTCTTTGCGATGCAGCTAACCCTACTAATTG | |
| | TATAGCCCCTGTTAATGGCTACTTTATTAAAACTAATAACA | |
| | CTAGGATTGTTGATGAGTGGTCATATACTGGCTCGTCCTTC | |
| | TATGCACCTGAGCCCATTACCTCCCTTAATACTAAGTATGT TGCACCACAGGTGACATACCAAAACATTTCTACTAACCTC | |
| | CCTCCTCCTCTTCTCGGCAATTCCACCGGGATTGACCTCCA | |
| | AGATGAGTTGGATGAGTTTTTCAAAAATGTTAGCACCAGT | |
| | ATACCTAATTTTGGTTCCCTAACACAGATTAATACTACATT | |
| | ACTCGATCTTACCTACGAGATGTTGTCTCTTCAACAAGTTG | |
| | TTAAAGCCCTTAATGAGTCTTACATAGACCTTAAAGAGCT | |
| | TGGCAATTATACTTATTACAACAAATGGCCGTGGTACATT | |
| | TGGCTTGGTTTCATTGCTGGGCTTGTTGCCTTAGCTCTATG | |
| | CGTCTTCTTCATACTGTGCTGCACTGGTTGTGGCACAAACT | |
| | GTATGGGAAAACTTAAGTGTAATCGTTGTTGTGATAGATA | |
| | CGAGGAATACGACCTCGAGCCGCATAAGGTTCATGTTCAC TAA | |
| | Inn | |
| ovel MERS S2 subunit trimeric | ATGATCCACTCCGTGTTCCTCCTCATGTTCCTGTTGACCCC | 22 |
| accine | CACTGAGTCAGACTGCAAGCTCCCGCTGGGACAGTCCCTG | |
| nucleotide) | TGTGCGCTGCCTGACACTCCTAGCACTCTGACCCCACGCTC | |
| | CGTGCGGTCGGTGCCTGGCGAAATGCGGCTGGCCTCCATC | |

CGTGCGGTCGGTGCCTGGCGAAATGCGGCTGGCCTCCATC

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TABLE 10-continued

| Strain | Nucleic Acid Sequence | SEQ I NO: |
|-------------------|---|--------------|
| | GCCTTCAATCACCCAATCCAAGTGGATCAGCTGAATAGCT | |
| | CGTATTTCAAGCTGTCCATCCCCACGAACTTCTCGTTCGGG | |
| | GTCACCCAGGAGTACATCCAGACCACAATTCAGAAGGTCA | |
| | CCGTCGATTGCAAGCAATACGTGTGCAACGGCTTCCAGAA | |
| | GTGCGAGCAGCTGCTGAGAGAATACGGGCAGTTTTGCAGC AAGATCAACCAGGCGCTGCATGGAGCTAACTTGCGCCAGG | |
| | ACGACTCCCGTGCGCAACCTCTTTGCCTCTGTGAAGTCATCC | |
| | CAGTCCTCCCCAATCATCCCCGGGATTCGGAGGGGGCTTCA | |
| | ACCTGACCCTCCTGGAGCCCGTGTCGATCAGCACCGGTAG | |
| | CAGATCGGCGCGCTCAGCCATTGAAGATCTTCTGTTCGAC | |
| | AAGGTCACCATCGCCGATCCGGGCTACATGCAGGGATACG | |
| | ACGACTGTATGCAGCAGGGACCAGCCTCCGCGAGGGACCT | |
| | CATCTGCGCGCAATACGTGGCCGGGTACAAAGTGCTGCCT CCTCTGATGGATGTGAACATGGAGGCCGCTTATACTTCGT | |
| | CCCTGCTCGGCTCTATCGCCGGCGTGGGGTGGACCGCCGG | |
| | CCTGTCCTCCTTCGCCGCTATCCCCTTTGCACAATCCATTT | |
| | TCTACCGGCTCAACGGCGTGGGCATTACTCAACAAGTCCT | |
| | GTCGGAGAACCAGAAGTTGATCGCAAACAAGTTCAATCA | |
| | GGCCCTGGGGGCCATGCAGACTGGATTCACTACGACTAAC | |
| | GAAGCGTTCCAGAAGGTCCAGGACGCTGTGAACAACAAC | |
| | GCCCAGGCGCTCTCAAAGCTGGCCTCCGAACTCAGCAACA | |
| | CCTTCGGAGCCATCAGCGCATCGATCGGTGACATAATTCA GCGGCTGGACGTGCTGGAGCAGGACGCCCAGATCGACCG | |
| | CCTCATCAACGGACGGCTGACCACCTTGAATGCCTTCGTG | |
| | GCACAACAGCTGGTCCGGAGCGAATCAGCGGCACTTTCCG | |
| | CCCAACTCGCCAAGGACAAAGTCAACGAATGCGTGAAGG | |
| | CCCAGTCCAAGAGGTCCGGTTTCTGCGGTCAAGGAACCCA | |
| | TATTGTGTCCTTCGTCGTGAACGCGCCCAACGGTCTGTACT | |
| | TTATGCACGTCGGCTACTACCCGAGCAATCATATCGAAGT | |
| | GGTGTCCGCCTACGGCCTGTGCGATGCCGCTAACCCCACT AACTGTATTGCCCCTGTGAACGGATATTTTATTAAGACCA | |
| | ACTGTATTGCCCCTGTGAACGGATATTTTATTAAGACCA ACAACACCCCGCATTGTGGACGAATGGTCATACACCGGTTC | |
| | GTCCTTCTACGCGCCCGAGCCCATCACTTCACTGAACACC | |
| | AAATACGTGGCTCCGCAAGTGACCTACCAGAACATCTCCA | |
| | CCAATTTGCCGCCGCCGCTGCTCGGAAACAGCACCGGAAT | |
| | TGATTTCCAAGATGAACTGGACGAATTCTTCAAGAACGTG | |
| | TCCACTTCCATTCCCAACTTCGGAAGCCTGACACAGATCA | |
| | ACACCACCCTTCTCGACCTGACCTACGAGATGCTGAGCCT | |
| | TCAACAAGTGGTCAAGGCCCTGAACGAGAGCTACATCGAC CTGAAGGAGCTGGGCAACTATACCTACTACAACAAGTGGC | |
| | CGGACAAGATTGAGGAGATTCTGTCGAAAAATCTACCACAAGTGGC | |
| | TGAAAACGAGATCGCCAGAATCAAGAAGCTTATCGGCGA | |
| | AGCC | |
| IERS SO Full- | ATGGAAACCCCTGCCCAGCTGCTGTTCCTGCTGCTGCTGTG | 23 |
| ength Spike | GCTGCCTGATACCACCGGCAGCTATGTGGACGTGGGCCCC | |
| rotein | GATAGCGTGAAGTCCGCCTGTATCGAAGTGGACATCCAGC | |
| nucleotide, codon | AGACCTTTTTCGACAAGACCTGGCCCAGACCCATCGACGT | |
| ptimized) | GTCCAAGGCCGACGGCATCATCTATCCACAAGGCCGGACC | |
| | TACAGCAACATCACCATTACCTACCAGGGCCTGTTCCCAT ATCAAGGCGACCACGGCGATATGTACGTGTACTCTGCCGG | |
| | CCACGCCACCGGCACCACCACCCCAGAAACTGTTCGTGGCC | |
| | AACTACAGCCAGGACGTGAAGCAGTTCGCCAACGGCTTCG | |
| | TCGTGCGGATTGGCGCCGCTGCCAATAGCACCGGCACAGT | |
| | GATCATCAGCCCCAGCACCAGCGCCACCATCCGGAAGATC | |
| | TACCCCGCCTTCATGCTGGGCAGCTCCGTGGGCAATTTCA | |
| | GCGACGGCAAGATGGGCCGGTTCTTCAACCACACCCTGGT | |
| | GCTGCTGCCCGATGGCTGTGGCACACTGCTGAGAGCCTTC | |
| | TACTGCATCCTGGAACCCAGAAGCGGCAACCACTGCCCTG CCGGCAATAGCTACACCAGCTTCGCCACCTACCACACACC | |
| | CCGGCAATAGCTACACCAGCTTCGCCACCTACCACACACC CGCCACCGATTGCTCCGACGGCAACTACAACCCGGAACGCC | |
| | AGCCTGAACAGCTTCAAAGAGTACTTCAACCTGCGGAACT | |
| | GCACCTTCATGTACACCTACAATATCACCGAGGACGAGAT | |
| | CCTGGAATGGTTCCGCATCACCCAGACCGCCCAGGGCGTG | |
| | CACCTGTTCAGCAGCAGATACGTGGACCTGTACGGCGGCA | |
| | ACATGTTCCAGTTTGCCACCCTGCCCGTGTACGACACCATC | |
| | AAGTACTACAGCATCATCCCCCACAGCATCCGGTCCATCC | |
| | AGAGCGACAGAAAAGCCTGGGCCGCCTTCTACGTGTACAA | |
| | GCTGCAGCCCCTGACCTTCCTGCTGGACTTCAGCGTGGAC GGCTACATCAGACGGGCCATCGACTGCGGCTTCAACGACC | |
| | GGCTACATCAGACGGGCCATCGACTGCGGCTTCAACGACC TGAGCCAGCTGCACTGCTCCTACGAGAGCTTCGACGTGGA | |
| | AAGCGGCGTGTACAGCGTGTCCAGCTTCGAGGCCAAGCCT | |
| | AGCGGCAGCGTGGTGGAACAGGCTGAGGGCGTGGAATGC | |
| | | |
| | GACTTCAGCCCTCTGCTGAGCGGCACCCCTCCCCAGGTGT | |

TABLE 10-continued

| train | Nucleic Acid Sequence | SEQ I NO: |
|-------|---|--------------|
| | CCTGACCAAGCTGCTGAGCCTGTTCTCCGTGAACGACTTC | |
| | ACCTGTAGCCAGATCAGCCCTGCCGCCATTGCCAGCAACT | |
| | GCTACAGCAGCCTGATCCTGGACTACTTCAGCTACCCCCT | |
| | GAGCATGAAGTCCGATCTGAGCGTGTCCTCCGCCGGACCC | |
| | ATCAGCCAGTTCAACTACAAGCAGAGCTTCAGCAACCCTA | |
| | CCTGCCTGATTCTGGCCACCGTGCCCCACAATCTGACCAC | |
| | CATCACCAAGCCCCTGAAGTACAGCTACATCAACAAGTGC | |
| | AGCAGACTGCTGTCCGACGACCGGACCGAAGTGCCCCAGC TCGTGAACGCCAACCAGTACAGCCCCTGCGTGTCCATCGT | |
| | GCCCAGCACCGTGTGGGAGGACGGCGACTACTACAGAAA | |
| | GCAGCTGAGCCCCCTGGAAGGCGGCGGATGGCTGGTGGCT | |
| | TCTGGAAGCACAGTGGCCATGACCGAGCAGCTGCAGATG | |
| | GGCTTTGGCATCACCGTGCAGTACGGCACCGACACCAACA | |
| | GCGTGTGCCCCAAGCTGGAATTCGCCAATGACACCAAGAT | |
| | CGCCAGCCAGCTGGGAAACTGCGTGGAATACTCCCTGTAT | |
| | GGCGTGTCCGGACGGGGCGTGTTCCAGAATTGCACAGCAG | |
| | TGGGAGTGCGGCAGCAGAGATTCGTGTACGATGCCTACCA | |
| | GAACCTCGTGGGCTACTACAGCGACGACGGCAATTACTAC | |
| | TGCCTGCGGGCCTGTGTGTCCGTGCCCGTGTCCGTGATCTA | |
| | CGACAAAGAGACAAAGACCCACGCCACACTGTTCGGCTCC CTCCCCCTCCCACACTGCCCCCCCCCC | |
| | GTGGCCTGCGAGCACATCAGCTCCACCATGAGCCAGTACT CCCGCTCCACCCGGTCCATGCTGAAGCGGAGAGATAGCAC | |
| | CTACGGCCCCCTGCAGACACCTGTGCGGATGTGTGCTGGGC | |
| | CTCGTGAACAGCTCCCTGTTTGTGGAAGATGCAAGCTGC | |
| | CCCTGGGCCAGAGCCTGTGTGCCCTGCCAGATACCCCTAG | |
| | CACCCTGACCCCTAGAAGCGTGCGCTCTGTGCCCGGCGAA | |
| | ATGCGGCTCGCCTCTATCGCCTTCAATCACCCCATCCAGGT | |
| | GGACCAGCTGAACTCCAGCTACTTCAAGCTGAGCATCCCC | |
| | ACCAACTTCAGCTTCGGCGTGACCCAGGAGTACATCCAGA | |
| | CCACAATCCAGAAAGTGACCGTGGACTGCAAGCAGTACGT | |
| | GTGCAACGGCTTTCAGAAGTGCGAACAGCTGCTGCGCGAG | |
| | TACGGCCAGTTCTGCAGCAAGATCAACCAGGCCCTGCACG | |
| | GCGCCAACCTGAGACAGGATGACAGCGTGCGGAACCTGTT | |
| | CGCCAGCGTGAAAAGCAGCCAGTCCAGCCCCATCATCCCT | |
| | GGCTTCGGCGGCGACTTTAACCTGACCCTGCTGGAACCTG TGTCCATCAGCACCGGCTCCAGAAGCGCCCAGATCCGCCAT | |
| | CGAGGACCTGCTGTTCGACAAGGGCCAGATCCGCCAT | |
| | GGCTACATGCAGGGCTACGACGATGCATGCAGCAGGGCC | |
| | CAGCCAGCGCCAGGGATCTGATCTGTGCCCCAGTATGTGGC | |
| | CGGCTACAAGGTGCTGCCCCCCTGATGGACGTGAACATG | |
| | GAAGCCGCCTACACCTCCAGCCTGCTGGGCTCTATTGCTG | |
| | GCGTGGGATGGACAGCCGGCCTGTCTAGCTTTGCCGCCAT | |
| | CCCTTTCGCCCAGAGCATCTTCTACCGGCTGAACGGCGTG | |
| | GGCATCACACAGGGGGGGGGGGGGGAGAACCAGAAGCTG | |
| | ATCGCCAACAAGTTTAACCAGGCACTGGGCGCCATGCAGA | |
| | CCGGCTTCACCACCACCAACGAGGCCTTCAGAAAGGTGCA | |
| | GGACGCCGTGAACAACGCCCAGGCTCTGAGCAAGCT GGCCTCCGAGCTGAGCAATACCTTCGGCGCCATCAGCGCC | |
| | TCCATCGGCGACATCATCCAGCGGCTGGACGTGCTGGAAC | |
| | AGGACGCCCAGATCGACCGGCTGATCAACGGCAGACTGA | |
| | CCACCCTGAACGCCTTCGTCGCACAGCAGCTCGTGCCGGAG | |
| | CGAATCTGCCGCTCTGTCTGCTCAGCTGGCCAAGGACAAA | |
| | GTGAACGAGTGCGTGAAGGCCCAGTCCAAGCGGAGCGGC | |
| | TTTTGTGGCCAGGGCACCCACATCGTGTCCTTCGTCGTGAA | |
| | TGCCCCCAACGGCCTGTACTTTATGCACGTGGGCTATTACC | |
| | CCAGCAACCACATCGAGGTGGTGTCCGCCTATGGCCTGTG | |
| | CGACGCCGCCAATCCTACCAACTGTATCGCCCCCGTGAAC | |
| | GGCTACTTCATCAAGACCAACAACACCCGGATCGTGGACG | |
| | AGTGGTCCTACACAGGCAGCAGCTTCTACGCCCCCGAGCC | |
| | CATCACCTCCCTGAACACCAAATACGTGGCCCCCCAAGTG | |
| | ACATACCAGAACATCTCCACCAACCTGCCCCCTCCACTGC TGGGAAATTCCACCGGCATCGACTTCCAGGACGAGCTGGA | |
| | TGGGAAATTCCACCGGCATCGACTTCCAGGACGAGCTGGA CGAGTTCTTCAAGAACGTGTCCACCTCCATCCCCAAGTTCG | |
| | GCAGCCTGACCCAGATCAACACCACCACCTGGCAGCCTGAC | |
| | CTACGAGATGCTGTCCCTGCAACAGGTCGTGAAAGCCCTG | |
| | AACGAGAGCTACATCGACCTGAAAGAGCTGGGGAACTAC | |
| | ACCTACTACAACAAGTGGCCTTGGTACATTTGGCTGGGCT | |
| | TTATCGCCGGCCTGGTGGCCCTGGCCCTGTGCGTGTTCTTC | |
| | ATCCTGTGCTGCACCGGCTGCGGCACCAATTGCATGGGCA | |
| | AGCTGAAATGCAACCGGTGCTGCGACAGATACGAGGAAT | |

TABLE 10-continued

| Strain | Nucleic Acid Sequence | SEQ NO : |
|----------------------------|--|-------------|
| ; | Betacoronavirus mRNA Sequences | |
| gb KJ156934.1 : 21405-2546 | 6 AUGAUACACUCAGUGUUUCUACUGAUGUUCUUGUUAAC | 65 |
| Middle | ACCUACAGAAAGUUACGUUGAUGUAGGGCCAGAUUCUG | 00 |
| East respiratory | UUAAGUCUGCUUGUAUUGAGGUUGAUAUACAACAGACC | |
| syndrome | UUCUUUGAUAAAACUUGGCCUAGGCCAAUUGAUGUUUC | |
| coronavirus | UAAGGCUGACGGUAUUAUAUACCCUCAAGGCCGUACAU | |
| isolate | AUUCUAACAUAACUAUCACUUAUCAAGGUCUUUUUCCCU | |
| Riyadh 14 2013, | AUCAGGGAGACCAUGGUGAUAUGUAUGUUUACUCUGCA | |
| spike protein | GGACAUGCUACAGGCACAACUCCACAAAAGUUGUUUGU | |
| (nucleotide) | AGCUAACUAUUCUCAGGACGUCAAACAGUUUGCUAAUG | |
| , | GGUUUGUCGUCCGUAUAGGAGCAGCUGCCAAUUCCACUG | |
| | GCACUGUUAUUAUUAGCCCAUCUACCAGCGCUACUAUAC | |
| | GAAAAAUUUACCCUGCUUUUAUGCUGGGUUCUUCAGUU | |
| | GGUAAUUUCUCAGAUGGUAAAAUGGGCCGCUUCUUCAA | |
| | UCAUACUCUAGUUCUUUUGCCCGAUGGAUGUGGCACUU | |
| | UACUUAGAGCUUUUUAUUGUAUUCUAGAGCCUCGCUCU | |
| | GGAAAUCAUUGUCCUGCUGGCAAUUCCUAUACUUCUUU | |
| | UGCCACUUAUCACACUCCUGCAACAGAUUGUUCUGAUGG | |
| | CAAUUACAAUCGUAAUGCCAGUCUGAACUCUUUUAAGG | |
| | AGUAUUUUAAUUUACGUAACUGCACCUUUAUGUACACU | |
| | UAUAACAUUACCGAAGAUGAGAUUUUAGAGUGGUUUGG | |
| | CAUUACACAAACUGCUCAAGGUGUUCACCUCUUCUCAUC | |
| | UCGGUAUGUUGAUUUGUACGGCGGCAAUAUGUUUCAAU | |
| | UUGCCACCUUGCCUGUUUAUGAUACUAUUAAGUAUUAU | |
| | UCUAUCAUUCCUCACAGUAUUCGUUCUAUCCAAAGUGAU | |
| | AGAAAAGCUUGGGCUGCCUUCUACGUAUAUAAACUUCA | |
| | ACCGUUAACUUUCCUGUUGGAUUUUUCUGUUGAUGGUU | |
| | AUAUACGCAGAGCUAUAGACUGUGGUUUUAAUGAUUUG | |
| | UCACAACUCCACUGCUCAUAUGAAUCCUUCGAUGUUGAA | |
| | UCUGGAGUUUAUUCAGUUUCGUCUUUCGAAGCAAAACC | |
| | UUCUGGCUCAGUUGUGGAACAGGCUGAAGGUGUUGAAU | |
| | GUGAUUUUUCACCUCUUCUGUCUGGCACACCUCCUCAGG | |
| | UUUAUAAUUUCAAGCGUUUGGUUUUUACCAAUUGCAAU | |
| | UAUAAUCUUACCAAAUUGCUUUCACUUUUUUCUGUGAA | |
| | UGAUUUUACUUGUAGUCAAAUAUCUCCAGCAGCAAUUG | |
| | CUAGCAACUGUUAUUCUUCACUGAUUUUUGGAUUAUUUU | |
| | UCAUACCCACUUAGUAUGAAAUCCGAUCUCAGUGUUAG | |
| | UUCUGCUGGUCCAAUAUCCCAGUUUAAUUAUAAACAGU | |
| | CCUUUUCUAAUCCCACAUGUUUGAUCUUAGCGACUGUUC | |
| | CUCAUAACCUUACUACUAUUACUAAGCCUCUUAAGUACA | |
| | GCUAUAUUAACAAGUGCUCUCGUCUUCUUUCUGAUGAU | |
| | CGUACUGAAGUACCUCAGUUAGUGAACGCUAAUCAAUA | |
| | CUCACCCUGUGUAUCCAUUGUCCCAUCCACUGUGUGGGA | |
| | AGACGGUGAUUAUUAUAGGAAACAACUAUCUCCACUUG | |
| | | |
| | AAGGUGGUGGCUGGCUUGUUGCUAGUGGCUCAACUGUU | |
| | GCCAUGACUGAGCAAUUACAGAUGGGCUUUGGUAUUAC AGUUCAAUAUGGUACAGACACCAAUAGUGUUUGCCCCA | |
| | | |
| | AGCUUGAAUUUGCUAAUGACACAAAAAUUGCCUCUCAA | |
| | UUAGGCAAUUGCGUGGAAUAUUCCCUCUAUGGUGUUUC | |
| | GGGCCGUGGUGUUUUUCAGAAUUGCACAGCUGUAGGUG | |
| | UUCGACAGCAGCGCUUUGUUUAUGAUGCGUACCAGAAU | |
| | UUAGUUGGCUAUUAUUCUGAUGAUGGCAACUACUACUG | |
| | UCUGCGUGCUUGUGUUAGUGUUCCUGUUUCUGUCAUCU | |
| | AUGAUAAAGAAACUAAAACCCACGCUACUCUAUUUGGU | |
| | AGUGUUGCAUGUGAACACAUUUCUUCUACCAUGUCUCA | |
| | AUACUCCCGUUCUACGCGAUCAAUGCUUAAACGGCGAGA | |
| | UUCUACAUAUGGCCCCCUUCAGACACCUGUUGGUUGUGU | |
| | CCUAGGACUUGUUAAUUCCUCUUUGUUCGUAGAGGACU | |
| | GCAAGUUGCCUCUCGGUCAAUCUCUCUGUGCUCUUCCUG | |
| | ACACACCUAGUACUCUCACACCUCGCAGUGUGCGCUCUG | |
| | UGCCAGGUGAAAUGCGCUUGGCAUCCAUUGCUUUUAAU | |
| | CAUCCCAUUCAGGUUGAUCAACUUAAUAGUAGUUAUUU | |
| | UAAAUUAAGUAUACCCACUAAUUUUUCCUUUGGUGUGA | |
| | CUCAGGAGUACAUUCAGACAACCAUUCAGAAAGUUACU | |
| | GUUGAUUGUAAACAGUACGUUUGCAAUGGUUUCCAGAA | |
| | GUGUGAGCAAUUACUGCGCGAGUAUGGCCAGUUUUGUU | |
| | CCAAAAUAAACCAGGCUCUCCAUGGUGCCAAUUUACGCC | |
| | AGGAUGAUUCUGUACGUAAUUUGUUUGCGAGCGUGAAA | |
| | AGCUCUCAAUCAUCUCCUAUCAUACCAGGUUUUGGAGGU | |
| | GACUUUAAUUUGACACUUCUAGAACCUGUUUCUAUAUC | |
| | UACUGGCAGUCGUAGUGCACGUAGUGCUAUUGAGGAUU | |
| | UGCUAUUUGACAAAGUCACUAUAGCUGAUCCUGGUUAU | |
| | AUGCAAGGUUACGAUGAUUGUAUGCAGCAAGGUCCAGC | |

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TABLE 10-continued

| Betacoronavirus Nucleic Acid Sequence | | |
|---|---|---------------|
| Strain | Nucleic Acid Sequence | SEQ ID NO: |
| Strain | Nucleic Acid Sequence AUCAGCUCGUGAUUAUUUGUGUGCUCAAUAUGUGGCUG GUUAUAAAGUAUUACUUCAUCUUUGCUUGGAUGUUAAUAUG GAAGCCGCGUAUACUUCAUCUUUGCUUGGAGCAUAGCA GGUGUUGGCUGGACUGCUGCUUAUCCUCUUUGCUGCU AUUCCAUUUGCACAGAGUAUYUUUUAUAGGUUAAACGG UGUUGGCAUGCACAGAGUUCUUUCAGAGAACCAAA AGCUUAUUCCCAUACAGUUCUUUCAGAGAACCAAA AGCUUAUUCACGACUUCAUACAACUAAUGAAGCUUUUCG GAAGGUUCAGGAAUCAACUAAUGAAGCUUUUCG GAAGGUUCCGCCUCUUUGAGACAACACUAAUGCACAGGCUC UAUCCAAAUUAGCUGUCGAACACACUAAUACUUUUGGU GCUAUUUCCGCAUCAUAAGGCCCCAAAUAGACAGACUUAU UAAUGGCGUUUCGAUCAAACCUAAUGACUUUUGGU GAUGUUCCGAAUAAGUCAUACAACGACUUAU UAAUGGCGUUUGGACAACACUAAAUGACUUUUGUUGCAUGCC AAUUGGCCGUUUGGAUUAAUGAGUGUCCAAGGCA AAGCUUUGUUGUUGUAAAUGCCCUAAGGCACACAU AUUGGCUCUUUGUUGUUAAAUGCCCUAAGGCACACAU AUUGUUCUUUUGUUGUUAAAUGCCCCUAAUGGCUUUA CUUUAUUGUUGUUGUUAAAUGCCCUUUUGCGAUGACCUAU UUAAUACAAUAACCUACUUUUUGCGAUGACUAACC AAAACUUUUUUGUUGUUGUUGUUGAUAGGUGGCCAUUUUU AUACUAAUAACACUAGGUUUGUCCUUCAAGAGUUGGUCAU UUUUUCAAUAAUAACCUACUUUCAAAGAUUGUUGAUUAGCUUUUUUUU | |
| MERS S FL SPIKE 2cEMC/2012 (XBaI change(U to G)) (nucleotide) | UACGAGGAAAACUUAAGUGUAAUCGUUGUGUGUAUAA UACGAGGAAUACGACCUCGAGCCGCAUAAGGUUCAUGU UCACUAA AUGAUACACUCAGUCUUCACUCGAUGUUCUUCUUGUUAAC ACCUACAGAAAGUUACGUUGAUGUAGGUCCUUCUUCUU UUAAGUCUGCUUGUAUUGACGUUGAUGUACAACAGACU UUCUUUGAUAAAACUUUGCCUAAGCCCGUACAU AUUCUAACAUAACUAUCACUUAUCAAGGUCUUUUUCCU AUCAGGAGACCAUGGUGUAUAUACAACAGCUUUUUCCU AUCAGGAGACCAUGUUAUCACUUAUCAAGGUCUUUUUCCU AUCAGGAGACCAUGUUAUCACUUAUCAAGGUCUUUUUCCU GGACAUGCUACAGUCACACUCACAAAAGUUUUCACUGCA GGACAUGCUACAGUCACAACUCCACAAAAGUUUUCACUUGCA GGUUUGUUCGUCCGUAUAGAGCUGCAAUUCACUUG GACAUGUUAUUAUAGCCCUCUAACAGUUUUCACUUG GAAAAAUUUACCCUGCUUUUAUGCGGGUUCUUCAGUU GGUAAUUUCUCAGAUGUAAAAUGGGCCGCUUCUUCAA UCAUACUCUAGUUCUUUUGCCGAUGGAUGUGGACUUUUAGG GAAUUUUCUCAGAUGUGAAAAUGGGCCGCUUCUUCAA UCAUACUCUAGUUCUUUUGCUGGAUGUGGACUUUUAGG CAAUUACAUUGUCCUGCUGCAACAGAUUCUUUUUUU UGCCACUUUUUAUUGUAACGGCGCCUCUUUUAAGG CAAUUACAUUGUCCUGCUGCAACAGAUUGUUCUGAUGG AGUAUUUUAAUUUACGUAACGCGCGCUUCUUAAGG CAAUUACAAUGGUAUUUAUGUAACUUCUUU UGCCACCUUAUCACACUCUCAAGUUUUAAGG CAUUACAAUUGUCCUGCUGCAACAGAUUUUUAAGG AGUAUUUUAAUUUACGUAACGCGCGCCUCUUCAAU UUGCCACCUUACGUCAAGGUGUUCAACUUUUAAGG CAUUACACUGUCUCAAGGUGUUCAACUUUUAAGG CAUUACACUGUCUCAAGGUGUUCACCUUUUAAGG CAUUACACUUGCCUCAAGGUGUUCACCUUUUCAAU UUGCCACCUUGCUCAAGGUGUUCACCUCUUCCAUC UCGGUAUGUGGCUGCCUUCUACGUAUUAAAGUAUUAA UUGCCACUUGCCUCAAGGUGUUCACUUCUCAUCAAU UUGCGACUUGGCUGCUUUCAGUUUUAAAGUGUU AUAAACUUCCCUCUACGUAUUAAAGUGUUCAAUGAU AUAUACGCAGGCUAUAGAUUCUUCGUUCAAUGUU AUAUACCUCCUCUCAUAGAUUCUUCGAUGUUGAA UCUGGAGUUAUUCAGUUUCAGUUUUAAAGUGUU AUAUAACUUCCUCUUCGUUCUACGUUUCAAUGUUGAA UCUGGAGUUAUUCAGUUUCGUCUUCGAAGGGUGUAAACUUCA UUCUGGCCACUUCUUCGUCUUCGAAGGUGUUGAA UUCUACACUCCUCUUCGGCACACCUCCUCAGG UUUAUAAAUUUCACUUUCGUUUCG | 66 |

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TABLE 10-continued Betacoronavirus Nucleic Acid Sequence

| Strain | Nucleic Acid Sequence | SEQ ID NO: |
|--------------------------------|--|---------------|
| | GCUAUAUUAACAAGUGCUCUCGUCUUCUUUCUGAUGAU CGUACUGAAGUACCUCAGUUAGUGAACGCUAAUCAAUA | |
| | CUCACCCUGUGUAUCCAUUGUCCCAUCCACUGUGUGGGA | |
| | AGACGGUGAUUAUUAUAGGAAACAACUAUCUCCACUUG | |
| | AAGGUGGUGGCUUGCUUGUUGCUAGUGGCUCAACUGUU | |
| | GCCAUGACUGAGCAAUUACAGAUGGGCUUUGGUAUUAC AGUUCAAUAUGGUACAGACACCAAUAGUGUUUGCCCCA | |
| | AGUUGAAUUUGCUAAUGACACAAAAAUUGCCUCUCAA | |
| | UUAGGCAAUUGCGUGGAAUAUUCCCUCUAUGGUGUUUC | |
| | GGGCCGUGGUGUUUUUCAGAAUUGCACAGCUGUAGGUG | |
| | UUCGACAGCAGCGCUUUGUUUAUGAUGCGUACCAGAAU UUAGUUGGCUAUUAUUCUGAUGAUGGCAACUACUACUG | |
| | UUUGCGUGCUUGUGUUAGUGUUCCUGUUUCUGUCAUCU | |
| | AUGAUAAAGAAACUAAAACCCACGCUACUCUAUUUGGU | |
| | AGUGUUGCAUGUGAACACAUUUCUUCUACCAUGUCUCA | |
| | AUACUCCCGUUCUACGCGAUCAAUGCUUAAACGGCGAGA | |
| | UUCUACAUAUGGCCCCCUUCAGACACCUGUUGGUUGUGU CCUAGGACUUGUUAAUUCCUCUUUGUUCGUAGAGGACU | |
| | GCAAGUUGCCUCUUGGUCAAUCUCUCUGUGCUCUUCCUG | |
| | ACACACCUAGUACUCUCACACCUCGCAGUGUGCGCUCUG | |
| | UUCCAGGUGAAAUGCGCUUGGCAUCCAUUGCUUUUAAU | |
| | CAUCCUAUUCAGGUUGAUCAACUUAAUAGUAGUUAUUU | |
| | UAAAUUAAGUAUACCCACUAAUUUUUCCUUUGGUGUGA CUCAGGAGUACAUUCAGACAACCAUUCAGAAAGUUACU | |
| | GUUGAUUGUAAACAGUACGUUUGCAAUGGUUUCCAGAA | |
| | GUGUGAGCAAUUACUGCGCGAGUAUGGCCAGUUUUGUU | |
| | CCAAAAUAAACCAGGCUCUCCAUGGUGCCAAUUUACGCC | |
| | AGGAUGAUUCUGUACGUAAUUUGUUUGCGAGCGUGAAA AGCUCUCAAUCAUCUCCUAUCAUACCAGGUUUUGGAGGU | |
| | GACUJUJAAUJUGACACUUCUGGAACCUGUJUCUAUAUC | |
| | UACUGGCAGUCGUAGUGCACGUAGUGCUAUUGAGGAUU | |
| | UGCUAUUUGACAAAGUCACUAUAGCUGAUCCUGGUUAU | |
| | AUGCAAGGUUACGAUGAUUGCAUGCAGGCAAGGUCCAGC | |
| | AUCAGCUCGUGAUCUUAUUUGUGCUCAAUAUGUGGCUG GUUACAAAGUAUUACCUCCUCUUAUGGAUGUUAAUAUG | |
| | GAAGCCGCGUAUACUUCAUCUUUGCUUGGCAGCAUAGCA | |
| | GGUGUUGGCUGGACUGCUGGCUUAUCCUCCUUUGCUGCU | |
| | AUUCCAUUUGCACAGAGUAUCUUUUAUAGGUUAAACGG | |
| | UGUUGGCAUUACUCAACAGGUUCUUUCAGAGAACCAAA AGCUUAUUGCCAAUAAGUUUAAUCAGGCUCUGGGAGCU | |
| | AUGCAAACAGGCUUCACUACAACUAAUGAAGCUUUUCA | |
| | GAAGGUUCAGGAUGCUGUGAACAACAAUGCACAGGCUC | |
| | UAUCCAAAUUAGCUAGCGAGCUAUCUAAUACUUUUGGU | |
| | GCUAUUUCCGCCUCUAUUGGAGACAUCAUACAACGUCUU GAUGUUCUCGAACAGGACGCCCAAAUAGACAGACUUAU | |
| | UAAUGGCCGUUUGACAACACUAAAUGCUUUUGUUGCAC | |
| | AGCAGCUUGUUCGUUCCGAAUCAGCUGCUCUUUCCGCUC | |
| | AAUUGGCUAAAGAUAAAGUCAAUGAGUGUGUCAAGGCA | |
| | CAAUCCAAGCGUUCUGGAUUUUGCGGUCAAGGCACACAU AUAGUGUCCUUUGUUGUAAAUGCCCCUAAUGGCCUUUA | |
| | CUUCAUGCAUGUUGGUUAUUACCCUAGCAACCACAUUGA | |
| | GGUUGUUUCUGCUUAUGGUCUUUGCGAUGCAGCUAACC | |
| | CUACUAAUUGUAUAGCCCCUGUUAAUGGCUACUUUAUU | |
| | AAAACUAAUAACACUAGGAUUGUUGAUGAGUGGUCAUA | |
| | UACUGGCUCGUCCUUCUAUGCACCUGAGCCCAUUACCUC CCUUAAUACUAAGUAUGUUGCACCACAGGUGACAUACCA | |
| | AAACAUUUCUACUAACCUCCCUCCUCCUCUUCUCGGCAA | |
| | UUCCACCGGGAUUGACUUCCAAGAUGAGUUGGAUGAGU | |
| | UUUUCAAAAAUGUUAGCACCAGUAUACCUAAUUUUGGU | |
| | UCCCUAACACAGAUUAAUACUACAUUACUCGAUCUUACC | |
| | UACGAGAUGUUGUCUCUCAACAAGUUGUUAAAGCCCU UAAUGAGUCUUACAUAGACCUUAAAGAGCUUGGCAAUU | |
| | AUACUUAUUACAACAAAUGGCCGUGGUACAUUUGGCUU | |
| | GGUUUCAUUGCUGGGCUUGUUGCCUUAGCUCUAUGCGU | |
| | CUUCUUCAUACUGUGCUGCACUGGUUGUGGCACAAACUG | |
| | UAUGGGAAAACUUAAGUGUAAUCGUUGUUGUGAUAGAU ACGAGGAAUACGACCUCGAGCCGCAUAAGGUUCAUGUUC | |
| | ACGAGGAADACGACCUCGAGCCGCADAAGGUUCAUGUUC | |
| Novel_MERS_S2_subunit_trimeric | AUGAUCCACUCCGUGUUCCUCCUCAUGUUCCUGUUGACC | 67 |
| vaccine | CCCACUGAGUCAGACUGCAAGCUCCCGCUGGGACAGUCC | |
| (nucleotide) | CUGUGUGCGCUGCCUGACACUCCUAGCACUCUGACCCCA | |
| | CGCUCCGUGCGGUCGGUGCCUGGCGAAAUGCGGCUGGCC UCCAUCGCCUUCAAUCACCCAAUCCAAGUGGAUCAGCUG | |
| | CONTRACTOR CALCENATION CALCUNATION CALCUNA | |

TABLE 10-continued

| train | Nucleic Acid Sequence | SEQ NO : |
|------------------|---|-------------|
| | • | |
| | UCGUUCGGGGUCACCCAGGAGUACAUCCAGACCACAAUU CAGAAGGUCACCGUCGAUUGCAAGCAAUACGUGUGCAAC | |
| | GGCUUCCAGAAGUGCGAGCAGCUGCUGAGAGAAUACGG | |
| | GCAGUUUUGCAGCAAGAUCAACCAGGCGCUGCAUGGAGC | |
| | UAACUUGCGCCAGGACGACUCCGUGCGCAACCUCUUUGC | |
| | CUCUGUGAAGUCAUCCCAGUCCUCCCCAAUCAUCCCGGG | |
| | AUUCGGAGGGGACUUCAACCUGACCCUCCUGGAGCCCGU | |
| | GUCGAUCAGCACCGGUAGCAGAUCGGCGCGCUCAGCCAU | |
| | UGAAGAUCUUCUGUUCGACAAGGUCACCAUCGCCGAUCC GGGCUACAUGCAGGGAUACGACGACUGUAUGCAGCAGG | |
| | GGGCUACAUGCAGGGAUACGACGACUGUAUGCAGCAGG GACCAGCCUCCGCGAGGGACCUCAUCUGCGCGCAAUACG | |
| | UGGCCGGGUACAAAGUGCUGCCUCCUCUGAUGGAUGUG | |
| | AACAUGGAGGCCGCUUAUACUUCGUCCCUGCUCGGCUCU | |
| | AUCGCCGGCGUGGGGUGGACCGCCGGCCUGUCCUCCUUC | |
| | GCCGCUAUCCCCUUUGCACAAUCCAUUUUCUACCGGCUC | |
| | AACGGCGUGGGCAUUACUCAACAAGUCCUGUCGGAGAAC | |
| | CAGAAGUUGAUCGCAAACAAGUUCAAUCAGGCCCUGGG | |
| | GGCCAUGCAGACUGGAUUCACUACGACUAACGAAGCGUU | |
| | CCAGAAGGUCCAGGACGCUGUGAACAACAACGCCCAGGC GCUCUCAAAGCUGGCCUCCGAACUCAGCAACACCUUCGG | |
| | AGCCAUCAGCGCGAUCGGUCGGUGACAUAAUUCAGCGGCU | |
| | GGACGUGCUGGAGCAGGACGCCCAGAUCGACCGCCUCAU | |
| | CAACGGACGGCUGACCACCUUGAAUGCCUUCGUGGCACA | |
| | ACAGCUGGUCCGGAGCGAAUCAGCGGCACUUUCCGCCCA | |
| | ACUCGCCAAGGACAAAGUCAACGAAUGCGUGAAGGCCCA | |
| | GUCCAAGAGGUCCGGUUUCUGCGGUCAAGGAACCCAUAU | |
| | | |
| | UAUGCACGUCGGCUACUACCCCGAGCAAUCAUAUCGAAGU GGUGUCCGCCUACGGCCUGUGCGAUGCCGCUAACCCCAC | |
| | UAACUGUAUUGCCCCUGUGAACGGAUAUUUUAUUAAGA | |
| | CCAACAACACCCGCAUUGUGGACGAAUGGUCAUACACCG | |
| | GUUCGUCCUUCUACGCGCCCGAGCCCAUCACUUCACUGA | |
| | ACACCAAAUACGUGGCUCCGCAAGUGACCUACCAGAACA | |
| | UCUCCACCAAUUUGCCGCCGCCGCUGCUCGGAAACAGCA | |
| | CCGGAAUUGAUUUCCAAGAUGAACUGGACGAAUUCUUC | |
| | AAGAACGUGUCCACUUCCAUUCCCAACUUCGGAAGCCUG | |
| | ACACAGAUCAACACCACCCUUCUCGACCUGACCUACGAG AUGCUGAGCCUUCAACAAGUGGUCAAGGCCCUGAACGAG | |
| | AUGUUGAGUUUGAGUUGAGUGUGGGUAAGGUUUGAGUAGG AGCUACAUCGACCUGAAGGAGCUGGGCAACUAUACCUAC | |
| | UACAACAAGUGGCCGGACAAGAUUGAGGAGAUUCUGUC | |
| | GAAAAUCUACCACAUUGAAAACGAGAUCGCCAGAAUCA | |
| | AGAAGCUUAUCGGCGAAGCC | |
| RS_S0_Full- | AUGGAAACCCCUGCCCAGCUGCUGCUGCUGCUGCUGCUG | 68 |
| ngth Spike | UGGCUGCCUGAUACCACCGGCAGCUAUGUGGACGUGGGC | |
| otein | CCCGAUAGCGUGAAGUCCGCCUGUAUCGAAGUGGACAUC | |
| ucleotide, codon | CAGCAGACCUUUUUCGACAAGACCUGGCCCAGACCCAUC | |
| timized) | GACGUGUCCAAGGCCGACGGCAUCAUCUAUCCACAAGGC | |
| | CGGACCUACAGCAACAUCACCAUUACCUACCAGGGCCUG UUCCCAUAUCAAGGCGACCACGGCGAUAUGUACGUGUAC | |
| | UCUGCCGGCCACGCCACCGGCACCACACCACACCACAGAAACUG | |
| | UUCGUGGCCAACUACAGCCAGGACGUGAAGCAGUUCGCC | |
| | AACGGCUUCGUCGUGCGGAUUGGCGCCCGCUGCCAAUAGC | |
| | ACCGGCACAGUGAUCAUCAGCCCCAGCACCAGCGCCACC | |
| | AUCCGGAAGAUCUACCCCGCCUUCAUGCUGGGCAGCUCC | |
| | GUGGGCAAUUUCAGCGACGGCAAGAUGGGCCGGUUCUU | |
| | CAACCACACCCUGGUGCUGCUGCCCGAUGGCUGUGGCAC | |
| | ACUGCUGAGAGCCUUCUACUGCAUCCUGGAACCCAGAAG | |
| | CGGCAACCACUGCCCUGCCGGCAAUAGCUACACCAGCUU CGCCACCUACCACACACCCGCCACCGAUUGCUCCGACGG | |
| | CAACUACAACCGGAACGCCAGCCUGAACAGCUUCAAAGA | |
| | GUACUUCAACCUGCGGAACUGCACCUUCAUGUACACCUA | |
| | CAAUAUCACCGAGGACGAGAUCCUGGAAUGGUUCGGCA | |
| | UCACCCAGACCGCCCAGGGCGUGCACCUGUUCAGCAGCA | |
| | GAUACGUGGACCUGUACGGCGGCAACAUGUUCCAGUUU | |
| | GCCACCCUGCCCGUGUACGACACCAUCAAGUACUACAGC | |
| | AUCAUCCCCCACAGCAUCCGGUCCAUCCAGAGCGACAGA | |
| | AAAGCCUGGGCCGCCUUCUACGUGUACAAGCUGCAGCCC CUGACCUUCCUGCUGGACUUCAGCGUGGACGGCUACAUC | |
| | CUGACCUUCCUGCUGGACUUCAGCGUGGACGGCUACAUC AGACGGGCCAUCGACUGCGGCUUCAACGACCUGAGCCAG | |
| | CUGCACUGCUCCUACGAGGCUUCGACGUGGAAAGCGGC | |
| | GUGUACAGCGUGUCCAGCUUCGAGGCCAAGCCUAGCGGC | |
| | AGCGUGGUGGAACAGGCUGAGGGCGUGGAAUGCGACUU | |
| | | |
| | CAGCCCUCUGCUGAGCGGCACCCCUCCCCAGGUGUACAA | |

TABLE 10-continued

| | | SEQ I |
|--------|--|-------|
| Strain | Nucleic Acid Sequence | NO : |
| | GACCAAGCUGCUGAGCCUGUUCUCCGUGAACGACUUCAC | |
| | CUGUAGCCAGAUCAGCCCUGCCGCCAUUGCCAGCAACUG | |
| | CUACAGCAGCCUGAUCCUGGACUACUUCAGCUACCCCCU | |
| | GAGCAUGAAGUCCGAUCUGAGCGUGUCCUCCGCCGGACC | |
| | CAUCAGCCAGUUCAACUACAAGCAGAGCUUCAGCAACCC | |
| | UACCUGCCUGAUUCUGGCCACCGUGCCCCACAAUCUGAC | |
| | CACCAUCACCAAGCCCCUGAAGUACAGCUACAUCAACAA | |
| | GUGCAGCAGACUGCUGUCCGACGACCGACCGAAGUGCC | |
| | | |
| | CAUCGUGCCCAGCACCGUGUGGGAGGACGGCGACUACUA CAGAAAGCAGCUGAGCCCCCUGGAAGGCGGCGGAUGGCU | |
| | GGUGGCUUCUGGAAGCACAGUGGCCAUGACCGAGCAGCU | |
| | GCAGAUGGGCUUUGGCAUCACCGUGCAGUACGGCACCGA | |
| | CACCAACAGCGUGUGCCCCAAGCUGGAAUUCGCCAAUGA | |
| | CACCAAGAUCGCCAGCCAGCUGGGAAACUGCGUGGAAUA | |
| | CUCCCUGUAUGGCGUGUCCCGGACGGGGCGUGUUCCAGAA | |
| | UUGCACAGCAGUGGGAGUGCGGCAGCAGAGAUUCGUGU | |
| | ACGAUGCCUACCAGAACCUCGUGGGCUACUACAGCGACG | |
| | ACGGCAAUUACUACUGCCUGCGGGCCUGUGUGUCCGUGC | |
| | CCGUGUCCGUGAUCUACGACAAAGAGACAAAGACCCACG | |
| | CCACACUGUUCGGCUCCGUGGCCUGCGAGCACAUCAGCU | |
| | CCACCAUGAGCCAGUACUCCCGCUCCACCCGGUCCAUGC | |
| | UGAAGCGGAGAGAUAGCACCUACGGCCCCCUGCAGACAC | |
| | CUGUGGGAUGUGUGCUGGGCCUCGUGAACAGCUCCCUGU | |
| | UUGUGGAAGAUUGCAAGCUGCCCCUGGGCCAGAGCCUGU | |
| | GUGCCCUGCCAGAUACCCCUAGCACCCUGACCCCUAGAA | |
| | GCGUGCGCUCUGUGCCCGGCGAAAUGCGGCUGGCCUCUA | |
| | UCGCCUUCAAUCACCCCAUCCAGGUGGACCAGCUGAACU | |
| | CCAGCUACUUCAAGCUGAGCAUCCCCACCAACUUCAGCU | |
| | UCGGCGUGACCCAGGAGUACAUCCAGACCACAAUCCAGA | |
| | AAGUGACCGUGGACUGCAAGCAGUACGUGUGCAACGGC | |
| | UUUCAGAAGUGCGAACAGCUGCUGCGCGAGUACGGCCAG | |
| | UUCUGCAGCAAGAUCAACCAGGCCCUGCACGGCGCCAAC | |
| | CUGAGACAGGAUGACAGCGUGCGGAACCUGUUCGCCAGC | |
| | GUGAAAAGCAGCCAGUCCAGCCCCAUCAUCCCUGGCUUC | |
| | GGCGGCGACUUUAACCUGACCCUGCUGGAACCUGUGUCC | |
| | AUCAGCACCGGCUCCAGAAGCGCCAGAUCCGCCAUCGAG | |
| | GACCUGCUGUUCGACAAAGUGACCAUUGCCGACCCCGGC | |
| | UACAUGCAGGGCUACGACGAUUGCAUGCAGGAGGGCCCA | |
| | GCCAGCGCCAGGGAUCUGAUCUGUGCCCAGUAUGUGGCC | |
| | GGCUACAAGGUGCUGCCCCCCUGAUGGACGUGAACAUG | |
| | GAAGCCGCCUACACCUCCAGCCUGCUGGGCUCUAUUGCU | |
| | GGCGUGGGAUGGACAGCCGGCCUGUCUAGCUUUGCCGCC | |
| | | |
| | GUGGGCAUCACACAACAGGUGCUGAGCGAGAACCAGAA | |
| | | |
| | GCAGACCGGCUUCACCACCACCACGAGGCCUUCAGAAA | |
| | GGUGCAGGACGCCGUGAACAACACGCCCAGGCUCUGAG CAAGCUGGCCUCCGAGCUGAGCAAUACCUUCGGCGCCAU | |
| | CAGCGCCUCCAUCGGCGACAUCAUCCAGCGGCUGGACGU | |
| | GCUGGACAGGACGCCCAGAUCGACGGCUGGACGGCUGGACGG | |
| | CAGACUGAACAGGACGCCCAGAUCGACGGCUGAUCAACGG CAGACUGACCACCCCUGAACGCCUUCGUGGCACAGCAGCU | |
| | CGUGCGGAGCGAAUCUGCCGCUCUGUCUGCUCAGCUGGC | |
| | CAAGGACAAAGUGAACGAGUGCGUGAAGGCCCAGUCCA | |
| | AGCGGAGCGGCUUUUGUGGCCAGGGCACCCACAUCGUGU | |
| | CCUUCGUCGUGAAUGCCCCCAACGGCCUGUACUUUAUGC | |
| | ACGUGGGCUAUUACCCCAGCAACCACAUCGAGGUGGUGU | |
| | CCGCCUAUGGCCUGUGCGACGCCGCCAAUCCUACCAACU | |
| | GUAUCGCCCCCGUGAACGGCUACUUCAUCAAGACCAACA | |
| | ACACCCGGAUCGUGGACGAGUGGUCCUACACAGGCAGCA | |
| | GCUUCUACGCCCCCGAGCCCAUCACCUCCCUGAACACCA | |
| | | |
| | | |
| | | |
| | UCGACUUCCAGGACGAGCUGGACGAGUUCUUCAAGAACG | |
| | UGUCCACCUCCAUCCCCAACUUCGGCAGCCUGACCCAGA | |
| | UCAACACCACUCUGCUGGACCUGACCUACGAGAUGCUGU | |
| | CCCUGCAACAGGUCGUGAAAGCCCUGAACGAGAGCUACA | |
| | UCGACCUGAAAGAGCUGGGGAACUACACCUACUACAACA | |
| | AGUGGCCUUGGUACAUUUGGCUGGGCUUUAUCGCCGGCC | |
| | NGENGGCCCNGGCCCNGNGCGNGNNCNNCANGCNGCA | |
| | GCACCGGCUGCGGCACCAAUUGCAUGGGCAAGCUGAAAU | |
| | GCAACCGGUGCUGCGACAGAUACGAGGAAUACGACCUGG | |
| | AACCUCACAAAGUGCAUGUGCAC | |

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TABLE 11

| | | SEQ II |
|---|---|--------|
| Strain | Amino Acid Sequence | NO: |
| gb KJ156934.1 : 21405-25466 Middle East respiratory syndrome coronavirus isolate Riyadh_14_2013, spike protein (amino acid) | MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKT WPRPIDVSKADGIIYPQGRTYSNITITYQGLFPYQGDHGDMY VYSAGHATGTTPQKLFVANYSQDVKQFANGFVVHIGAAANS TGTVIISPSTSATIRKIYPAPMLGSSVGNFSDGKMGRPFNHTL VLLPDGCGTLLRAFYCILEPRSGNHCPACNSYTSFATYHTPA TDCSDGNYNRNASLNSFKEYFNLRNCTFMYTYNITEDEILEW FGITQTAQGVHLFSSRYVDLYGGNMFQPATLPVVDTIKYTSII PHSIRSIQSDRKAWAAFYVYKLQPLTFLLDFSVDGYIRRAIDC GFNDLSQLHCSYESFDVESGVYSVSSFEAKPSGSVVEQABGV ECDFSPLLSGTPPQVYNFKRLVFTNCNYNLTKLLSLFSVNDFt CSGISPAAIASNCYSSILDYFSYVBLSMKSDLSVSSAGFISQFN YKQSFSNPTCLILATVPHNLTTITKPLKYSYINKCSRLSDDRT EVPQLVNNQYSPCVSIVPSTWEDGDYYRKQLSPLEGGGW LVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKLEFANDT KIASQLGMCVEYSLYGVSGRGVFQNCTAVGVRQQFFVDA YQNLVGYYSDGNYYCLRACVSVPSVIDVERTTHATLFG SVACHHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCULGL VNSSLFVEDCKLDLGQSLCALPDTPSTLTPRSVRSVPGEMRLA SIAPNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYIQTTIQKVTV DCKQYVCNGFQKCEQLLREYGQPCSKINGALHGANLRQDDS VRNLFASVKSSQSSPIIPGFGGDPNLTLLEPVSISTGSRSARSAI EDLLFDKVTIADFGYMQGYDDCMQQGPASARDLICAQVVA GYKVLPPLMDVNMEAAYTSSLLGSIAGVGWTAGLSSFAAIFF AQSIFYLLNGVGITQQUSENQKLIANKNQALGAMQTGFTT TNEAFrKVQDAVNNAQALSKLASELSNTFGAISASIGDIIQR LDVLEQDAQIDRLINGRLTTLNAFVAQUVRSESAALSAQLA KDKVNECVKAQSKRSGFCQGTHIVSFVNAPNGLYFMHV GYYPSNHIEVVSAYGLCDAANPTNCIAPVNGQFIKTNNTRIV DEWSYTGSSFYAPEPITSLNKKVVAPQVTYQNISTNLPPPLLG NSTGIDFQDELDEFFKNVSTSIPNFSGTQUTISTNLPPLLG VSYCALNESYIDLKELGNYTYNKWPWIWLGFIAGLVA LALCVFFILCCTGCGTNCMGKLKCNRCCDRYEEVDLEPHKV HVH | 24 |
| MERS S FL SPIKE 2cEMC/2012 (XBaI change(T to G)) (amino acid) | MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKT WRPPIDVSKADGIIYPQGRTYSNITITYQGLFPYQGDHGDMY VYSAGHATGTTPQKLFVANYSQDVKQFANGFVVRIGAAANS TGTVIISPSTSATIRKIYPAPMLGSSVGNFSDGKMGRFFNHTL VLLPDGCGTLLRAFYCLLEPRSGNHCPACNSYTSFATYHTPA TDCSDGNYNRNASLNSFKEYPNLRNCTFMYTYNITEDEILEW FGITQTAQGVHLFSSRYVDLYGGMMFQFATLPVYDTIKYYSII PHSIRSIQSDRKAWAAFYVYKLQPLTFLLDFSVDGYIRRAIDC GFNDLSQLHCSYESFDVBSGVYSVSSFEAKPSGSVVEQABGV ECDFSPLLSGTPPQVYNFKRLVFTNCNYNLTKLLSLFSVNDFT CSQISPAATASNCYSSLILDYFSYPLSMKSDLSVSSAGPISQFN YKQSFSNFTCLILATVPHNLTTITKPLKYSYINKCSRLLSDDRT EVPQLVNANQYSPCVSIVFSTWEDGDYYRKQLSPLEGGGW LVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKLEFANDT KIASQLGNCVEYSLYGVSGRGVFQNCTAVGVRQQFFVDA YQNLVGYYSDDGNYYCLRACVSVPVSVIDKETKTHATLFG SVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCVLGL VNSSLFVEDCKLDLGQSLCALPDTPSTITPRSVRSVPGBMRLA SIAFNHPIQVDQLNSSYFKLSIPTNFFGVTQEYIQTTIQKVTV DCKQVVCNGFQKCEQLLREYGQFCSKINQALHGANLRQDDS VRNLFASVKSSQSSPIIPGFGGDFNLTLLEPVSISTGSRSARSAI EDLLFDKVTIADFGYMQGYDCMQGPASARDLCAQYVA GYKVLPPLMVNMEAAYTSSLLGSLAVFFALGAMQTGFT THEAFQKVQDAVNNNAQALSKLASELSNTFGAISASIGDIIQR LDVLEQDAQIDRLINGRLTTLNAFVAQQLVRSESAALSAQLA KDKVNECVKAQSKRSGCGQGTHIVSFVNAPNGLYFMW GYYPSNHIEVSAYGLCDAANPTNCIAPVNGYFIKTNNTRIV DEKSYTGSSFYAPEPITSLINFFGSLTQINTTILDLTYEMLS LQQVVALNESYIDLKELGNYTYNKWPYIWLGFIAGLVA LALCVFFILCTGCGTNCMGKLKCNRCCDRYEEYDLEPHKV HVH | 25 |
| Novel_MERS_S2_subunit_trimeric vaccine (amino acid) | MIHSVFLLMFLLTPTESDCKLPLGQSLCALPDTPSTLTPRSVR SVPGEMRLASIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYI QTTIQKVTVDCKQYVCNGFQKCEQLLREYGQFCSKINQALH GANLRQDDSVRNLFASVKSSQSSPIIPGFGGDFNLTLLEPVSIS TGSRSARSAIEDLLFDKVTIADPGYMQGYDDCMQQGPASAR DLICAQYYAGYKVLPPLMDVNMEAAYTSSLLGSIAGVGWTA GLSSFAAIPFAQSIFYRLMGVGITQQVLSENQKLIANKFNQAL | 26 |

| Betacoronavirus Amino Acid Sequences | | |
|--|--|---------------|
| Strain | Amino Acid Sequence | SEQ ID NO: |
| | GAMQTGFTTTNEAFQKVQDAVNNNAQALSKLASELSNTFG AISASIGDIIQRLDVLEQDAQIDRLINGRLTTLNAFVAQQLVRS ESAALSAQLAKDKVNECVKAQSKRSGFCGQGTHIVSFVVNA PNGLYFMHVGYYPSNHIEVVSAYGLCDAANPTNCIAPVNGY FIKTNNTRIVDEWSYTGSSFYAPEPITSLNTKYVAPQVTYQNI STNLPPPLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQINTTL LDLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKWPDKIE EILSKIYHIENEIARIKKLIGEA | |
| Isolate Al- Hasa_1_2013 (NCBI accession #AGN70962) | MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKT WPRIDVSKADGIIYPQGRTYSNITIITYQGLFPYQGDHGDMY VYSAGHATGTTPQKLFVANYSQDVKQFANGFVVRIGAAANS TGTVIISPSTSATIRKIYPAPMLGSSVGNFSDGKMGRFFNHTL VLLPDGCGTLLRAFYCILBFRSGNHCPACMSYTSFATYHTPA TDCSDGNYNRNASLNSFKEYFNLFNCTFMYTYNITEDEILEW FGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVVDTIKYYSII PHSIRSIQSDRKAWAAFYVYKLQPLTFLLDFSVDGYIRRAIDC GFNDLSQLHCSYESFDVESGVYSVSSFEAKPSGSVVEQAEGV ECDFSPLLSGTPQVYNFKRLVFTNCNYNLTKLSLFSVNDFT CSQISPAAIASNCYSSLIDYFSYDLSMKSDLSVSSAGPISQFN YKQFFSNFTCLILATVPHNLTTITKPLKYSYINKCSRLLSDDRT EVPQLVNANQYSPCVSIVPSTVWEDGDYYRKQLSPLEGGGW LVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKLEFANDT KIASQLGNCVEYSLYGVSGRGVFQNCTAVGVRQQRFVYDA YQNLVGYSDDGNYYCLRACVSVPSVIVDKETKTHATLFG SVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCVLGL VNSSLFVEDCKLPLGQSLCALPDTPSTLTPRSVRSVPGEMRLA SIAPNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYIQTTIQKVTV DCKQYVCNGFQKCEQLLREYGQFCSKINQALHGANLRQDDS VRNLFASVKSSQSSPIIPGFGDDNLTLLEPVSISTGSRSARSAI EDLLFDKVTIADFGYQQTDCMQQGPASARDLICAQYVA GYKVLPPLMDVNMEAAYTSSLGSIAGVGNTAGLSSFAAIFF AQSIFYRLMGVGITQQVLSENQKLIANKFNQALGANQTGFT TNEAFRKVQDAVNNAQALSKLASELSNTFGAISASIGDIIQR LDVLEQVAQSKRSGFCQGTHIVSFVNAPNGLYFMHV GYYFSNHIEVVSAYGLCDANPTNCIAPVMGYFIKNNTRIV DEWSYTGSSFYAPEPITSLNTKYVAPHVTYQNISTNLPPPLLG NSTGIDFQDELDEFFKNVSTSIDFNSLSTQINTTLLDFYELS LQQVVKALNESYIDLKELGNYTYNKWPWYIWLGFIAGLVA LALCVFFILCCTGCGTNCMGKLKCNRCCDRYEEYDLEPHKV HVH | 27 |
| Middle East respiratory syndrome coronavirus S protein UniProtKB- R9UQ53 | MIHSVFLLMPLLTPTESYVDVGPDSVKSACIEVDIQQTFPDKT WPRPIDVSKADGIIYPQGRTYSNITITYQGLPPVQGDHGDMY VYSAGHATGTTPQKLFVANYSQDVKQFANGFVVRIGAAANS TGTVIISPSTSATIRKIYPAPMLGSSVGNFSDGKMGRFPNHTL VLLPGCGTLLRAFYCILEPRSGNHCPAGNSYTSFATYHTPA TDCSDGNYNRNASLNSFKEYFNLFNCTFMYTYNITEDEILEW FGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYSII PHSIRSIQSDRKAMAAFYYYKLQPLTFLDFSVDGYIRRAIDC GFNDLSQLHCSYESFDVESGVYSVSSFAKPSGSVVEQAEGV ECDFSPLLSGTPPQYNFRRLVFTNCNYNLTKLLSLFSVNDFT CSQISPAAIASNCYSSLILDYFSYPLSMKSDLSVSSAGPISQPN YKQFFSNFTCLILATVPHNLTTITKPLKYSYINKCSRLLSDDRT EVPQLVNANQYSPCVSIVPSTWEDGDYYRKQLSPLEGGBW LVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKLEFANDT KIASQLGNCVEYSLIGVSGRGVFQNCTAVGVRQQFFVDA YQNLVGYYSDDGNYYCLRACVSVPVSVIYDKETKTHATLFG SVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCVLGL VNSSLFVEDCKLPLGQSLREVGQFCSKINQALHGANLRQDDS VRNLFASVKSSQSSPIIPGFGGDFNLTLLEPVSISTGSRSARSAI EDLLFPKVQDANNNAQALSKLASELSNTFGAISASIGDIQR LVASGSTVAMTSQLGLREYGQFCSKINQALGAMQTGFTT TNEAFRKVQDAVNNAQALSKLASELSNTFGAISASIGDIQR LDVLGYYSDGGTUQVSENQKLIANKFNQALGAMQTGFTT TNEAFRKVQDAVNNAQALSKLASELSNTFGAISASIGDIQR LDVLFYSNGGTQQVLSENQKLIANKFNQALGAMQTGFTT TNEAFRKVQDAVNNAQALSKLASELSNTFGAISASIGDIQR LDVLEQDAQIDRLINGRITTLNAFVAQLVRSESAALSAQLA KDKVNECVKAQSKRSGFCQGTHIVSFVNAPNGLYFMHV GYYPSNHIEVVSAYGLCDAANPTNCIAPVMGYFIKTNNTRIV DEWSYTGSSFYAPEPITSLNYVNAPHYQNISTNLPPPLLG NSTGIDFQDELDEFFKNYSTSIPNFGSLQINTTLLDLTYEMLS LQQVVKALMESYIDLKELGNYTYNKWPWIWLGFIAGLVA | 28 |

TABLE 11-continued

| Betacoronavirus Amino Acid Sequences | | |
|--|--|---------------|
| Strain | Amino Acid Sequence | SEQ II NO: |
| | LALCVFFILCCTGCGTNCMGKLKCNRCCDRYEEYDLEPHKV HVH | |
| Human SARS coronavirus (SARS-CoV) (Severe acute respiratory syndrome coronavirus) Spike glycoprotein UniProtKB- P59594 | MFIFLLFLTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYY PDEIFRSDTLYLTQDLFLPFYSNVTGFHTINHTGONPVIPFKDG IYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNSTNVVIRAC NFELCDNFFFAVSKPMGTQTHTMIFDNAFNCTFEYISDAFSLD VSEKSGNFKHLREFVFKNKDGFLYVYKGYQFIDVVRDLPSGF NTLKPIFKLPLGINITNFRAILTAFSPAQDIWGTSAAAYFVGYL KPTTFMLKYDENGTITDAVDCSQNPLAELKCSVKSFEIDKGI YQTSNFRVVPSGDVVRPNITNLCPFGEVFNATKFPSVYAWE RKKISNCVADYSULYNSTFFSTFKCYGVSATKLNDLCFSNVY ADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAW NTRNIDATSTGNYNYKYRYLRHGKLRPFERDISNVPFSPDGK PCTPPALNCYWPLNDYGFYTTGIGYQPYRVVUSFELLNAP ATVCGFKLSTDLIKNQCVNFNENGLTGTGVLTPSSKRFQPFQ QFGRDVSDFTDSVRDPKTSEILDISPCSFGGVSVITPGTNASSE VAVLYQDVNCTDVSTAIHADQLTPAWRIYSTGNNVFQTQAG CLIGAEHVDTSYECDIPIGAGICASYHTVSLLRSTSQKSIVAYT MSLGADSSIAYSNNTIAIFTNFSISITTEVMPVSMAKTSVDCN MYICGDSTECANLLQYGSFCTQLNRALSGIAAEQDRNTREV FAQVKQWKKTPTLKYFGGFNFSQILPDFLKPTKRSFIEDLLFN KVTLADAGFMKQYGECLGDINARDLICAQKFNGLTVLPPLL TDDMIAAYTAALVSGTATAGWTFGAGAALQIPFAMQMAYR FNGIGUTQNVLYENXGLANGFKAISQIQESLTTTSTLGKL QDVNQNAQALNTLVKQLSNFGAISSVLNDILSRLDKVEAE VQLDRLITGRLQSLQTVTVQLLRAAEIRASANLAATKMSEC VLGQSKRVDFCGKGYHLMSFPQAAPHGVVFLHVTYVPSQER NFTTAPAICHEGKAYFPREGVFVPNGTSWFITQNFFSQIITT DNTFVSGNCDVIGIINNTVDPLQPELDSFKEELDKYFKNH TSPDVDLGDISGINASVVNIQKEIDRLNEVFKHH TSPDVDLGDISGINASVVNIQKEIDRLNESKLDLJESLDLQE LGKYEQYIKWPYVLGFIAGLIAIVMVTILLCCMTSCCSCL KGACSCGSCCKFDEDDSEPVLKGVKLHYT | 29 |
| Human coronavirus OC43 (HCoV-OC43) Spike glycoprotein UniProtKB- P36334 | MFLILLISLPTAFAVIGDLKCTSDNINDKDTGPPPISTDTVDVT NGLGTYVVLDRVYLNTTLFLNGYYPTSGSTYRNMALKGSVL LSRLWFKPPFLSDFINGIFAKVKNTKVIKDRVMYSEFPAITIGS TFVNTSYSVVVQPRTINSTQDGDNKLQGLLEVSVCQYNMCE YPQTICHPNLGNHRKELMHLDTGVVSCLYKRNFTYDVNAD YLYPHFYQEGGTFYAYFTDTGVVTKFLFNVYLGMALSHYV MPLTCNSKLTLEYWVTPLTSRQYLLAFNQDGIIPNAEDCMSD FMSEIKCKTQSIAPPTGVYELNGYTVQPIADVYRKKPNLPNC NIEAWLMDKSVPSPLNMERKTFSNCNFINSSLMSFIQADSFT CNNIDAKIYGMCFSSITIDKFAIPNGRKUDLQLGNLGYLQSF NYRIDTTATSCQLYYNLPAANVSVSRPNSTWNKRFGFIEDS VFKPRPAGVLTNHDVVYAQHCFKAPKNFCPCKLNGSCVGSG PGKNNGIGTCPAGTNYLTCDNLCTPQPITFTGTYKCPQTKSL VGIGEHCSGLAVKSDYCGGNSCTCRPQAFLGWSADSCLQED KCNIFANFILHDVNSQLLYSNGNLYGFRDYIJINRTFMI RSCYSGRVSAPHANSEPALLFRNIKCNYVFINSLTRQLQFI NYFDSYLGCVNAYNSTAISVQTCDLTVGSGYCVDYSKNRR SRGAITTGYRFTNFEPFTVNSVNDSLEPVGGLYHQIPSEFTIG NMVEFIQTSSPKVTIDCAAFVCGDYAACKSQLVEYGSFCDNI NAILTEVNELLDTQLQVANSLMNGVTLSTKLKDGVFRNVD DINFSPVLGCLGSECSKASSRSAIEDLLFDKVKLSDVGFVEAY NNCTGGAEIRDLICVQSYKGIKVLPPLLSENQISGYTLAATSA SLFPPWTAAAGVPFYLNVQYRINGLAVQSSRINFCGNGNHIIS LVQNAPYGLYFINFEPFTVKVTARVSPGLCIAGDRGHAVS QQLSDSTLVKFSAQAMEKVNECVKSQSSRINFCGNGNHIIS LVQNAPGLYFIHFSYVPTKYVTARVSPGLCIAGDRGIAPKS GYFVNVNNTWMYTGSGYYPEPITENNVVMSTCAVNYTK APYVMLNTSIPNLPDFKEELDQWFKNQTSVAPDLSLDYINVT FLDLQVEMNRLQEAIKVLNQSYINLKDIGTYEYVKWPWVV WLLICLAGVAMLVLEFFICCCTGGGTSCFKKCGGCCDDYTG YQELVIKTSHDD | 30 |
| Human coronavirus HKU1 (isolate N5) (HCoV- HKU1) Spike glycoprotein | MFLIIFILPTTLAVIGDFNCTNSFINDYNKTIPRISEDVVDVSLG LGTYYVLNRVYLNTTLLFTGYPFKSGANFRDLALKGSIVLST LWYKPPFLSDFNNGIFSKVKNTKLYVNNTLYSEFSTIVIGSVF VNTSYTIVVQPHNGILEITACQYTMCEYPHTVCKSKGSIRNES WHIDSSEPLCLFKKNFTYNVSADWLYFHFYQERGVFYAYYA DVGMPTTFLFSLYLGTILSHYYVMPLTCNAISSNTDNETLEY | 31 |

TABLE 11-continued

| Be | Betacoronavirus Amino Acid Sequences | | |
|------------------------|---|---------------|--|
| Strain | Amino Acid Sequence | SEQ ID NO: | |
| UniProtKB- Q0ZME7 | WVTPLSRRQVLLNFDEHGVITNAVDCSSSFLSEIQCKTQSFAP NTGVYDLSGFTVKFVATVYRRIPNLPDCDIDNMLNNVSVPSP LNWERRIFSNCNFNLSTLLRLVHVDSFSCNNLDKSKIFGSCFN SITVDKFAIPNRRDDLQLGSSGFLQSSNYKIDISSSSCQLYYS LPLVNVTINNENPSSWNRRYGFGSFNLSSYDVVYSDHCFSVN SDFCPCADPSVVNSCAKSKPPSAICPAGTKYRHCDLDTTLYV KNWCRCSCLPDPISTYSPNTCPQKKVVVGIGEHCPGLGINEE KCGTQLNHSSCPCSPDAFLGWSPDSCISNNRCNIPSNFIFNGIN SGTTCSNDLLYSNTEISTGVCVNYDLYGITGQGIFKEVSAAY YNNWQNLLYDSNGNIIGFKDFLTNKTYTILPCYSGRVSAAFY QNSSSPALLYNNKCSYVLNISFISQPFYDSYLGCVLNAVN LTSYSVSSCDLRMGSGFCIDYALPSSRKRRGISSPYRPVTFEP FNVSFVNDSVETVGGLFEIQIPTNFTIAGHEEFIQTSSPKVTIDC SAFVCSNYAACHDLSEYGTFCDNINSILNEVNDLLDITQLQV ANALMQGVTLSSNLNTNLHSDVDNIDFKSLLGCLGSQCGSSS RSLLEDLFNKVKLSDVGFVEAYNNCTGGSEIRDLLCVQSFN GIKVLPPILSETQISGYTTAATVAAMPPWSAAAGVPFSLNVQ YRINGLGVTMANAQALNSLLQQLFNKFGAISSSLGEILSRLDNLE AQVQIDRLINGRTALNAYVSQLSDITLIKAGASRAIEKVNE CVKSQSPRINFCGNGNHILSLVQNAPYGLLFIHFSYKPTSFKT VLVSPGLCLSGDRGIAPKQGYFIKQNDSWMFTGSSYYYPEPIS DKNVVFMNSCSVNFTKAPFIVLNNSIFNLSDFEAELSLWFKN HTSIAPNLTFNSHINATFLDLYYEMVIQESIKSLNSSFINLKEI GTYEMYVKWPWYIWLLVILFIIFLMILFFICCCTGCGSACFSK CHNCCDEYGGHNDFVIKASHDD | | |
| Novel_SARS_S2 | MFIFLLFLTLTSGSDLDRALSGIAAEQDRNTREVFAQVKQMY KTPTLKYFGGPNFSQILPDPLKPTKRSFIEDLLFNKVTLADAG FMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYT AALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQN VLYENQKQIANQFNKAISQIQESLTTTSTALGKLQDVVNQNA QALNTLVKQLSSNFGAISSVLNDILSRLDKVBAEVQIDRLITG RLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRV DFCGKGYHLMSFPQAAPHGVVFLHVTYVPSQERNFTTAPAIC HEGKAYFPREGYFVFNGTSWFITQRNFFSPQIITTDNTFVSGN CDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLG DISGINASVVNIQKEIDRLNEXKNLNESLIDLQELGKYEQYI KWPWYWLGFIAGLIAIVMVTILLCCMTSCCSCLKGACSCGS CCKFDEDDSEPVLKGVKLHYT | 32 | |
| Novel_MERS_S2 | MIHSVFLLMFLLTPTESDCKLPLGQSLCALPDTPSTLTPRSVR SVPGEMRLASIAFNHPIQVDQLNSSYFKLSIPTNPSFGVTQEYI QTTIQKVTVDCKQYVCNGFQKCEQLLREYGQPCSKINQALH GANLRQDDSVRNLFASVKSSQSSPIIPGFGGDFNLTLLEPVSIS TGSRSARSAIEDLLFDKVTIADPGYMQGYDDCMQQGPASAR DLICAQYVAGYKVLPPLMDVNMEAAYTSSLLGSIAGVGWTA GLSSPAAIPFAQSIFYRLNGVGITQQVLSENQKLIANKFNQAL GAMQTGFTTTNEAFQKVQDAVNNNAQALSKLASELSNTFG AISASIGDIIQRLDVLEQDAQIDRLINGRLTTLNAFVAQQLVRS ESAALSAQLAKDKVNECVKAQSKRSGPCGQGTHIVSFVVNA PNGLYFMHVGYYPSNHIEVVSAYGLCDANPTNCIAFVNGY FIKTNNTRIVDEWSYTGSSFYAPEPITSLNTKYVAPQVTYQNI STNLPPPLLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQINTTL LDLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKWP | 33 | |
| Novel_Trimeric_SARS_S2 | MFIFLLFLTLTSGSDLDRALSGIAAEQDRNTREVFAQVKQMY KTPTLKYFGGFNFSQILPDPLKPTKRSFIEDLLFNKVTLADAG FMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYT AALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQN VLYENQKQIANQFNKAISQIQESLTTTSTALGKLQDVVNQNA QALNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITG RLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRV DFCGKGYHLMSFPQAAPHGVVFLHVTYVPSQERNFTAPAIC HEGKAYFPREGVFVFNGTSWFITQRNFFSPQIITTDNTFVSGN CDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLG DISGINASVVNIQKEIDRLNEVAKNLESSLIDLQELGKYEQYI KWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCLKGACSCGS CCKFDEDDSEPVLKGVKLHYT | 34 | |

TABLE 12

| enBank ccession | Country | Collection Date | Release Date | Virus Name |
|--------------------|-------------------|-----------------|--------------|--|
| FY13307 | United | 2012 Sep. 11 | 2012 Dec. 5 | Betacoronavirus England 1, |
| FS88936 | Kingdom | 2012 Jun. 13 | 2012 Sep. 27 | complete genome Human betacoronavirus 2c |
| GG22542 | United | 2012 Sep. 19 | 2013 Feb. 27 | EMC/2012, complete genome Human betacoronavirus 2c England- |
| HY21469 | Kingdom Jordan | 2012 | 2014 May 4 | Qatar/2012, complete genome Human betacoronavirus 2c Jordan- N3/2012 isolate MG167, complete |
| GH58717 | Jordan | 2012 April | 2013 Mar. 25 | genome Human betacoronavirus 2c Jordan- |
| GV08444 | Saudi Arabia | 2013 May 7 | 2013 Sep. 17 | N3/2012, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GV08546 | Saudi Arabia | 2013 May 11 | 2013 Sep. 17 | Hasa_12_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GV08535 | Saudi Arabia | 2013 May 12 | 2013 Sep. 17 | Hasa_15_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GV08558 | Saudi Arabia | 2013 May 15 | 2013 Sep. 17 | Hasa_16_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GV08573 | Saudi Arabia | 2013 May 23 | 2013 Sep. 17 | Hasa_17_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GV08480 | Saudi Arabia | 2013 May 23 | 2013 Sep. 17 | Hasa_18_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GN70962 | Saudi Arabia | 2013 May 9 | 2013 Jun. 10 | Hasa_19_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GV08492 | Saudi Arabia | 2013 May 30 | 2013 Sep. 17 | Hasa_1_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| HI48517 | Saudi Arabia | 2013 May 2 | 2014 Feb. 6 | Hasa_21_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GN70951 | Saudi Arabia | 2013 Apr. 21 | 2013 Jun. 10 | Hasa_25_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GN70973 | Saudi Arabia | 2013 Apr. 22 | 2013 Jun. 10 | Hasa_2_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GN70929 | Saudi Arabia | 2013 May 1 | 2013 Jun. 10 | Hasa_3_2013, complete genome Middle East respiratory syndrome coronavirus isolate Al- |
| GV08408 | Saudi Arabia | 2012 Jun. 19 | 2013 Sep. 17 | Hasa_4_2013, complete genome Middle East respiratory syndrome coronavirus isolate Bisha_1_2012, |
| GV08467 | Saudi Arabia | 2013 May 13 | 2013 Sep. 17 | complete genome Middle East respiratory syndrome coronavirus isolate |
| ID50418 | United Kingdom | 2013 Feb. 10 | 2014 Jun. 18 | Buraidah_1_2013, complete genome Middle East respiratory syndrome coronavirus isolate England/2/2013, |
| ID81451 | United Kingdom | 2013 Feb. 10 | 2015 Jan. 18 | complete genome Middle East respiratory syndrome coronavirus isolate England/3/2013, |
| JD81440 | United Kingdom | 2013 Feb. 13 | 2015 Jan. 18 | complete genome Middle East respiratory syndrome coronavirus isolate England/4/2013, |
| HB33326 | France | 2013 May 7 | 2013 Dec. 7 | complete genome Middle East respiratory syndrome coronavirus isolate FRA/UAE, |
| Z48760 | USA | 2014 June | 2014 Dec. 14 | complete genome Middle East respiratory syndrome coronavirus isolate Florida/USA- 2_Saudi Arabia_2014, complete |
| GV08455 | Saudi Arabia | 2013 Jun. 4 | 2013 Sep. 17 | genome Middle East respiratory syndrome coronavirus isolate Hafr-Al- |
| HI48561 | Saudi Arabia | 2013 Aug. 5 | 2014 Feb. 6 | Batin_1_2013, complete genome Middle East respiratory syndrome coronavirus isolate Hafr-Al- |

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TABLE 12-continued

| GenBank Accession | Country | Collection Date | Release Date | Virus Name |
|----------------------|-----------------|-----------------|--------------|---|
| AHI48539 | Saudi Arabia | 2013 Aug. 28 | 2014 Feb. 6 | Middle East respiratory syndrome coronavirus isolate Hafr-Al- |
| \IZ744 17 | France | 2013 Apr. 26 | 2015 Mar. 10 | Batin_6_2013, complete genome Middle East respiratory syndrome coronavirus isolate Hu-France (UAE) - FRA1_1627- 2013_BAL_Sanger, complete |
| AIZ74433 | France | 2013 May 7 | 2015 Mar. 10 | genome Middle East respiratory syndrome coronavirus isolate Hu-France - FRA2_130569-2013_IS_HTS, |
| AIZ74439 | France | 2013 May 7 | 2015 Mar. 10 | complete genome Middle East respiratory syndrome coronavirus isolate Hu-France - FRA2_130569-2013_InSpu_Sanger, |
| AIZ7445 0 | France | 2013 May 7 | 2015 Mar. 10 | complete genome Middle East respiratory syndrome coronavirus isolate Hu-France - FRA2_130569-2013_Isolate_Sanger, |
| KK52602 | Saudi Arabia | 2015 Feb. 10 | 2015 Jun. 8 | complete genome Middle East respiratory syndrome coronavirus isolate Hu/Riyadh_KSA_2959_2015, |
| AKK52612 | Saudi Arabia | 2015 Mar. 1 | 2015 Jun. 8 | complete genome Middle East respiratory syndrome coronavirus isolate Hu/Riyadh_KSA_4050_2015, |
| AHN10812 | Saudi Arabia | 2013 Nov. 6 | 2014 Mar. 24 | complete genome Middle East respiratory syndrome coronavirus isolate Jeddah_1_2013, complete genome |
| AD55071 | Saudi Arabia | 2014 Apr. 21 | 2014 Nov. 12 | Middle East respiratory syndrome coronavirus isolate Jeddah_C10306/KSA/2014-04-20, |
| AID55066 | Saudi Arabia | 2014 | 2014 Nov. 12 | complete genome Middle East respiratory syndrome coronavirus isolate Jeddah_C7149/KSA/2014-04-05, |
| AID55067 | Saudi Arabia | 2014 | 2014 Nov. 12 | complete genome Middle East respiratory syndrome coronavirus isolate Jeddah_C7569/KSA/2014-04-03, |
| AID55068 | Saudi Arabia | 2014 Apr. 7 | 2014 Nov. 12 | complete genome Middle East respiratory syndrome coronavirus isolate Jeddah_C7770/KSA/2014-04-07, |
| AID55069 | Saudi Arabia | 2014 Apr. 12 | 2014 Nov. 12 | complete genome Middle East respiratory syndrome coronavirus isolate Jeddah_C8826/KSA/2014-04-12, |
| AID55070 | Saudi Arabia | 2014 Apr. 14 | 2014 Nov. 12 | complete genome Middle East respiratory syndrome coronavirus isolate Jeddah_C9055/KSA/2014-04-14, |
| AHE78108 | Saudi Arabia | 2013 Nov. 5 | 2014 May 1 | complete genome Middle East respiratory syndrome coronavirus isolate MERS-CoV- |
| KL59401 | South Korea | 2015 May 20 | 2015 Jun. 9 | Jeddah-human-1, complete genome Middle East respiratory syndrome coronavirus isolate MERS- CoV/KOR/KNIH/002_05_2015, |
| LD51904 | Thailand | 2015 Jun. 17 | 2015 Jul. 7 | complete genome Middle East respiratory syndrome coronavirus isolate MERS- CoV/THA/CU/17_06_2015, complete genome |
| AID55072 | Saudi Arabia | 2014 Apr. 15 | 2014 Nov. 12 | Middle East respiratory syndrome coronavirus isolate Makkah_C9355/KSA/Makkah/2014- |
| AHC74088 | Qatar | 2013 Oct. 13 | 2013 Dec. 23 | 04-15, complete genome Middle East respiratory syndrome coronavirus isolate Qatar3, complete genome |

| 2 | 8 | 9 |
|---|---|---|
| _ | v | / |

TABLE 12-continued

| ccession | Country | Collection Date | Release Date | Virus Name |
|-----------------|----------------------------|-----------------|--------------|--|
| AHC74098 | Qatar | 2013 Oct. 17 | 2013 Dec. 23 | Middle East respiratory syndrome coronavirus isolate Qatar4, complete |
| AHI48572 | Saudi Arabia | 2013 Aug. 15 | 2014 Feb. 6 | genome Middle East respiratory syndrome coronavirus isolate |
| GV08379 | Saudi Arabia | 2012 Oct. 23 | 2013 Sep. 17 | Riyadh_14_2013, complete genome Middle East respiratory syndrome coronavirus isolate Riyadh_1_2012, |
| AID55073 | Saudi Arabia | 2014 Apr. 22 | 2014 Nov. 12 | complete genome Middle East respiratory syndrome coronavirus isolate Riyadh_2014KSA_683/KSA/2014, |
| GV08584 | Saudi Arabia | 2012 Oct. 30 | 2013 Sep. 17 | complete genome Middle East respiratory syndrome coronavirus isolate Riyadh_2_2012, |
| GV0839 0 | Saudi Arabia | 2013 Feb. 5 | 2013 Sep. 17 | complete genome Middle East respiratory syndrome coronavirus isolate Riyadh_3_2013, |
| AHI48605 | Saudi Arabia | 2013 Mar. 1 | 2014 Feb. 6 | complete genome Middle East respiratory syndrome coronavirus isolate Riyadh_4_2013, |
| AHI48583 | Saudi Arabia | 2013 Jul. 2 | 2014 Feb. 6 | complete genome Middle East respiratory syndrome coronavirus isolate Riyadh_5_2013, |
| AHI48528 | Saudi Arabia | 2013 Jul. 17 | 2014 Feb. 6 | complete genome Middle East respiratory syndrome coronavirus isolate Riyadh_9_2013, |
| AHI48594 | Saudi Arabia | 2013 Jun. 12 | 2014 Feb. 6 | complete genome Middle East respiratory syndrome coronavirus isolate Taif_1_2013, |
| AHI48550 | Saudi Arabia | 2013 Jun. 12 | 2014 Feb. 6 | complete genome Middle East respiratory syndrome coronavirus isolate Wadi-Ad- |
| AI¥60558 | United Arab Emirates | 2014 Mar. 7 | 2014 Dec. 6 | Dawasir_1_2013, complete genome Middle East respiratory syndrome coronavirus strain Abu Dhabi/Gayathi_UAE_2_2014, |
| AIY60538 | United Arab Emirates | 2014 Apr. 10 | 2014 Dec. 6 | complete genome Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_16_2014, complete genome |
| AIY60528 | United Arab Emirates | 2014 Apr. 10 | 2014 Dec. 6 | Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_18_2014, complete |
| AI¥60588 | United Arab Emirates | 2014 Apr. 13 | 2014 Dec. 6 | genome Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_26_2014, complete |
| AIY60548 | United Arab Emirates | 2014 Apr. 19 | 2014 Dec. 6 | genome Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_30_2014, complete |
| AFY60568 | United Arab Emirates | 2014 Apr. 17 | 2014 Dec. 6 | genome Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_33_2014, complete |
| AI¥60518 | United Arab Emirates | 2014 Apr. 7 | 2014 Dec. 6 | genome Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_8_2014, complete |
| AIY60578 | United Arab Emirates | 2013 Nov. 15 | 2014 Dec. 6 | genome Middle East respiratory syndrome coronavirus strain Abu Dhabi_UAE_9_2013, complete |
| KJ80137 | China | 2015 May 27 | 2015 Jun. 5 | genome Middle East respiratory syndrome coronavirus strain ChinaGD01, |
| AHZ64057 | USA | 2014 May 10 | 2014 May 14 | complete genome Middle East respiratory syndrome coronavirus strain Florida/USA- 2_Saudi Arabia_2014, complete |
| KM76229 | Oman | 2013 Oct. 28 | 2015 Jun. 23 | genome Middle East respiratory syndrome coronavirus strain |

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|---|---|---|
| - | - | |

TABLE 12-continued

| GenBank Accession | Country | Collection Date | Release Date | Virus Name |
|----------------------|----------------------------|-----------------|--------------|--|
| AKM76239 | Oman | 2013 Dec. 28 | 2015 Jun. 23 | Hu/Oman_2285_2013, complete genome Middle East respiratory syndrome coronavirus strain Hu/Oman_2874_2013, complete |
| AKI29284 | Saudi Arabia | 2015 Jan. 6 | 2015 May 27 | genome Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA- 2049/2015, complete genome |
| AKI29265 | Saudi Arabia | 2015 Jan. 21 | 2015 May 27 | Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA- 2343/2015, complete genome |
| AKI29255 | Saudi Arabia | 2015 Jan. 21 | 2015 May 27 | Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA- 2345/2015, complete genome |
| AKI29275 | Saudi Arabia | 2015 Jan. 26 | 2015 May 27 | Middle East respiratory syndrome coronavirus strain Hu/Riyadh-KSA- 2466/2015, complete genome |
| AKK52582 | Saudi Arabia | 2015 Feb. 10 | 2015 Jun. 8 | Middle East respiratory syndrome coronavirus strain Hu/Riyadh_KSA_2959_2015, complete genome |
| AKK52592 | Saudi Arabia | 2015 Mar. 1 | 2015 Jun. 8 | Middle East respiratory syndrome coronavirus strain Hu/Riyadh_KSA_4050_2015, complete genome |
| AHZ58501 | USA | 2014 Apr. 30 | 2014 May 13 | Middle East respiratory syndrome coronavirus strain Indiana/USA- 1_Saudi Arabia_2014, complete genome |
| AGN52936 | United Arab Emirates | 2013 | 2013 Jun. 10 | Middle East respiratory syndrome coronavirus, complete genome |

| TABLE | 12 |
|-------|----|
| IADUG | 13 |

| - | MeV Nucleic Acid Sequences | |
|-------------------|---|---------------|
| Description | Sequence | SEQ II NO: |
| GC_F_MEASLES_B3.1 | TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT | 35 |
| Sequence, NT (5' | CACTATAGGGAAATAAGAGAGAAAAGAAGAGTAAGAA | |
| UTR, ORF, 3' | GAAATATAAGAGCCACCATGGGTCTCAAGGTGAACGTC | |
| UTR) | TCTGCCGTATTCATGGCAGTACTGTTAACTCTCCAAACA | |
| Sequence Length: | CCCGCCGGTCAAATTCATTGGGGCAATCTCTCTAAGAT | |
| 1864 | AGGGGTAGTAGGAATAGGAAGTGCAAGCTACAAAGTT | |
| | ATGACTCGTTCCAGCCATCAATCATTAGTCATAAAATT | |
| | AATGCCCAATATAACTCTCCTCAATAACTGCACGAGGG | |
| | TAGAGATTGCAGAATACAGGAGACTACTAAGAACAGTT | |
| | TTGGAACCAATTAGGGATGCACTTAATGCAATGACCCA | |
| | GAACATAAGGCCGGTTCAGAGCGTAGCTTCAAGTAGGA | |
| | GACACAAGAGATTTGCGGGAGTAGTCCTGGCAGGTGCG | |
| | GCCCTAGGTGTTGCCACAGCTGCTCAGATAACAGCCGG | |
| | CATTGCACTTCACCGGTCCATGCTGAACTCTCAGGCCAT | |
| | CGACAATCTGAGAGCGAGCCTGGAAACTACTAATCAGG | |
| | CAATTGAGGCAATCAGACAAGCAGGGCAGGAGATGAT | |
| | ATTGGCTGTTCAGGGTGTCCAAGACTACATCAATAATG | |
| | AGCTGATACCGTCTATGAACCAGCTATCTTGTGATCTA | |
| | ATCGGTCAGAAGCTCGGGCTCAAATTGCTTAGATACTA | |
| | TACAGAAATCCTGTCATTATTTGGCCCCAGCCTACGGG | |
| | ACCCCATATCTGCGGAGATATCTATCCAGGCTTTGAGTT | |
| | ATGCACTTGGAGGAGATATCAATAAGGTGTTAGAAAAG | |
| | CTCGGATACAGTGGAGGCGATTTACTAGGCATCTTAGA | |
| | GAGCAGAGGAATAAAGGCTCGGATAACTCACGTCGAC | |
| | ACAGAGTCCTACTTCATAGTCCTCAGTATAGCCTATCCG | |
| | ACGCTGTCCGAGATTAAGGGGGGTGATTGTCCACCGGCT | |
| | AGAGGGGGTCTCGTACAACATAGGCTCTCAAGAGTGGT | |
| | ATACCACTGTGCCCAAGTATGTTGCAACCCAAGGGTAC | |
| | CTTATCTCGAATTTTGATGAGTCATCATGTACTTTCATG | |
| | CCAGAGGGGGACTGTGTGCAGCCAAAATGCCTTGTACCC | |
| | GATGAGTCCTCTGCTCCAAGAATGCCTCCGGGGGTCCA | |

TABLE 13-continued

| SEQ ID | | | |
|---------------------------------------|---|-----|--|
| Description | Sequence | NO: | |
| | CCAAGTCCTGTGCTCGTACACTCGTATCCGGGTCTTTTG GGAACCGGTTCATTTTATCACAAGGGAACCTAATAGCC AATTGTGCATCAATTCTTTGTAAGGGTACCAAACAGGT ACGATTATTAATCAAGACCCTGACAAGATCCAACACGG GCGTGGCGACCATCCAAGTCGGCGCGGGGGGGGGG | | |
| GC_F_MEASLES_B3.1 ORF Sequence, NT | ACCCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGC ATGGGTCTCAAGGTGAACGTCTCTGCCGTATTCATGGC AGTACTGTTAACTCTCCAAAGACACCCGCCGGTCAAATTC ATTGGGGCAATCTCTCTAAGATAAGGGTAGTAGGAATA GAAGTCAACAAGTCTGCAGAGGTAGTAGGAATA GGAAGTACTACAAAGTTATGAACCGTTCCAGCCA TCAATCATTAGTCACAAAGTTATGAACCCAATAAACTCT CCTCAATAACTGCACGAGGGTAGAAGATTGCGAGAATAAC GGAGCTACTAAGAACAGTTTGGGAACCAATAAGGCCGGGTCA GAGCGTAGCTCCAGGCAGGGCACAAGAGATTGCG GGAGTAGTCCTGGCAGGTGCGGCCCTAGGTGTTGCCAC AGCTGCTCAGATAACAGCCGGCATTGCACTTCACCGGT CCATGCTGAACTACTAACAGCCGGCATTGCACTTCACCGGT CCATGCTGAACTACTAACAGCCGGCATTGCACTTCACGGGT GCCGGAAACTACTAATCAGGCAATGAGGCAATCG GCCCGGAACTACTAATCAGGCAATTGAGGCAATCG GCCCAGGCAAGCTACTAATCAGGCCATCAGAACCGG CCCAAGCTACTAATAATGAGCTGATACCGTCTATG AACCAGCTACTACTAATCAGGCCACAAATCGGAGGA TTCCAAATTGCTTAGGATCTAATCGGTCAGAAGCTGG GCTCAAATTGCTAGGTATATTGGCTCTGGCGACA TATCTATCCAGGCTTTGAGTTATGCACTGGGAGG GCTCGGATACTCACGTCTAGGACCCCATATCGGGGAGA TATCTATCCAGGCTTTGAGTTATGCACTGGGAGG GCTCGGATAACTCACGTCGACACAGGTCCTACTT ATTGGCCCCAGCTTCGAGACCCGATACGGTGG GCTCGGATAACTCACGTCGACACAGGTCCTACTTCAT AGGGGTGATTGTCCACGGGCTAGCTGGAC GCTCGGATAACTCACGTCGACACAGGTCCTACTTCAT AGGGGTGATTGTCCACGGGCTACGTGCTGGTC AACATAGGCTCTCAAGAGGGCCTACTTCAT AGGGGTGATTGTCCACGGGCACAGGGCCTCGTGC AACATAGGCTCCCAAGGGGCCCCACTACTTGA GTATGTTGCAACCTAGGCCAAGGGCCTCGTGC CAAGAATGCCTCCAGAGGGGCCCCCAATTTG ACACACGAGACCTAATTCCCGACGAGGGCCTGGTC CAAGAATGCCTCGGGGGTCCCCCAAGTCCTGGCCCA GTATGTTGCAACCTAATGCCAAGGGCCCTGGTC CAAGAATGCCTCGGGGGTCCCCCAAGTCCTGGCCGA GTCGGGAGCAAAATGCCTTATTCGCGAGGGCCTGGTC CCGGGAGCAGAGGCTACCTACTTGGCAACCAGGGCCTGGCTG CTGCGGAGCAGGAGCAACCCAATGGCCTGGCC | 36 | |
| mRNA Sequence | G*GGGAAATAAGAGAGAAAAGAAGAGGTAAGAAGAAT ATAAGAGCCACCATGGGTCTCAAGGTGAACGTCTCTGC CGTATTCATGGGCAGTACTGTTAACTCTCCAAACACCCG CCGGTCAAATCATTGGGCCAATCTCTCTAAGATAGGG GTAGTAGGAATAGGAAGTGCAAGCTACAAAGTTATGA CTCGTTCCAGCCATCAATCATTAGTCATAAAATTAATGC CCAATATAACTCTCCTCAATAACTGCACGAGGGTAGAG ATTGCAGAATACAGGAGACTACTAAAGAACAGTTTTGGA ACCAATTAGGGAGTGCACTTAATGCACCAGAACA TAAGGCCGGTTCAGAGCGTAGCTTCAAGTAGGAGACAC AAGAGATTGCGGGAGTAGTCCTGGCAGGTCGGCCCT | 37 | |

TABLE 13-continued

| | | SEQ ID |
|--|---|--------|
| escription | Sequence | NO: |
| Jescription | AGGTGTTGCCACAGCTGCTCAGATAACAGCCGGCATTG CACTTCACCGGTCCATGCTGAACTCTCAGGCCATCGAC AATCTGAGAGCGAGCCTGGAACTACTAATAATGAGCA TGAGGCAATCAGACAAGCAGGCAGGAGAGAGATGATATTG GCTGTTCAGGGTGTCCAAGACTACATCAATAATGAGCT GATACCGTCATGAACCAGCTATCTTGGATCTAATG GTCAGAAGCTCGGGCTCAAATTGCTTAGATACTATACA GAAATCCTGTCATTATTTGGCCCCAGCCTACGGGACCC CATATCTGCGGAGATATCATCACGGCTTGGAGTTATGC ACTTGGAGGAGATACTATCCAGGCTTTGAGATATGC ACTTGGAGGAGATCAATAAGGTGTTAGAAAAGCCG GATACAGTGGAGCGATTACTAGGGCATCTTAGAGAGC AGAGGAATAAAGGCTCGGATAACTCACGGCGACAGG AGTCCTACTTCATAGGGGGTGATACCCACGGCTAGAG GGGGTCTGTACAACATAGGCTCTCAAGAGTGGTATAC CACTGCGCCAAGATAGGCTCTCAAGAGTGGTATAC CACTGCCCAAGATAGGCCCCCAGAGAGGGTGCACCAA GGGGGTCGTCGTACAACATAGGCCTCTCAAGAGTGGTATAC CACTGCCCAAGATATGCCACCGGGGTCCCCCAG AGGCGACTGTGCGACAACATGGCCTTGAAGTGGTCACCGAG GGGTCCTGTCGTACAACATGGCCTTCGGGGGTCCACCAA GTCCTGTGCTCGAAGAATGCCTTCGGGGGTCCACCAA GTCCTGTGCTCGAAGAATGCCTTGCGGGGTCCACCAA GTCCTGTGCTCGAAGAATGCCTTGCGGGGTCCACCAA GTCCTGTGCTCGTACACGGAAGCCTAATAGCCACTA GTGCACAATTCTTTGTAAGTGTTACCCAACAGGTAG ATTATAATCAAGACCCTGGAAGTGCACACAATG GTGCACCAAGTCGGGGCCACAAATGCCTACCGGAGCGC GTGTACTTGGCGCGGAGCAGGAGGAGTATCCGGGACGC GTGTACTCGCACGAAGATGCCTACGGGATGCCACAAT TGCGCGAATGGCTGCGGGGCCCCCCCATATCA TTGCGCGAATGGCGCGGGAGCAGAGGAGTATCCAGACGCC GTGTACTGCCCAGGAATTGGACGGCGTGTGTGCGAG CAATTGCCAAATTGGAGGACCCAACGAAATCCGGGATGCC CAAGGGCCTGGAGCTAGGGACCCACTTTCGGGAATG CAATGCCAAGCATGGCTCCCCCCCTTTCGCGAGGTGACGCC GCGGGCCTGGACGACAAACTCGGGCCTTCTGCGGAAGG CAATGCCAAGCAAGGATCCCACGACAAGTTGG CAATGCCAAATCCTAGGAACCCCACCTTTCCAGAGAA CATCAAAACCCAGGCCTAAAGGCCGACAAATTGGGGAACAGTGG TATCTACAGACCAGGCCTAAAGGCTGACGACAAGTTGG CACGAGCCTGGTGACACAAAAGGCAGAACTTACAGGAAA CATCAAAACCCATGGCACAAACGCCTGCCCCCCCCTTGCGGCCCCCCCC | NG : |
| C_F_MEASLES_D8 Sequence, NT (5' JTR, ORF, 3' JTR) Sequence Length: .864 | CCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGCAAAAA | 38 |

TABLE 13-continued

| | | SEQ ID |
|---------------------|---|--------|
| Description | Sequence | NO : |
| | | |
| | ACATTGCTGCCGATCACTGCCCGGTGGTCGAGGTGAAT GGCGTGACCATCCAAGTCGGGAGCAGGAGGTATCCGG | |
| | ACGCTGTGTACTTGCACAGGATTGACCTCGGTCCTCCC | |
| | ATATCTTTCGAGAGGTTGGACGTAGGGACAAATCTGGG | |
| | GAATGCAATTGCTAAGTTGGAGGATGCCAAGGAATTGT | |
| | TGGAGTCATCGGACCAGATATTGAGGAGTATGAAAGGT | |
| | TTATCGAGCACTAGTATAGTTTACATCCTGATTGCAGTG | |
| | TGTCTTGGAGGATTGATAGGGATCCCCGCTTTAATATGT | |
| | TGCTGCAGGGGGCGTTGTAACAAGAAGGGAGAACAAG | |
| | | |
| | GGAACATCAAAATCCTATGTAAGGTCACTCTGATGATA ATAGGCTGGAGCCTCGGTGGCCAAGCTTCTTGCCCCTT | |
| | GGGCCTCCCCCAGCCCCTCCTCCCCCTTCCTGCACCCGT | |
| | ACCCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGC | |
| C F MEASLES D8 | ATGGGTCTCAAGGTGAACGTCTCTGTCATATTCATGGC | 39 |
| RF Sequence, NT | AGTACTGTTAACTCTTCAAACACCCCACCGGTCAAATCC | |
| , | ATTEGGGCAATCTCTCTAAGATAGGGGTGGTAGGGGTA | |
| | GGAAGTGCAAGCTACAAAGTTATGACTCGTTCCAGCCA | |
| | TCAATCATTAGTCATAAAGTTAATGCCCAATATAACTCT | |
| | CCTCAACAATTGCACGAGGGTAGGGATTGCAGAATACA | |
| | GGAGACTACTGAGAACAGTTCTGGAACCAATTAGAGAT | |
| | GCACTTAATGCAATGACCCAGAATATAAGACCGGTTCA | |
| | GAGTGTAGCTTCAAGTAGGAGACACAAGAGATTTGCGG | |
| | GAGTTGTCCTGGCAGGTGCGGCCCTAGGCGTTGCCACA GCTGCTCAAATAACAGCCGGTATTGCACTTCACCAGTC | |
| | CATGCTGAACTCTCAAGCCATCGACAATCTGAGAGCGA | |
| | GCCTAGAAACTACTAATCAGGCAATTGAGGCAATCAGA | |
| | CAAGCAGGGCAGGAGATGATATTGGCTGTTCAGGGTGT | |
| | CCAAGACTACATCAATAATGAGCTGATACCGTCTATGA | |
| | ATCAACTATCTTGTGATTTAATCGGCCAGAAGCTAGGG | |
| | CTCAAATTGCTCAGATACTATACAGAAATCCTGTCATT | |
| | ATTTGGCCCCAGCTTACGGGACCCCATATCTGCGGAGA | |
| | TATCTATCCAGGCTTTGAGCTATGCGCTTGGAGGAGAA ATCAATAAGGTGTTGGAAAAGCTCGGATACAGTGGAG | |
| | GTGATCTACTGGGCATCTTAGAGAGCAGAGGAATAAAG | |
| | GCCCGGATAACTCACGTCGACACAGAGTCCTACTTCAT | |
| | TGTACTCAGTATAGCCTATCCGACGCTATCCGAGATTA | |
| | AGGGGGTGATTGTCCACCGGCTAGAGGGGGTCTCGTAC | |
| | AACATAGGCTCTCAAGAGTGGTATACCACTGTGCCCAA | |
| | GTATGTTGCAACCCAAGGGTACCTTATCTCGAATTTTGA | |
| | TGAGTCATCATGCACTTTCATGCCAGAGGGGACTGTGT | |
| | GCAGCCAGAATGCCTTGTACCCGATGAGTCCTCTGCTC | |
| | | |
| | TACACTCGTATCCGGGTCTTTCGGGAACCGGTTCATTTT ATCACAGGGGAACCTAATAGCCAATTGTGCATCAATCC | |
| | TTTGCAAGTGTTACACAACAGGAACAATCATTAATCAA | |
| | GACCCTGACAAGATCCTAACATACATTGCTGCCGATCA | |
| | CTGCCCGGTGGTCGAGGTGAATGGCGTGACCATCCAAG | |
| | TCGGGAGCAGGAGGTATCCGGACGCTGTGTACTTGCAC | |
| | AGGATTGACCTCGGTCCTCCCATATCTTTGGAGAGGTT | |
| | GGACGTAGGGACAAATCTGGGGGAATGCAATTGCTAAGT | |
| | TGGAGGATGCCAAGGAATTGTTGGAGTCATCGGACCAG | |
| | ATATTGAGGAGTATGAAAGGTTTATCGAGCACTAGTAT | |
| | AGTTTACATCCTGATTGCAGTGTGTCTTGGAGGATTGAT AGGGATCCCCGCTTTAATATGTTGCTGCAGGGGGGGCGTT | |
| | GTAACAAGAAGGGAGAACAAGTTGGTATGTCAAGACC | |
| | AGGCCTAAAGCCTGATCTTACAGGAACATCAAAATCCT | |
| | ATGTAAGGTCACTCTGA | |
| GC F MEASLES D8 | G*GCGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT | 40 |
| NRNA Sequence | ATAAGAGCCACCATGGGTCTCAAGGTGAACGTCTCTGT | |
| (assumes T100 tail) | CATATTCATGGCAGTACTGTTAACTCTTCAAACACCCAC | |
| Sequence Length: | CGGTCAAATCCATTGGGGGCAATCTCTCTAAGATAGGGG | |
| 1925 | TGGTAGGGGTAGGAAGTGCAAGCTACAAAGTTATGACT | |
| | CGTTCCAGCCATCAATCATTAGTCATAAAGTTAATGCC | |
| | | |
| | TTGCAGAATACAGGAGACTACTGAGAACAGTTCTGGAA CCAATTAGAGATGCACTTAATGCAATGACCCAGAATAT | |
| | AAGACCGGTTCAGAGTGTAGCTTCAAGTAGGAGAGACACA | |
| | AGAGATTTGCGGGGAGTTGTCCTGGCAGGTGCGGCCCTA | |
| | GGCGTTGCCACAGCTGCTCAAATAACAGCCGGTATTGC | |
| | ACTTCACCAGTCCATGCTGAACTCTCAAGCCATCGACA | |

ACTTCACCAGTCCATGCTGAACTCTCAAGCCATCGACA ATCTGAGAGCGAGCCTAGAAACTACTAATCAGGCAATT

TABLE 13-continued

| escription | Sequence | SEQ ID NO: |
|--------------------|--|---------------|
| | GAGGCAATCAGACAAGCAGGGCAGGAGATGATATTGG | |
| | CTGTTCAGGGTGTCCAAGACTACATCAATAATGAGCTG | |
| | ATACCGTCTATGAATCAACTATCTTGTGATTTAATCGGC | |
| | CAGAAGCTAGGGCTCAAATTGCTCAGATACTATACAGA | |
| | AATCCTGTCATTATTTGGCCCCAGCTTACGGGACCCCAT ATCTGCGGAGATATCTATCCAGGCTTTGAGCTATGCGC | |
| | TTGGAGGAGATATCAATAAGGTGTTGGAAAAGCTCGGA | |
| | TACAGTGGAGGTGATCTACTGGGCATCTTAGAGAGCAG | |
| | AGGAATAAAGGCCCGGATAACTCACGTCGACACAGAG | |
| | TCCTACTTCATTGTACTCAGTATAGCCTATCCGACGCTA TCCGAGATTAAGGGGGTGATTGTCCACCGGCTAGAGGG | |
| | GGTCTCGTACAACATAGGCTCTCAAGAGTGGTATACCA | |
| | CTGTGCCCAAGTATGTTGCAACCCAAGGGTACCTTATC | |
| | TCGAATTTTGATGAGTCATCATGCACTTTCATGCCAGAG | |
| | GGGACTGTGTGCAGCCAGAATGCCTTGTACCCGATGAG | |
| | TCCTCTGCTCCAAGAATGCCTCCGGGGGTCCACTAAGT CCTGTGCTCGTACACTCGTATCCGGGTCTTTCGGGAACC | |
| | GGTTCATTTTATCACAGGGGAACCTAATAGCCAATTGT | |
| | GCATCAATCCTTTGCAAGTGTTACACAACAGGAACAAT | |
| | CATTAATCAAGACCCTGACAAGATCCTAACATACATTG | |
| | CTGCCGATCACTGCCCGGTGGTCGAGGTGAATGGCGTG ACCATCCAAGTCGGGAGCAGGAGGTATCCGGACGCTGT | |
| | GTACTTGCACAGGATTGACCTCGGTCCTCCCATATCTTT | |
| | GGAGAGGTTGGACGTAGGGACAAATCTGGGGAATGCA | |
| | ATTGCTAAGTTGGAGGATGCCAAGGAATTGTTGGAGTC | |
| | ATCGGACCAGATATTGAGGAGTATGAAAGGTTTATCGA | |
| | GCACTAGTATAGTTTACATCCTGATTGCAGTGTGTCTTG GAGGATTGATAGGGATCCCCGCTTTAATATGTTGCTGC | |
| | AGGGGCGTTGTAACAAGAAGGGAGAACAAGTTGGTA | |
| | TGTCAAGACCAGGCCTAAAGCCTGATCTTACAGGAACA | |
| | TCAAAATCCTATGTAAGGTCACTCTGATGATAATAGGC | |
| | TGGAGCCTCGGTGGCCAAGCTTCTTGCCCCTTGGGCCTC CCCCCAGCCCCTCCTCCCTGCACCCGTACCCCCG | |
| | TGGTCTTTGAATAAAGTCTGAGTGGGCGGCAAAAAAAA | |
| | ААААААААААААААААААААААААААААААААААААА | |
| | | |
| | ААААААААААААААААААТСТАG | |
| H MEASLES B3 | TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT | 41 |
| quence, NT (5' | CACTATAGGGAAATAAGAGAGAAAAGAAGAGTAAGAA | |
| R, ORF, 3' | GAAATATAAGAGCCACCATGTCACCGCAACGAGACCG | |
| R) | GATAAATGCCTTCTACAAAGATAACCCTTATCCCAAGG GAAGTAGGATAGTTATTAACAGAGAACATCTTATGATT | |
| uence Length: 5 | GACAGACCCTATGTTCTGCTGGCTGTCTGTTCGTCGTCATG | |
| 2065 | TTTCTGAGCTTGATCGGATTGCTGGCAATTGCAGGCATT | |
| | AGACTTCATCGGGCAGCCATCTACACCGCGGAGATCCA | |
| | TAAAAGCCTCAGTACCAATCTGGATGTGACTAACTCCA | |
| | TCGAGCATCAGGTCAAGGACGTGCTGACACCACTCTTT AAAATCATCGGGGGATGAAGTGGGCCTGAGAACACCTC | |
| | AGAGATTCACTGAGGGATGAAGTGGGCCTGAGAACACCTC AGAGATTCACTGACCTAGTGAAATTCATCTCGGACAAG | |
| | ATTAAATTCCTTAATCCGGATAGGGAGTACGACTTCAG | |
| | AGATCTCACTTGGTGCATCAACCCGCCAGAGAGGATCA | |
| | | |
| | GAAGAGCTCATGAATGCATTGGTGAACTCAACTCTACT GGAGACCAGAACAACCACTCAGTTCCTAGCTGTCTCAA | |
| | AGGGAAACTGCTCAGGGCCCACTACAATCAGAGGTCA | |
| | ATTCTCAAACATGTCGCTGTCCTTGTTGGACTTGTACTT | |
| | AGGTCGAGGTTACAATGTGTCATCTATAGTCACTATGA | |
| | CATCCCAGGGAATGTATGGGGGGAACCTACCTAGTTGAA AAGCCTAATCTGAACAGCAAAGGGTCAGAGTTGTCACA | |
| | AGCCTAATCTGAACAGCAAAGGGTCAGAGTTGTCACA | |
| | GAAACCCGGGTTTGGGGGGCTCCGGTGTTCCATATGACA | |
| | AACTATTTTGAGCAACCAGTCAGTAATGGTCTCGGCAA | |
| | CTGTATGGTGGCTTTGGGGGGGGGCTCAAACTCGCAGCCC | |
| | TTTGTCACGGGGACGATTCTATCATAATTCCCTATCAGG GATCAGGGAAAGGTGTCAGCTTCCAGCTCGTCAAGCTG | |
| | GATCAGGGAAAGGTGTCAGCTTCCAGCTCGTCAAGCTG | |
| | CCCCTTATCAACGGATGATCCAGTGGTAGACAGGCTTT | |
| | ACCTCTCATCTCACAGAGGTGTCATCGCTGACAATCAA | |
| | GCAAAATGGGCTGTCCCGACAACACGAACAGATGACA | |
| | AGTTGCGAATGGAGACATGCTTCCAGCAGGCGTGTAAA GGTAAAATCCAAGCACTCTGCGAGAATCCCGAGTGGGT | |
| | CONTRACTOR CONSCRETCION CONTRACTOR CONT | |
| | ACCATTGAAGGATAACAGGATTCCTTCATACGGGGTCC | |
| | ACCATTGAAGGATAACAGGATTCCTTCATACGGGGTCC TGTCTGTTGATCTGAGTCTGACGGTTGAGCTTAAAATCA | |

TABLE 13-continued

| Description | Sequence | SEQ ID NO: |
|----------------------------------|--|---------------|
| r | TCAGGGATGGACCTATACAAATCCAACTGCAACAATGT | |
| | GTATTGGCTGACTATTCCGCCAATGAGAAATCTAGCCT | |
| | TAGGCGTAATCAACACATTGGAGTGGATACCGAGATTC | |
| | AAGGTTAGTCCCAACCTCTTCACTGTCCCAATTAAGGA | |
| | AGCAGGCGAAGACTGCCATGCCCCAACATACCTACCTG CGGAGGTGGACGGTGATGTCAAACTCAGTTCCAACCTG | |
| | GTGATTCTACCTGGTCAAGATCTCCAATATGTTTTGGCA | |
| | ACCTACGATACCTCCAGGGTTGAGCATGCTGTGGTTTA | |
| | TTACGTTTACAGCCCAAGCCGCTCATTTTCTTACTTTA TCCTTTTACAGCCCCAAGCCGCTCATTTTCTTACTTTA | |
| | TCCTTTTAGGTTGCCTATAAAGGGGGGTCCCAATCGAAC TACAAGTGGAATGCTTCACATGGGATCAAAAACTCTGG | |
| | TGCCGTCACTTCTGTGTGCTTGCGGACTCAGAATCCGGT | |
| | GGACTTATCACTCACTCTGGGATGGTGGGCATGGGAGT | |
| | CAGCTGCACAGCTACCCGGGAAGATGGAACCAATCGC AGATAATGATAATAGGCTGGAGCCTCGGTGGCCAAGCT | |
| | TCTTGCCCCTTGGGCCTCCCCCCAGCCCCTCCTCCCCCTT | |
| | CCTGCACCCGTACCCCCGTGGTCTTTGAATAAAGTCTG | |
| | AGTCGGCGGC | |
| GC_H_MEASLES_B3 | ATGTCACCGCAACGAGACCGGATAAATGCCTTCTACAA | 42 |
| ORF Sequence, NT | AGATAACCCTTATCCCAAGGGAAGTAGGATAGTTATTA | |
| | ACAGAGAACATCTTATGATTGACAGACCCTATGTTCTG CTGGCTGTTCTGTT | |
| | TTGCTGGCAATTGCAGGCATTAGACTTCATCGGGCAGC | |
| | CATCTACACCGCGGAGATCCATAAAAGCCTCAGTACCA | |
| | ATCTGGATGTGACTAACTCCATCGAGCATCAGGTCAAG GACGTGCTGACACCACTCTTTAAAATCATCGGGGATGA | |
| | AGTGGGCCTGAGAACACCACTCAGAGATTCACCGGGGATGA | |
| | TGAAATTCATCTCGGACAAGATTAAATTCCTTAATCCG | |
| | GATAGGGAGTACGACTTCAGAGATCTCACTTGGTGCAT | |
| | CAACCCGCCAGAGAGGATCAAACTAGATTATGATCAAT ACTGTGCAGATGTGGCTGCTGAAGAGCTCATGAATGCA | |
| | TTGGTGAACTCAACTCTACTGGAGACCAGAACAACCAC | |
| | TCAGTTCCTAGCTGTCTCAAAGGGAAACTGCTCAGGGC | |
| | CCACTACAATCAGAGGTCAATTCTCAAACATGTCGCTG | |
| | TCCTTGTTGGACTTGTACTTAGGTCGAGGTTACAATGTG TCATCTATAGTCACTATGACATCCCAGGGAATGTATGG | |
| | GGGAACCTACCTAGTTGAAAAGCCTAATCTGAACAGCA | |
| | AAGGGTCAGAGTTGTCACAACTGAGCATGTACCGAGTG | |
| | TTTGAAGTAGGTGTGATCAGAAACCCGGGTTTGGGGGC TCCGGTGTTCCATATGACAAACTATTTTGAGCAACCAG | |
| | TCAGTAATGGTCTCCGGCAACTGTATGGTGGCTTTGGGG | |
| | GAGCTCAAACTCGCAGCCCTTTGTCACGGGGACGATTC | |
| | TATCATAATTCCCTATCAGGGATCAGGGAAAGGTGTCA | |
| | GCTTCCAGCTCGTCAAGCTGGGTGTCTGGAAATCCCCA ACCGACATGCAATCCTGGGTCCCCTTATCAACGGATGA | |
| | TCCAGTGGTAGACAGGCTTTACCTCTCATCTCACAGAG | |
| | GTGTCATCGCTGACAATCAAGCAAAATGGGCTGTCCCG | |
| | ACAACACGAACAGATGACAAGTTGCGAATGGAGACAT | |
| | GCTTCCAGCAGGCGTGTAAAAGGTAAAATCCAAGCACTC TGCGAGAATCCCCGAGTGGGTACCATTGAAGGATAACAG | |
| | GATTCCTTCATACGGGGTCCTGTCTGTTGATCTGAGTCT | |
| | GACGGTTGAGCTTAAAATCAAAATTGCTTCGGGATTCG | |
| | GGCCATTGATCACACACGGCTCAGGGATGGACCTATAC AAATCCAACTGCAACAATGTGTATTGGCTGACTATTCC | |
| | GCCAATGAGAAAATCTAGCCTTAGGCGTAATCAACACAT | |
| | TGGAGTGGATACCGAGATTCAAGGTTAGTCCCAACCTC | |
| | TTCACTGTCCCAATTAAGGAAGCAGGCGAAGACTGCCA | |
| | TGCCCCAACATACCTACCTGCGGAGGTGGACGGTGATG TCAAACTCAGTTCCAACCTGGTGATTCTACCTGGTCAA | |
| | GATCTCCAATATGTTTTGGCAACCTACGATACCTCCAG | |
| | GGTTGAGCATGCTGTGGTTTATTACGTTTACAGCCCAA | |
| | GCCGCTCATTTTCTTACTTTTATCCTTTTAGGTTGCCTAT | |
| | AAAGGGGGTCCCAATCGAACTACAAGTGGAATGCTTCA CATGGGATCAAAAACTCTGGTGCCGTCACTTCTGTGTG | |
| | CTTGCGGACTCAGAATCCGGTGGACTTATCACTCACTCT | |
| | GGGATGGTGGGCATGGGAGTCAGCTGCACAGCTACCCG GGAAGATGGAACCAATCGCAGATAA | |
| | | |
| GC_H_MEASLES_B3 mRNA Sequence | G*GGGAAATAAGAGAGAAAAGAGAGAGAAGAAGAAAAT ATAAGAGCCACCATGTCACCGCAACGAGACCGGATAA | 43 |
| • | ATGCCTTCTACAAAGATAACCCTTATCCCAAGGGAAGT | |
| Sequence Length: | AGGATAGTTATTAACAGAGAACATCTTATGATTGACAG | |
| 126 | ACCCTATGTTCTGCTGGCTGTTCTGTTCGTCATGTTTCT | |
| | GAGCTTGATCGGATTGCTGGCAATTGCAGGCATTAGAC | |

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TABLE 13-continued

| MeV Nucleic Acid Sequences | | |
|----------------------------|---|---------------|
| Description | Sequence | SEQ II NO: |
| | TTCATCGGGCAGCCATCTACACCGCGGAGATCCATAAA | |
| | AGCCTCAGTACCAATCTGGATGTGACTAACTCCATCGA | |
| | GCATCAGGTCAAGGACGTGCTGACACCACTCTTTAAAA TCATCGGGGATGAAGTGGGCCTGAGAACACCTCAGAG | |
| | ATTCACTGACCTAGTGAAATTCATCTCGGACAAGATTA | |
| | AATTCCTTAATCCGGATAGGGAGTACGACTTCAGAGAT | |
| | CTCACTTGGTGCATCAACCCGCCAGAGAGGATCAAACT AGATTATGATCAATACTGTGCAGATGTGGCTGCTGAAG | |
| | AGATTATGATGAATACTGIGCAGATGIGGCIGCIGAAG | |
| | ACCAGAACAACCACTCAGTTCCTAGCTGTCTCAAAGGG | |
| | AAACTGCTCAGGGCCCACTACAATCAGAGGTCAATTCT | |
| | CAAACATGTCGCTGTCCTTGTTGGACTTGTACTTAGGTC GAGGTTACAATGTGTCATCTATAGTCACTATGACATCC | |
| | CAGGGAATGTATGGGGGGAACCTACCTAGTTGAAAAGCC | |
| | TAATCTGAACAGCAAAGGGTCAGAGTTGTCACAACTGA | |
| | GCATGTACCGAGTGTTTGAAGTAGGTGTGATCAGAAAC | |
| | CCGGGTTTGGGGGGCTCCGGTGTTCCATATGACAAACTA TTTTGAGCAACCAGTCAGTAATGGTCTCGGCAACTGTA | |
| | TGGTGGCTTTGGGGGGGGGGGGGGGGGGGGGGGGGGGCCCTTTGT | |
| | CACGGGGACGATTCTATCATAATTCCCTATCAGGGATC | |
| | AGGGAAAGGTGTCAGCTTCCAGCTCGTCAAGCTGGGTG | |
| | TCTGGAAATCCCCAACCGACATGCAATCCTGGGTCCCC TTATCAACGGATGATCCAGTGGTAGACAGGCTTTACCT | |
| | CTCATCTCACAGAGGTGTCATCGCTGACAGGCTTTACCT | |
| | AATGGGCTGTCCCGACAACACGAACAGATGACAAGTTG | |
| | CGAATGGAGACATGCTTCCAGCAGGCGTGTAAAGGTAA | |
| | AATCCAAGCACTCTGCGAGAATCCCGAGTGGGTACCAT TGAAGGATAACAGGATTCCTTCATACGGGGTCCTGTCT | |
| | GTTGATCTGAGTCTGACGGTTGAGCTTAAAATCAAAAT | |
| | TGCTTCGGGATTCGGGCCATTGATCACACGCGCTCAG | |
| | GGATGGACCTATACAAATCCAACTGCAACAATGTGTAT | |
| | TGGCTGACTATTCCGCCAATGAGAAATCTAGCCTTAGG CGTAATCAACACATTGGAGTGGATACCGAGATTCAAGG | |
| | TTAGTCCCAACCTCTTCACTGTCCCAATTAAGGAAGCA | |
| | GGCGAAGACTGCCATGCCCCAACATACCTACCTGCGGA | |
| | GGTGGACGGTGATGTCAAACTCAGTTCCAACCTGGTGA | |
| | TTCTACCTGGTCAAGATCTCCAATATGTTTTGGCAACCT ACGATACCTCCAGGGTTGAGCATGCTGTGGTTTATTAC | |
| | GTTTACAGCCCAAGCCGCTCATTTTCTTACTTTATCCT | |
| | TTTAGGTTGCCTATAAAGGGGGTCCCAATCGAACTACA | |
| | AGTGGAATGCTTCACATGGGATCAAAAACTCTGGTGCC | |
| | GTCACTTCTGTGTGCTTGCGGACTCAGAATCCGGTGGA CTTATCACTCACTCTGGGATGGTGGGCATGGGAGTCAG | |
| | CTTATCACTCACTCTGGGATGGTGGGCATGGGAGTCAG | |
| | AATGATAATAGGCTGGAGCCTCGGTGGCCAAGCTTCTT | |
| | GCCCCTTGGGCCTCCCCCAGCCCCTCCTCCCCTG | |
| | CACCCGTACCCCCGTGGTCTTTGAATAAAGTCTGAGTG | |
| | GGCGGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA | |
| | АЛЛООЧИЛЛИЧТООЧИЛЛИТОООТЛИЧТООЧИЛ АААААААААААААААААААААААААААААААААААА | |
| | TAG | |
| C H MEASLES D8 | TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT | 44 |
| equence, NT (5' | CACTATAGGGAAATAAGAGAGAAAAGAGAGAGAAGAA | |
| R, ORF, 3' | GAAATATAAGAGCCACCATGTCACCACAACGAGACCG | |
| IR) | GATAAATGCCTTCTACAAAGACAACCCCCCATCCTAAGG GAAGTAGGATAGTTATTAACAGAGAACATCTTATGATT | |
| equence Length: 065 | GAAGTAGGATAGTTATTAACAGAGAACATCTTATGATT GATAGACCTTATGTTTTGCTGGCTGTTCTATTCGTCATG | |
| | TTTCTGAGCTTGATCGGGTTGCTAGCCATTGCAGGCATT | |
| | AGACTTCATCGGGCAGCCATCTACACCGCAGAGATCCA | |
| | | |
| | TCGAGCATCAGGTTAAGGACGTGCTGACACCACTCTTC AAGATCATCGGTGATGAAGTGGGCTTGAGGACACCTCA | |
| | GAGATTCACTGACCTAGTGAAGTTCATCTCTGACAAGA | |
| | TTAAATTCCTTAATCCGGACAGGGAATACGACTTCAGA | |
| | GATCTCACTTGGTGTATCAACCCGCCAGAGAGAATCAA | |
| | ATTGGATTATGATCAATACTGTGCAGATGTGGCTGCTG AAGAACTCATGAATGCATTGGTGAACTCAACTC | |
| | GAGACCCAGGGCAACCAATGCATGGGGGAACTCAACTCTACTG | |
| | GGGAAACTGCTCAGGGCCCACTACAATCAGAGGCCAAT | |
| | TCTCAAACATGTCGCTGTCCCTGTTGGACTTGTATTTAA | |
| | GTCGAGGTTACAATGTGTCATCTATAGTCACTATGACA | |
| | TCCCAGGGAATGTACGGGGGGAACTTACCTAGTGGAAAA | |
| | GCCTAATCTGAGCAGCAAAGGGTCAGAGTTGTCACAAC | |

TABLE 13-continued

| Description | Sequence | SEQ ID NO: |
|-----------------|---|---------------|
| Jesei peron | ~ | 10. |
| | AATCCGGGTTTGGGGGGCTCCGGTATTCCATATGACAAA CTATCTTGAGCAACCAGTCAGTAATGATTTCAGCAACT | |
| | GCATGGTGGCTTTGGGGGGGGCTCAAGTTCGCAGCCCTC | |
| | TGTCACAGGGAAGATTCTATCACAATTCCCTATCAGGG | |
| | ATCAGGGAAAGGTGTCAGCTTCCAGCTTGTCAAGCTAG | |
| | GTGTCTGGAAATCCCCCAACCGACATGCAATCCTGGGTC CCCCTATCAACGGATGATCCAGTGATAGACAGGCTTTA | |
| | CCTCTCATCTCACAGAGGGCGTTATCGCTGACAATCAAG | |
| | CAAAATGGGCTGTCCCGACAACACGGACAGATGACAA | |
| | GTTGCGAATGGAGACATGCTTCCAGCAGGCGTGTAAGG | |
| | GTAAAATCCAAGCACTTTGCGAGAATCCCGAGTGGACA | |
| | CCATTGAAGGATAACAGGATTCCTTCATACGGGGTCTT GTCTGTTGATCTGAGTCTGACAGTTGAGCTTAAAATCA | |
| | AAATTGTTTCAGGATTCGGGCCATTGATCACACACGGT | |
| | TCAGGGATGGACCTATACAAATCCAACCACAACAATAT | |
| | GTATTGGCTGACTATCCCGCCAATGAAGAACCTGGCCT | |
| | TAGGTGTAATCAACACATTGGAGTGGATACCGAGATTC | |
| | AAGGTTAGTCCCAACCTCTTCACTGTTCCAATTAAGGA AGCAGGCGAGGACTGCCCATGCCCCAACATACCTACCTG | |
| | CGGAGGTGGATGGTGATGTCAAACTCAGTTCCAATCTG | |
| | GTGATTCTACCTGGTCAAGATCTCCAATATGTTCTGGCA | |
| | ACCTACGATACTTCCAGAGTTGAACATGCTGTAGTTTAT | |
| | TACGTTTACAGCCCAAGCCGCTCATTTTCTTACTTTAT | |
| | CCTTTTAGGTTGCCTGTAAGGGGGGTCCCCATTGAATTA CAAGTGGAATGCTTCACATGGGACCAAAAACTCTGGTG | |
| | CCGTCACTTCTGTGTGTGCTTGCGGACTCAGAATCTGGTGG | |
| | ACATATCACTCACTCTGGGATGGTGGGCATGGGAGTCA | |
| | GCTGCACAGCCACTCGGGAAGATGGAACCAGCCGCAG | |
| | ATAGTGATAATAGGCTGGAGCCTCGGTGGCCAAGCTTC | |
| | TTGCCCCTTGGGCCTCCCCCAGCCCCTCCTCCCCTTCC TGCACCCGTACCCCGTGGTCTTTGAATAAAGTCTGAG | |
| | TGGGCGGC | |
| C_H_MEASLES_D8 | ATGTCACCACAACGAGACCGGATAAATGCCTTCTACAA | 45 |
| RF Sequence, NT | AGACAACCCCCATCCTAAGGGAAGTAGGATAGTTATTA | |
| | ACAGAGAACATCTTATGATTGATAGACCTTATGTTTTGC | |
| | TGGCTGTTCTATTCGTCATGTTTCTGAGCTTGATCGGGT TGCTAGCCATTGCAGGCATTAGACTTCATCGGGCAGCC | |
| | ATCTACACCGCAGAGATCCATAAAAGCCTCAGCACCAA | |
| | TCTGGATGTAACTAACTCAATCGAGCATCAGGTTAAGG | |
| | ACGTGCTGACACCACTCTTCAAGATCATCGGTGATGAA | |
| | GTGGGCTTGAGGACACCTCAGAGATTCACTGACCTAGT | |
| | GAAGTTCATCTCTGACAAGATTAAATTCCTTAATCCGG ACAGGGAATACGACTTCAGAGATCTCACTTGGTGTATC | |
| | ACCCCGCCAGAGAGAATCAAATTGGATTATGATCAATA | |
| | CTGTGCAGATGTGGCTGCTGAAGAACTCATGAATGCAT | |
| | TGGTGAACTCAACTCTACTGGAGACCAGGGCAACCAAT | |
| | CAGTTCCTAGCTGTCTCAAAGGGAAACTGCTCAGGGCC | |
| | CACTACAATCAGAGGCCAATTCTCAAACATGTCGCTGT CCCTGTTGGACTTGTATTTAAGTCGAGGTTACAATGTGT | |
| | CATCTATAGTCACTATGACATCCCAGGGAATGTACGGG | |
| | GGAACTTACCTAGTGGAAAAGCCTAATCTGAGCAGCAA | |
| | AGGGTCAGAGTTGTCACAACTGAGCATGCACCGAGTGT | |
| | TTGAAGTAGGTGTTATCAGAAATCCGGGTTTGGGGGGCT | |
| | CCGGTATTCCATATGACAAACTATCTTGAGCAACCAGT CAGTAATGATTTCAGCAACTGCATGGTGGCTTTGGGGGG | |
| | AGCTCAAGTTCGCAGCCCTCTGTCACAGGGAAGATTCT | |
| | ATCACAATTCCCTATCAGGGATCAGGGAAAGGTGTCAG | |
| | CTTCCAGCTTGTCAAGCTAGGTGTCTGGAAATCCCCCAA | |
| | CCGACATGCAATCCTGGGTCCCCCTATCAACGGATGAT | |
| | | |
| | CGTTATCGCTGACAATCAAGCAAAATGGGCTGTCCCGA CAACACGGACAGATGACAAGTTGCGAATGGAGACATG | |
| | CAACACGGACAGATGACAAGTTGCGAATGGAGACATG CTTCCAGCAGGCGTGTAAGGGTAAAATCCAAGCACTTT | |
| | GCGAGAATCCCGAGTGGACACCATTGAAGGATAACAG | |
| | GATTCCTTCATACGGGGTCTTGTCTGTTGATCTGAGTCT | |
| | GACAGTTGAGCTTAAAATCAAAATTGTTTCAGGATTCG | |
| | GGCCATTGATCACACACGGTTCAGGGATGGACCTATAC | |
| | AAATCCAACCACAACAATATGTATTGGCTGACTATCCC | |
| | GCCAATGAAGAACCTGGCCTTAGGTGTAATCAACACAT TGGAGTGGATACCGAGATTCAAGGTTAGTCCCAACCTC | |
| | TTCACTGTTCCAATTAAGGAAGCAGGCGAGGACTGCCA | |
| | TGCCCCAACATACCTACCTGCGGAGGTGGATGGTGATG | |
| | | |
| | TCAAACTCAGTTCCAATCTGGTGATTCTACCTGGTCAAG | |

| Description | Sequence | SEQ ID |
|----------------------------------|--|--------|
| Description | Sequence GTTGAACATGCTGTAGTTTATTACGTTTACAGCCCAAGC CGCTCATTTTCTTACTTTATTACCTTTTAGGTTGCCTGTAA | NO : |
| | GGGGGGTCCCCATTGAATTACAAGTGGAATGCTTCACA | |
| | TGGGACCAAAAACTCTGGTGCCGTCACTTCTGTGTGCCTT GCGGACTCAGAATCTGGTGGACATATCACTCACTCTGG | |
| | GATGGTGGGCATGGGAGTCAGCTGCACAGCCACTCGGG | |
| | AAGATGGAACCAGCCGCAGATAG | |
| GC_H_MEASLES_D8 mRNA Sequence | G*GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT ATAAGAGCCACCATGTCACCACAACGAGACCGGATAA | 46 |
| | ATGCCTTCTACAAAGACAACCCCCATCCTAAGGGAAGT | |
| Sequence Length: 2126 | AGGATAGTTATTAACAGAGAACATCTTATGATTGATAG ACCTTATGTTTGCTGGCTGTTCTATTCGTCATGTTTCTG | |
| | AGCTTGATCGGGTTGCTAGCCATTGCAGGCATTAGACT | |
| | TCATCGGGCAGCCATCTACACCGCAGAGATCCATAAAA GCCTCAGCACCAATCTGGATGTAACTAACTCAATCGAG | |
| | CATCAGGTTAAGGACGTGCTGACACCACTCTTCAAGAT CATCGGTGATGAAGTGGGCTTGAGGACACCTCAGAGAT | |
| | TCACTGACCTAGTGAAGTGGGGCTTGAGGACACCTCAGAGAT | |
| | TTCCTTAATCCGGACAGGGAATACGACTTCAGAGATCT | |
| | CACTTGGTGTATCAACCCGCCAGAGAGAATCAAATTGG ATTATGATCAATACTGTGCAGATGTGGCTGCTGAAGAA | |
| | CTCATGAATGCATTGGTGAACTCAACTCTACTGGAGAC | |
| | CAGGGCAACCAATCAGTTCCTAGCTGTCTCAAAGGGAA | |
| | ACTGCTCAGGGCCCACTACAATCAGAGGCCCAATTCTCA AACATGTCGCTGTCCCTGTTGGACTTGTATTTAAGTCGA | |
| | GGTTACAATGTGTCATCTATAGTCACTATGACATCCCA | |
| | GGGAATGTACGGGGGAACTTACCTAGTGGAAAAGCCT | |
| | AATCTGAGCAGCAAAGGGTCAGAGTTGTCACAACTGAG CATGCACCGAGTGTTTGAAGTAGGTGTTATCAGAAATC | |
| | CGGGTTTGGGGGGCTCCGGTATTCCATATGACAAACTAT | |
| | CTTGAGCAACCAGTCAGTAATGATTTCAGCAACTGCAT | |
| | GGTGGCTTTGGGGGGAGCTCAAGTTCGCAGCCCTCTGTC ACAGGGAAGATTCTATCACAATTCCCTATCAGGGATCA | |
| | GGGAAAGGTGTCAGCTTCCAGCTTGTCAAGCTAGGTGT | |
| | CTGGAAATCCCCAACCGACATGCAATCCTGGGTCCCCC | |
| | TATCAACGGATGATCCAGTGATAGACAGGCTTTACCTC TCATCTCACAGAGGCGTTATCGCTGACAATCAAGCAAA | |
| | ATGGGCTGTCCCGACAACACGGACAGATGACAAGTTGC | |
| | GAATGGAGACATGCTTCCAGCAGGCGTGTAAGGGTAA | |
| | AATCCAAGCACTTTGCGAGAATCCCGAGTGGACACCAT TGAAGGATAACAGGATTCCTTCATACGGGGTCTTGTCT | |
| | GTTGATCTGAGTCTGACAGTTGAGCTTAAAATCAAAAT | |
| | TGTTTCAGGATTCGGGCCATTGATCACACACGGTTCAG | |
| | GGATGGACCTATACAAATCCAACCACAACAATATGTAT TGGCTGACTATCCCGCCAATGAAGAACCTGGCCTTAGG | |
| | TGTAATCAACACATTGGAGTGGATACCGAGATTCAAGG | |
| | TTAGTCCCAACCTCTTCACTGTTCCAATTAAGGAAGCA | |
| | GGCGAGGACTGCCATGCCCCAACATACCTACCTGCGGA GGTGGATGGTGATGTCAAACTCAGTTCCAATCTGGTGA | |
| | TTCTACCTGGTCAAGATCTCCAATATGTTCTGGCAACCT | |
| | ACGATACTTCCAGAGTTGAACATGCTGTAGTTTATTAC GTTTACAGCCCAAGCCGCTCATTTTCTTACTTTATCCT | |
| | TTTAGGTTGCCTGTAAGCCGCTCATTTTCTTACTTTTATCCT | |
| | AGTGGAATGCTTCACATGGGACCAAAAACTCTGGTGCC | |
| | GTCACTTCTGTGTGCGTCGGACTCAGAATCTGGTGGA | |
| | CATATCACTCACTCTGGGATGGTGGGCATGGGAGTCAG CTGCACAGCCACTCGGGAAGATGGAACCAGCCGCAGA | |
| | TAGTGATAATAGGCTGGAGCCTCGGTGGCCAAGCTTCT | |
| | TGCCCCTTGGGCCTCCCCCCAGCCCCTCCTCCCTCCT GCACCCGTACCCCCGTGGTCTTTGAATAAAGTCTGAGT | |
| | GCACCCCGTACCCCCGTGGTCTTTGAATAAAGTCTGAGT GGGCGCCAAAAAAAAAA | |
| | АААААААААААААААААААААААААААААААААААА | |
| | ААААААААААААААААААААААААААААААААААААА | |
| | MeV mRNA Sequences | |

GC_F_MEASLES_B3.1 Sequence, NT (5' UTR, ORF, 3' UTR) Sequence Length: 1864 UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC UCACUAUAGGGAAUAAGAGAGAAAAGAAGAGUAAG AAGAAUAUAAGAGCCACCAUGGUCUCAAGGUGAA CGUUCUGCCGUAUUCAUGGCAUCUGUUAACUCUC CAAACACCCGCCGGUCAAUUCAUUGGGGCAUCUCU CUAAGAUAGGGGUAGUAGAAUAGGAAGUGCAAGCU ACAAAGUUAUGACUCGUUCCAGCCAUCAAUCAUUAGU

TABLE 13-continued

| | MeV Nucleic Acid Sequences | |
|------------------|---|--------------|
| escription | Sequence | SEQ I NO: |
| | CAUAAAAUUAAUGCCCAAUAUAACUCUCCUCAAUAAC | |
| | UGCACGAGGGUAGAGAUUGCAGAAUACAGGAGACUA | |
| | CUAAGAACAGUUUUGGAACCAAUUAGGGAUGCACUU | |
| | AAUGCAAUGACCCAGAACAUAAGGCCGGUUCAGAGCG UAGCUUCAAGUAGGAGACACAAGAGAUUUGCCGGGAG | |
| | UAGUCCUGGCAGGUGCGGCCCUAGGUGUUGCCACAGC | |
| | UGCUCAGAUAACAGCCGGCAUUGCACUUCACCGGUCC | |
| | AUGCUGAACUCUCAGGCCAUCGACAAUCUGAGAGCGA | |
| | GCCUGGAAACUACUAAUCAGGCAAUUGAGGCAAUCAG ACAAGCAGGGCAGG | |
| | UGUCCAAGACUACAUCAAUAAUGAGCUGAUACCGUCU | |
| | AUGAACCAGCUAUCUUGUGAUCUAAUCGGUCAGAAGC | |
| | UCGGGCUCAAAUUGCUUAGAUACUAUACAGAAAUCCU | |
| | GUCAUUAUUUGGCCCCAGCCUACGGGACCCCAUAUCU | |
| | GCGGAGAUAUCUAUCCAGGCUUUGAGUUAUGCACUU GGACGAGAUAUCAAUAAGGUGUUAGAAAAGCUCGGA | |
| | UACAGUGGAGGCGAUUUACUAGGCAUCUUAGAGAGGC | |
| | AGAGGAAUAAAGGCUCGGAUAACUCACGUCGACACAG | |
| | AGUCCUACUUCAUAGUCCUCAGUAUAGCCUAUCCGAC | |
| | GCUGUCCGAGAUUAAGGGGGUGAUUGUCCACCGGCUA | |
| | GAGGGGGUCUCGUACAACAUAGGCUCUCAAGAGUGG | |
| | UAUACCACUGUGCCCAAGUAUGUUGCAACCCAAGGGU ACCUUAUCUCGAAUUUUGAUGAGUCAUCAUGUACUU | |
| | UCAUGCCAGAGGGGACUGUGUGCAGCCAAAAUGCCUU | |
| | GUACCCGAUGAGUCCUCUGCUCCAAGAAUGCCUCCGG | |
| | GGGUCCACCAAGUCCUGUGCUCGUACACUCGUAUCCG | |
| | GGUCUUUUGGGAACCGGUUCAUUUUAUCACAAGGGA | |
| | ACCUAAUAGCCAAUUGUGCAUCAAUUCUUUGUAAGU GUUACACAACAGGUACGAUUAUUAAUCAAGACCCUGA | |
| | CAAGAUCCUAACAUACAUUGCUGCCGAUCGCUGCCCG | |
| | GUAGUCGAGGUGAACGGCGUGACCAUCCAAGUCGGGA | |
| | GCAGGAGGUAUCCAGACGCUGUGUACUUGCACAGAAU | |
| | UGACCUCGGUCCUCCCAUAUCAUUGGAGAGGUUGGAC | |
| | GUAGGGACAAAUCUGGGGAAUGCAAUUGCCAAAUUG GAGGAUGCCAAGGAAUUGUUGGAAUCAUCGGACCAG | |
| | AUAUUGAGAAGUAUGAAAGGUUUAUCGAGCACUAGC | |
| | AUAGUCUACAUCCUGAUUGCAGUGUGUCUUGGAGGG | |
| | UUGAUAGGGAUCCCCACUUUAAUAUGUUGCUGCAGG | |
| | GGGCGUUGUAACAAAAGGGAGAACAAGUUGGUAUG | |
| | UCAAGACCAGGCCUAAAGCCUGACCUUACAGGAACAU CAAAAUCCUAUGUAAGAUCGCUUUGAUGAUAAUAGG | |
| | CUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCUUGGGC | |
| | CUCCCCCCAGCCCUCCUCCCCUUCCUGCACCCGUACC | |
| | CCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCGGC | |
| C_F_MEASLES_B3.1 | AUGGGUCUCAAGGUGAACGUCUCUGCCGUAUUCAUGG | 70 |
| RF Sequence, NT | CAGUACUGUUAACUCUCCAAACACCCGCCGGUCAAAU | |
| | UCAUUGGGGCAAUCUCUCUAAGAUAGGGGUAGUAGG | |
| | AAUAGGAAGUGCAAGCUACAAAGUUAUGACUCGUUC CAGCCAUCAAUCAUUAGUCAUAAAAUUAAUGCCCAAU | |
| | AUAACUCUCCUCAAUAACUGCACGAGGGUAGAGAUUG | |
| | CAGAAUACAGGAGACUACUAAGAACAGUUUUGGAAC | |
| | CAAUUAGGGAUGCACUUAAUGCAAUGACCCAGAACAU | |
| | AAGGCCGGUUCAGAGCGUAGCUUCAAGUAGGAGACAC | |
| | AAGAGAUUUGCGGGAGUAGUCCUGGCAGGUGCGGCCC UAGGUGUUGCCACAGCUGCUCAGAUAACAGCCGGCAU | |
| | UGCACUUCACCGGUCCAUGCUGAACUCUCAGGCCAUC | |
| | GACAAUCUGAGAGCGAGCCUGGAAACUACUAAUCAGG | |
| | | |
| | CAAUUGAGGCAAUCAGACAAGCAGGGCAGGAGAUGA | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA UCUAAUCGGUCAGAAGCUCGGGCUCAAAUUGCUUAGA | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA UCUAAUCGGUCAGAAGCUCGGGCUCAAAUUGCUUAGA UACUAUACAGAAAUCCUGUCAUUAUUUGGCCCCAGCC UACGGGACCCCAUAUCUGCGGAGAUAUCUAUCCAGGC UUUGAGUUAUGCACUUGGAGGAGAUAUCAAUAAGGU | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA UCUAAUCGGUCAGAAGCUCGGGCUCAAAUUGCUUAGA UACUAUACAGAAAUCCUGUCAUUAUUUGGCCCCAGCC UACGGGACCCCAUAUCUGCGGAGAUAUCUAUCCAGGC UUUGAGUUAUGCACUUGGAGGAAUAUCAAUAAGGU GUUAGAAAAGCUCGGAUACAGUGGAGGCGAUUUACU | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA UCUAAUCGGUCAGAAGCUCGGGCUCAAAUUGCUUAGA UACUAUACAGAAAUCCUGUCAUUAUUUGGCCCCAGCC UACGGGACCCCAUAUCUGCGGGGAGAUAUCCAUGCC UUUGAGUUAUGCACUUGGAGGGAAUAUCAAUAAGGU GUUAGAAAAGCUCGGAUACAGUGGAGGCGAUUUACU AGGCAUCUUAGAGAGCAGAGGAAUAAAGGCUCGGAU | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA UCUAAUCGGUCAGAAGCUCGGGCUCAAAUUGCUUAGA UACUAUACAGAAAUCCUGUCAUUAUUUGGCCCCAGCC UACGGACCCCAUAUCUGGGGGGAUAUCUAUCCAGGC UUUGAGUUAUGCACUUGGAGGGGAUAUCAAUAAGGU GUUAGAAAAGCUCGGAUACAGUGGAGGCGUUUUACU AGGCAUCUUAGAGAGCAGAGGGAUUAAAGGCUCGGAU AACUCACGUCGACACAGAGUCCUACUUCAUAGUCCUC | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGUUACGGUCUAUGAACCAGCUAUCUUGUGA UCUAAUCGGUCAGAAGUCCGGCUCAAUUGCUUAGA UACUAUACAGAAAUCCUGUCAUUAUUUGGCCCAGCC UACGGGACCCCAUAUCUGCGGAGAUAUCUAUCCAGGC UUUGAGUUAUGCACUUGGAGGAGAUAUCAAUAAGGU GUUAGAAAAGCUCGGAUACAGUGGAGCGAUUUACU AGGCAUCUUAGAGAGCAGAGGAAUAAAGGCUCGGAU AACUCACGUCGACACAGAGGAAUAAAGGCUCCGGAU AAGUCACGUCGACACAGAGUCCUACUUCAUAGGCCUC AGUAUAGCCUAUCCGACGCUGUCCGAGAUUAAGGGGG | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA UCUAAUCGGUCAGAAGCUCGGGCUCAAAUUGCUUAGA UACUAUACAGAAAUCCUGUCAUUAUUUGGCCCCAGCC UACGGACCCCAUAUCUGGGGGGAUAUCUAUCCAGGC UUUGAGUUAUGCACUUGGAGGGGAUAUCAAUAAGGU GUUAGAAAAGCUCGGAUACAGUGGAGGCGUUUUACU AGGCAUCUUAGAGAGCAGAGGGAUUAAAGGCUCGGAU AACUCACGUCGACACAGAGUCCUACUUCAUAGUCCUC | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA UCUAAUCGGUCAGAAGCUCGGGCUCAAUUCUUGUGA UACUAUACAGAAAUCCUGUCAUUAUUUGCCCAGCC UACGGGACCCCAUAUCUGCGGAGAUAUUCUAUCCAGGC UUUGAAUUAUCCACUUGGAGGAAUAUCAAUAAGGU GUUAGAAAAGCUCGGAUACAGUGGAGGCGAUUUACU AGGCAUCUUAGAGAGCAGAGGGAAUAAAGGCUCGGAU AACUCACGUCGACACAAAGUCCUACUUCAUAGUCCUC AGUAUAGCCUAUCCGACGCUGUCCGAGAUUAAGGGG UGAUUGUCCACCGGCUAGAGGGGGUUCGUACAACAU AGGCUCUCAAAGUGGUAACACCUGGACUCGUACAACAU GUUGCAACCCAAGGGUACCUUGUCCGAAUUUUGAUG | |
| | UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA UCUAAUCGGUCAGAAGCUCGGGCUCAAAUUGCUUAGA UACUAUACAGAAAUCCUQUCAUUAUUUGGCCCCAGCC UACGGGACCCCAUAUCUGGGGGAAUAUCAUCAGGC UUUGAGUUAUGCACUUGGAGGAGAUAUCAAUAAGGU GUUAGAAAAGCUCGGAUACAGUGGGAGGCGAUUUACU AGGCAUCUUAAGAGGCGAGGGAUAAAGGCUCGGAU AACUCACGUCGACACAGAGUCCUACUUCAUAGUCCUC AGUAUAUCCGACCGACGCUGUCCGAGAUUAAGGGG UQAUUGUCCACCGGCUAGAGGGGGUCUCGUACAACAU AGGCUCUCAAGAGUGGUAUACCACUGUGCCCAAGUAU | |

| | | SEQ ID |
|------------------|--|--------|
| Description | Sequence | NO : |
| | CGUACACUCGUAUCCGGGUCUUUUGGGAACCGGUUCA | |
| | UUUUAUCACAAGGGAACCUAAUAGCCAAUUGUGCAUC | |
| | AAUUCUUUGUAAGUGUUACACAACAGGUACGAUUAU UAAUCAAGACCCUGACAAGAUCCUAACAUACAUUGCU | |
| | GCCGAUCGCUGCCCCGGUAGUCGAGGUGAACGGCGUGA | |
| | CCAUCCAAGUCGGGAGCAGGAGGUAUCCAGACGCUGU | |
| | GUACUUGCACAGAAUUGACCUCGGUCCUCCCAUAUCA | |
| | UUGGAGAGGUUGGACGUAGGGACAAAUCUGGGGAAU | |
| | GCAAUUGCCAAAUUGGAGGAUGCCAAGGAAUUGUUG | |
| | GAAUCAUCGGACCAGAUAUUGAGAAGUAUGAAAGGU | |
| | UUAUCGAGCACUAGCAUAGUCUACAUCCUGAUUGCAG | |
| | UGUGUCUUGGAGGGUUGAUAGGGAUCCCCACUUUAA | |
| | UAUGUUGCUGCAGGGGGGGGUUGUAACAAAAAGGGAG AACAAGUUGGUAUGUCAAGACCAGGCCUAAAGCCUGA | |
| | CCUUACAGGAACAUCAAAAUCCUAUGUAAGAUCGCUU | |
| | UGA | |
| | | |
| C_F_MEASLES_B3.1 | G*GCGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAA | 71 |
| nRNA Sequence | UAUAAGAGCCACCAUGGGUCUCAAGGUGAACGUCUCU | |
| | GCCGUAUUCAUGGCAGUACUGUUAACUCUCCAAACAC | |
| nRNA Sequence | CCGCCGGUCAAAUUCAUUGGGGCAAUCUCUCUAAGAU | |
| Length: 1925 | AGGGGUAGUAGGAAUAGGAAGUGCAAGCUACAAAGU | |
| | UAUGACUCGUUCCAGCCAUCAAUCAUUAGUCAUAAAA UUAAUGCCCAAUAUAACUCUCCUCAAUAACUGCACGA | |
| | GGGUAGAGAUUGCAGAAUACAGGAGACUACUAAGAA | |
| | CAGUUUUGGAACCAAUUAGGGAUGCACUUAAUGCAA | |
| | UGACCCAGAACAUAAGGCCGGUUCAGAGCGUAGCUUC | |
| | AAGUAGGAGACACAAGAGAUUUGCGGGAGUAGUCCU | |
| | GGCAGGUGCGGCCCUAGGUGUUGCCACAGCUGCUCAG | |
| | AUAACAGCCGGCAUUGCACUUCACCGGUCCAUGCUGA | |
| | ACUCUCAGGCCAUCGACAAUCUGAGAGCGAGCCUGGA | |
| | AACUACUAAUCAGGCAAUUGAGGCAAUCAGACAAGCA | |
| | GGGCAGGAGAUGAUAUUGGCUGUUCAGGGUGUCCAA GACUACAUCAAUAAUGAGCUGAUACCGUCUAUGAACC | |
| | AGCUAUCUUGUGAUCUAAUCGGUCAGAAGCUCGGGCU | |
| | CAAAUUGCUUAGAUACUAUACAGAAAUCCUGUCAUU | |
| | AUUUGGCCCCAGCCUACGGGACCCCAUAUCUGCGGAG | |
| | AUAUCUAUCCAGGCUUUGAGUUAUGCACUUGGAGGA | |
| | GAUAUCAAUAAGGUGUUAGAAAAGCUCGGAUACAGU | |
| | GGAGGCGAUUUACUAGGCAUCUUAGAGAGCAGAGGA | |
| | AUAAAGGCUCGGAUAACUCACGUCGACACAGAGUCCU | |
| | ACUUCAUAGUCCUCAGUAUAGCCUAUCCGACGCUGUC | |
| | CGAGAUUAAGGGGGUGAUUGUCCACCGGCUAGAGGG GGUCUCGUACAACAUAGGCUCUCAAGAGUGGUAUACC | |
| | ACUGUGCCCAAGUAUGUUGCAACCCCAAGGGUACCCUUA | |
| | UCUCGAAUUUUGAUGAGUCAUCAUGUACUUUCAUGCC | |
| | AGAGGGGACUGUGUGCAGCCAAAAUGCCUUGUACCCG | |
| | AUGAGUCCUCUGCUCCAAGAAUGCCUCCGGGGGGUCCA | |
| | CCAAGUCCUGUGCUCGUACACUCGUAUCCGGGUCUUU | |
| | UGGGAACCGGUUCAUUUUAUCACAAGGGAACCUAAU | |
| | AGCCAAUUGUGCAUCAAUUCUUUGUAAGUGUUACAC | |
| | AACAGGUACGAUUAUUAAUCAAGACCCUGACAAGAUC | |
| | CUAACAUACAUUGCUGCCGAUCGCUGCCCGGUAGUCG | |
| | AGGUGAACGGCGUGACCAUCCAAGUCGGGAGCAGGAG | |
| | GUAUCCAGACGCUGUGUACUUGCACAGAAUUGACCUC GGUCCUCCCAUAUCAUUGGAGAGGUUGGACGUAGGG | |
| | ACAAAUCUGGGGAAUGCAAUUGCCAAAUUGGAGGAU | |
| | GCCAAGGAAUUGUUGGAAUCAUCGGACCAGAUAUUG | |
| | AGAAGUAUGAAAGGUUUAUCGAGCACUAGCAUAGUC | |
| | UACAUCCUGAUUGCAGUGUGUCUUGGAGGGUUGAUA | |
| | GGGAUCCCCACUUUAAUAUGUUGCUGCAGGGGGGCGUU | |
| | GUAACAAAAAGGGAGAACAAGUUGGUAUGUCAAGAC | |
| | CAGGCCUAAAGCCUGACCUUACAGGAACAUCAAAAUC | |
| | CUAUGUAAGAUCGCUUUGAUGAUAAUAGGCUGGAGC | |
| | CUCGGUGGCCAAGCUUCUUGCCCCUUGGGCCUCCCCC | |
| | | |
| | UCUUUGAAUAAAGUCUGAGUGGGCGGCAAAAAAAAA AAAAAAAAAA | |
| | AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA | |
| | AAAAAAAAAAAAAAAAAAAAAUCUAG | |
| | | |
| GC_F_MEASLES_D8 | UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC | 72 |
| equence, NT (5' | UCACUAUAGGGAAAUAAGAGAGAAAAGAAGAGUAAG | |
| JTR, ORF, 3' | AAGAAAUAUAAGAGCCACCAUGGGUCUCAAGGUGAA | |

UTR, ORF, 3 UTR)

AAGAAAUAUAAGAGCCACCAUGGGUCUCAAGGUGAA CGUCUCUGUCAUAUUCAUGGCAGUACUGUUAACUCUU

| | | SEQ ID |
|------------------|--|--------|
| Description | Sequence | NO : |
| Sequence Length: | CAAACACCCACCGGUCAAAUCCAUUGGGGCAAUCUCU | |
| .864 | CUAAGAUAGGGGUGGUAGGGGUAGGAAGUGCAAGCU ACAAAGUUAUGACUCGUUCCAGCCAUCAAUCAUUAGU | |
| | CAUAAAGUUAAUGCCCAAUAUAACUCUCCUCAACAAU | |
| | UGCACGAGGGUAGGGAUUGCAGAAUACAGGAGACUA | |
| | CUGAGAACAGUUCUGGAACCAAUUAGAGAUGCACUU | |
| | AAUGCAAUGACCCAGAAUAUAAGACCGGUUCAGAGU | |
| | GUAGCUUCAAGUAGGAGACACAAGAGAUUUGCGGGA GUUGUCCUGGCAGGUGCGGCCCUAGGCGUUGCCACAG | |
| | CUGCUCAAAUAACAGCCGGUAUUGCACUUCACCAGUC | |
| | CAUGCUGAACUCUCAAGCCAUCGACAAUCUGAGAGCG | |
| | AGCCUAGAAACUACUAAUCAGGCAAUUGAGGCAAUCA | |
| | GACAAGCAGGGCAGGAGAUGAUAUUGGCUGUUCAGG | |
| | GUGUCCAAGACUACAUCAAUAAUGAGCUGAUACCGUC UAUGAAUCAACUAUCUUGUGAUUUAAUCGGCCAGAA | |
| | GCUAGGGCUCAAAUUGCUCAGAUACUAUACAGAAAUC | |
| | CUGUCAUUAUUUGGCCCCAGCUUACGGGACCCCAUAU | |
| | CUGCGGAGAUAUCUAUCCAGGCUUUGAGCUAUGCGCU | |
| | UGGAGGAGAUAUCAAUAAGGUGUUGGAAAAGCUCGG | |
| | AUACAGUGGAGGUGAUCUACUGGGCAUCUUAGAGAG CAGAGGAAUAAAGGCCCGGAUAACUCACGUCGACACA | |
| | GAGUCCUACUUCAUUGUACUCAGUAUAGCCUAUCCGA | |
| | CGCUAUCCGAGAUUAAGGGGGUGAUUGUCCACCGGCU | |
| | AGAGGGGGUCUCGUACAACAUAGGCUCUCAAGAGUG | |
| | GUAUACCACUGUGCCCAAGUAUGUUGCAACCCAAGGG | |
| | UACCUUAUCUCGAAUUUUGAUGAGUCAUCAUGCACUU | |
| | UCAUGCCAGAGGGGACUGUGUGCAGCCAGAAUGCCUU GUACCCGAUGAGUCCUCUGCUCCAAGAAUGCCUCCGG | |
| | GGGUCCACUAAGUCCUCUGCUCCAAGAAUGCCUCCGG GGGUCCACUAAGUCCUGUGCUCGUACACUCGUAUCCG | |
| | GGUCUUUCGGGAACCGGUUCAUUUUAUCACAGGGGA | |
| | ACCUAAUAGCCAAUUGUGCAUCAAUCCUUUGCAAGUG | |
| | UUACACAACAGGAACAAUCAUUAAUCAAGACCCUGAC | |
| | AAGAUCCUAACAUACAUUGCUGCCGAUCACUGCCCGG | |
| | UGGUCGAGGUGAAUGGCGUGACCAUCCAAGUCGGGA GCAGGAGGUAUCCGGACGCUGUGUACUUGCACAGGAU | |
| | UGACCUCGGUCCUCCCAUAUCUUUGGAGAGGUUGGAC | |
| | GUAGGGACAAAUCUGGGGAAUGCAAUUGCUAAGUUG | |
| | GAGGAUGCCAAGGAAUUGUUGGAGUCAUCGGACCAG | |
| | AUAUUGAGGAGUAUGAAAGGUUUAUCGAGCACUAGU | |
| | AUAGUUUACAUCCUGAUUGCAGUGUGUCUUGGAGGA | |
| | UUGAUAGGGAUCCCCGCUUUAAUAUGUUGCUGCAGG GGGCGUUGUAACAAGAAGGGAGAACAAGUUGGUAUG | |
| | UCAAGACCAGGCCUAAAGCCUGAUCUUACAGGAACAU | |
| | CAAAAUCCUAUGUAAGGUCACUCUGAUGAUAAUAGG | |
| | CUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCUUGGGC | |
| | CUCCCCCCAGCCCCUCCUCCCUCCUGCACCCGUACC | |
| | CCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCGGC | |
| C_F_MEASLES_D8 | AUGGGUCUCAAGGUGAACGUCUCUGUCAUAUUCAUG | 73 |
| RF Sequence, NT | GCAGUACUGUUAACUCUUCAAACACCCACCGGUCAAA | |
| | UCCAUUGGGGCAAUCUCUCUAAGAUAGGGGUGGUAG GGGUAGGAAGUGCAAGCUACAAAGUUAUGACUCGUU | |
| | CCAGCCAUCAAUCAUUAGUCAUAAAGUUAAUGCCCAA | |
| | UAUAACUCUCCUCAACAAUUGCACGAGGGUAGGGAUU | |
| | GCAGAAUACAGGAGACUACUGAGAACAGUUCUGGAA | |
| | CCAAUUAGAGAUGCACUUAAUGCAAUGACCCAGAAUA | |
| | UAAGACCGGUUCAGAGUGUAGCUUCAAGUAGGAGAC | |
| | ACAAGAGAUUUGCGGGAGUUGUCCUGGCAGGUGCGG CCCUAGGCGUUGCCACAGCUGCUCAAAUAACAGCCGG | |
| | UAUUGCACUUCACCAGUCCAUGCUGAACUCUCAAGCC | |
| | AUCGACAAUCUGAGAGCGAGCCUAGAAACUACUAAUC | |
| | AGGCAAUUGAGGCAAUCAGACAAGCAGGGCAGGAGA | |
| | UGAUAUUGGCUGUUCAGGGUGUCCAAGACUACAUCA | |
| | AUAAUGAGCUGAUACCGUCUAUGAAUCAACUAUCUU | |
| | GUGAUJUJAAUCGGCCAGAAGCUAGGGCUCAAAUUGC UCAGAUACUAUACAGAAAUCCUGUCAUUAUUUGGCCC | |
| | CAGCUUACGGGACCCCAUAUCUGCGGAGAUAUCUAUC | |
| | CAGGCUUUGAGCUAUGCGCUUGGAGGAGAUAUCAAU | |
| | AAGGUGUUGGAAAAGCUCGGAUACAGUGGAGGUGAU | |
| | CUACUGGGCAUCUUAGAGAGCAGAGGAAUAAAGGCCC | |
| | GGAUAACUCACGUCGACACAGAGUCCUACUUCAUUGU | |
| | ACUCAGUAUAGCCUAUCCGACGCUAUCCGAGAUUAAG GGGGUGAUUGUCCACCGGCUAGAGGGGGUCUCGUACA | |
| | | |
| | ACAUAGGCUCUCAAGAGUGGUAUACCACUGUGCCCAA | |

| | MeV Nucleic Acid Sequences | |
|---|---|---------------|
| Description | Sequence | SEQ ID NO: |
| | GAUGAGUCAUCAUGCACUUUCAUGCCAGAGGGGACUG UGUGCAGCCAGAAUGCCUUGUACCCGAUGAGUCCUCU GCUCCAAGAAUGCCUCCGGGGGUCCACUAAGUCCUGU GCUCGUACACUCGUAUCCGGGUCUUUCGGGAACCGGU UCAUUUUAUCACAGGGGAACCUAAUAGCCAAUUGUGC | |
| | AUCAAUCCUUUGCAAGUGUUACACAACAGGAACAAUC AUUAAUCAAGACCCUGACAAGAUCCUAACAUACAUUG CUGCCGAUCACUGCCCGGUGGUCGAGGUGAAUGGCGU GACCAUCCAAGUCGGGAGCAGGAGGUAUCCGGACGCU | |
| | GUGUACUUGCACAGGAUUGACCUCGGUCCUCCCAUAU CUUUGGACAGGUUGGACGUAGGACAAAUCUGGGGA AUGCAAUUGCUAAGUUGGAGGAUGCCAAGGAAUUGU UGGAGUCAUCGGACCAGAUAUUGAGGAGUAUGAAAG GUUUAUCGAGCACUAGUAUAGUUUACAUCCUGAUUG | |
| | CASUGUGUCUUUGGAGGAUUGAUAGGAUCCCGCUU UAAUAUGUUGCUGCAGGGGCGUUGUAACAAGAAGG GAGAACAAGUUGGUAUGUCAAGACCAGGCCUAAAGCC UGAUCUUACAGGAACAUCAAAAUCCUAUGUAAGGUC ACUCUGA | |
| GC_F_MEASLES_D8 mRMA Sequence (assumes T100 tail) Sequence Length: 1925 | G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAA UAUAAGAGCCACCAUGGGUCUCAAGGUGAACGUCUCU GUCAUAUUCAUGGCAGUACUGUUAACUCUUCAAACAC CCACCGGUCAAAUCCAUUGGGGCAAUCUCUCUAAGAU AGGGUGGUAGGGUAG | 74 |
| | GGGUAGGGAUUGCAGAAUACAGGAGACUACUGAGAA CAGUUCUGGAACCAAUUAGAGAUGCACUUAAUGCAA UGACCCAGAAUAUAAGACCGGUUCAGAGUGUAGCUUC AAGUAGGAGACACAAGAGAUUUGCGGGAGUUGUCCU | |
| | GGCAGGUGCGGCCCUAGGCGUUGCCACAGCUGCUCAA AUAACAGCCGGUAUUGCACUUCACCAGUCCAUGCUGA ACUCUCAAGCCAUCGACAAUCUGAGAGCGAGCCUAGA AACUACUAAUCAGGCAAUUGAGGCAAUCAGACAAGCA | |
| | GGGCAGGAGAUGAUAUUGGCUGUUCAGGGUGUCCAA GACUACAUCAAUAAUGAGCUGAUACCGUCUAUGAAUC AACUAUCUUGUGAUUUAAUCGGCCAGAAGCUAGGGC UCAAAUUGCUCAGAUACUAUACAGAAAUCCUGUCAUU AUUUGGCCCCAGCUACGGACCCCAUAUCUGCGGAG | |
| | AUAUCUAUCCAGGCUUUGAGCUAUGCGCUUGGAGGA GAUAUCAAUAAGGUGUUGGAAAAGCUCGGAUACAGU GGAGGUGAUCUACUGGGCAUCUUAGAGAGCAGAGGA | |
| | AUAAAGGCCCGGAUAACUCACGUCGACACAGAGUCCU ACUUCAUUGUACUCAGUAUAGCCUAUCCGACGCUAUC CGAGAUUAAGGGGGUGAUUGUCCACCGGCUAGAGGG GGUCUCGUACAACAUAGGCUCUCAAGAGUGGUAUACC | |
| | ACUGUGCCCAAGUAUGUUGCAACCCAAGGGUACCUUA UCUCGAAUUUUGAUGAGUCAUCAUGCACUUUCAUGCC AGAGGGGACUGUGUGCAGCCAGAAUGCCUUGUACCCG AUGAGUCCUCUGCUCCAAGAAUGCCUCCGGGGGUCCA | |
| | CUAAGUCCUGUGCUCGUACACUCGUAUCCGGGUCUUU CGGGAACCGGUUCAUUUUAUCACAGGGGAACCUAAUA GCCAAUUGUGCAUCAAUCCUUUGCAAGUGUUACACAA CAGGAACAAUCAUUAAUCAAGACCCUGACAAGAUCCU | |
| | AACAUACAUUGCUGCCGAUCACUGCCCGGUGGUCGAG GUGAAUGGCGUGACCAUCCAAGUCGGGAGCAGGAGG UAUCCGGACGCUGUGUACUUGCACAGGAUUGACCUCG | |
| | GUCCUCCCAUAUCUUUGGAGAGGUUGGACGUAGGGAC AAAUCUGGGGAAUGCAAUUGCUAAGUUGGAGGAUGC CAAGGAAUUGUUGGAGUCAUCGGACCAGAUAUUGAG GAGUAUGAAAGGUUUAUCGAGCACUAGUAUAGUUUA | |
| | CAUCCUGAUUGCAGUGUGUCUUGGAGGAUUGAUAGG GAUCCCCGCUUUAAUAUGUUGCUGCAGGGGGGCUUUGU AACAAGAAGGGAGAACAAGUUGGUAUGUCAAGACCA GGCCUAAAGCCUGAUCUUACAGGAACAUCAAAAUCCU | |
| | AUGUAAGGUCACUCUGAUGAUAAUAGGCUGGAGCCU CGGUGGCCAAGCUUCUUGCCCCUUGGGCCUCCCCCCA GCCCCUCCUCCCCUUCCUGCACCCGUACCCCCGUGGUC | |
| | UUUGAAUAAAGUCUGAGUGGGCGGCAAAAAAAAAA АЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛА | |

| Description | Sequence | SEQ ID NO: |
|------------------|---------------------------------------|---------------|
| | | |
| GC_H_MEASLES_B3 | UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC | 75 |
| Sequence, NT (5' | UCACUAUAGGGAAAUAAGAGAGAAAAGAAGAGUAAG | |
| UTR, ORF, 3' | AAGAAAUAUAAGAGCCACCAUGUCACCGCAACGAGAC | |
| UTR) | CGGAUAAAUGCCUUCUACAAAGAUAACCCUUAUCCCA | |
| Sequence Length: | AGGGAAGUAGGAUAGUUAUUAACAGAGAACAUCUUA | |
| 2065 | UGAUUGACAGACCCUAUGUUCUGCUGGCUGUUCUGUU | |
| 2065 | | |
| | CGUCAUGUUUCUGAGCUUGAUCGGAUUGCUGGCAAU | |
| | UGCAGGCAUUAGACUUCAUCGGGCAGCCAUCUACACC | |
| | GCGGAGAUCCAUAAAAGCCUCAGUACCAAUCUGGAUG | |
| | UGACUAACUCCAUCGAGCAUCAGGUCAAGGACGUGCU | |
| | GACACCACUCUUUAAAAUCAUCGGGGAUGAAGUGGGC | |
| | CUGAGAACACCUCAGAGAUUCACUGACCUAGUGAAAU | |
| | UCAUCUCGGACAAGAUUAAAUUCCUUAAUCCGGAUAG | |
| | GGAGUACGACUUCAGAGAUCUCACUUGGUGCAUCAAC | |
| | CCGCCAGAGAGGAUCAAACUAGAUUAUGAUCAAUACU | |
| | GUGCAGAUGUGGCUGCUGAAGAGCUCAUGAAUGCAU | |
| | UGGUGAACUCAACUCUACUGGAGACCAGAACAACCAC | |
| | UCAGUUCCUAGCUGUCUCAAAGGGAAACUGCUCAGGG | |
| | | |
| | | |
| | UGUCCUUGUUGGACUUGUACUUAGGUCGAGGUUACA | |
| | AUGUGUCAUCUAUAGUCACUAUGACAUCCCAGGGAAU | |
| | GUAUGGGGGAACCUACCUAGUUGAAAAGCCUAAUCU | |
| | GAACAGCAAAGGGUCAGAGUUGUCACAACUGAGCAU | |
| | GUACCGAGUGUUUGAAGUAGGUGUGAUCAGAAACCC | |
| | GGGUUUGGGGGCUCCGGUGUUCCAUAUGACAAACUA | |
| | UUUUGAGCAACCAGUCAGUAAUGGUCUCGGCAACUGU | |
| | AUGGUGGCUUUGGGGGAGCUCAAACUCGCAGCCCUUU | |
| | GUCACGGGGACGAUUCUAUCAUAAUUCCCUAUCAGGG | |
| | AUCAGGGAAAGGUGUCAGCUUCCAGCUCGUCAAGCUG | |
| | GGUGUCUGGAAAUCCCCAACCGACAUGCAAUCCUGGG | |
| | UCCCCUUAUCAACGGAUGAUCCAGUGGUAGACAGGCU | |
| | UUACCUCUCAUCUCACAGAGGUGUCAUCGCUGACAAU | |
| | CAAGCAAAAUGGGCUGUCCCGACAACACGAACAGAUG | |
| | | |
| | ACAAGUUGCGAAUGGAGACAUGCUUCCAGCAGGCGUG | |
| | UAAAGGUAAAAUCCAAGCACUCUGCGAGAAUCCCGAG | |
| | UGGGUACCAUUGAAGGAUAACAGGAUUCCUUCAUAC | |
| | GGGGUCCUGUCUGUUGAUCUGAGUCUGACGGUUGAG | |
| | CUUAAAAUCAAAAUUGCUUCGGGAUUCGGGCCAUUG | |
| | AUCACACGGCUCAGGGAUGGACCUAUACAAAUCCA | |
| | ACUGCAACAAUGUGUAUUGGCUGACUAUUCCGCCAAU | |
| | GAGAAAUCUAGCCUUAGGCGUAAUCAACACAUUGGA | |
| | GUGGAUACCGAGAUUCAAGGUUAGUCCCAACCUCUUC | |
| | ACUGUCCCAAUUAAGGAAGCAGGCGAAGACUGCCAUG | |
| | CCCCAACAUACCUACCUGCGGAGGUGGACGGUGAUGU | |
| | CAAACUCAGUUCCAACCUGGUGAUUCUACCUGGUCAA | |
| | GAUCUCCAAUAUGUUUUGGCAACCUACGAUACCUCCA | |
| | GGGUUGAGCAUGCUGUGGUUUAUUACGUUUACAGCC | |
| | CAAGCCGCUCAUUUUCUUACUUUUAUCCUUUUAGGUU | |
| | | |
| | GCCUAUAAAGGGGGUCCCAAUCGAACUACAAGUGGAA | |
| | UGCUUCACAUGGGAUCAAAAACUCUGGUGCCGUCACU | |
| | UCUGUGUGCUUGCGGACUCAGAAUCCGGUGGACUUAU | |
| | CACUCACUCUGGGAUGGUGGGCAUGGGAGUCAGCUGC | |
| | ACAGCUACCCGGGAAGAUGGAACCAAUCGCAGAUAAU | |
| | GAUAAUAGGCUGGAGCCUCGGUGGCCAAGCUUCUUGC | |
| | CCCUUGGGCCUCCCCCAGCCCCUCCUCCCCUUCCUGC | |
| | ACCCGUACCCCCGUGGUCUUUGAAUAAAGUCUGAGUG | |
| | GGCGGC | |
| GC H MEASLES B3 | AUGUCACCGCAACGAGACCGGAUAAAUGCCUUCUACA | 76 |
| | | /6 |
| ORF Sequence, NT | AAGAUAACCCUUAUCCCAAGGGAAGUAGGAUAGUUA | |
| | UUAACAGAGAACAUCUUAUGAUUGACAGACCCUAUG | |
| | UUCUGCUGGCUGUUCUGUUCGUCAUGUUUCUGAGCUU | |
| | GAUCGGAUUGCUGGCAAUUGCAGGCAUUAGACUUCA | |
| | UCGGGCAGCCAUCUACACCGCGGAGAUCCAUAAAAGC | |
| | CUCAGUACCAAUCUGGAUGUGACUAACUCCAUCGAGC | |
| | AUCAGGUCAAGGACGUGCUGACACCACUCUUUAAAAU | |
| | CAUCGGGGAUGAAGUGGGCCUGAGAACACCUCAGAGA | |
| | UUCACUGACCUAGUGAAAUUCAUCUCGGACAAGAUUA | |
| | ABUUCCUUAAUCCGGAUACGGACUACGGACUUCAGAG | |
| | | |

AAUUCCUUAAUCCGGAUAGGGAGUACGACUUCAGAG AUCUCACUUGGUGCAUCAACCCGCCAGAGAGGAUCAA ACUGGAGACCAGAACAACCACUCAGUUCCUAGCUGUC UCAAAGGGAAACUGCUCAGGGCCCACUACAAUCAGAG

TABLE 13-continued

| SEQ ID | | |
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| Description | Sequence | NO: |
| | GUCAAUUCUCAAACAUGUCGCUGUCCUUGUUGGACUU | |
| | GUACUUAGGUCGAGGUUACAAUGUGUCAUCUAUAGU | |
| | CACUAUGACAUCCCAGGGAAUGUAUGGGGGGAACCUAC | |
| | CUAGUUGAAAAGCCUAAUCUGAACAGCAAAGGGUCA GAGUUGUCACAACUGAGCAUGUACCGAGUGUUUGAA | |
| | GUAGGUGUGAUCAGAAACCCGGGUUUGGGGGGCUCCG | |
| | GUGUUCCAUAUGACAAACUAUUUUGAGCAACCAGUCA | |
| | GUAAUGGUCUCGGCAACUGUAUGGUGGCUUUGGGGG | |
| | AGCUCAAACUCGCAGCCCUUUGUCACGGGGACGAUUC | |
| | UAUCAUAAUUCCCUAUCAGGGAUCAGGGAAAGGUGU | |
| | CAGCUUCCAGCUCGUCAAGCUGGGUGUCUGGAAAUCC | |
| | CCAACCGACAUGCAAUCCUGGGUCCCCUUAUCAACGG | |
| | AUGAUCCAGUGGUAGACAGGCUUUACCUCUCAUCUCA CAGAGGUGUCAUCGCUGACAAUCAAGCAAAAUGGGCU | |
| | GUCCCGACAACACGAACAGAUGACAAGUUGCGAAUGG | |
| | AGACAUGCUUCCAGCAGGCGUGUAAAGGUAAAAUCCA | |
| | AGCACUCUGCGAGAAUCCCGAGUGGGUACCAUUGAAG | |
| | GAUAACAGGAUUCCUUCAUACGGGGUCCUGUCUGUUG | |
| | AUCUGAGUCUGACGGUUGAGCUUAAAAUCAAAAUUG | |
| | CUUCGGGAUUCGGGCCAUUGAUCACACACGGCUCAGG | |
| | GAUGGACCUAUACAAAUCCAACUGCAACAAUGUGUAU | |
| | UGGCUGACUAUUCCGCCAAUGAGAAAUCUAGCCUUAG GCGUAAUCAACACAUUGGAGUGGAUACCGAGAUUCA | |
| | AGGUUAGUCCCAACCUCUUCACUGUCCCAAUUAAGGA | |
| | AGCAGGCGAAGACUGCCAUGCCCCAACAUACCUACCU | |
| | GCGGAGGUGGACGGUGAUGUCAAACUCAGUUCCAACC | |
| | UGGUGAUUCUACCUGGUCAAGAUCUCCAAUAUGUUU | |
| | UGGCAACCUACGAUACCUCCAGGGUUGAGCAUGCUGU | |
| | GGUUUAUUACGUUUACAGCCCAAGCCGCUCAUUUUCU | |
| | UACUUUUAUCCUUUUAGGUUGCCUAUAAAGGGGGUC | |
| | CCAAUCGAACUACAAGUGGAAUGCUUCACAUGGGAUC AAAAACUCUGGUGCCGUCACUUCUGUGUGCCUUGCGGA | |
| | CUCAGAAUCCGGUGGACUUAUCACUCACUCUGGGAUG | |
| | GUGGGCAUGGGAGUCAGCUGCACAGCUACCCGGGAAG | |
| | AUGGAACCAAUCGCAGAUAA | |
| GC H MEASLES B3 | G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAA | 77 |
| mRNA Sequence | UAUAAGAGCCACCAUGUCACCGCAACGAGACCGGAUA | |
| (assumes T100 | AAUGCCUUCUACAAAGAUAACCCUUAUCCCAAGGGAA | |
| Tail) | GUAGGAUAGUUAUUAACAGAGAACAUCUUAUGAUUG | |
| Sequence Length: | ACAGACCCUAUGUUCUGCUGGCUGUUCUGUUCGUCAU | |
| 2126 | GUUUCUGAGCUUGAUCGGAUUGCUGGCAAUUGCAGG | |
| | CAUUAGACUUCAUCGGGCAGCCAUCUACACCGCGGAG AUCCAUAAAAGCCUCAGUACCAAUCUGGAUGUGACUA | |
| | ACUCCAUCGAGCAUCAGGUCAAGGACGUGCUGACACC | |
| | ACUCUUUAAAAUCAUCGGGGAUGAAGUGGGCCUGAG | |
| | AACACCUCAGAGAUUCACUGACCUAGUGAAAUUCAUC | |
| | UCGGACAAGAUUAAAUUCCUUAAUCCGGAUAGGGAG | |
| | UACGACUUCAGAGAUCUCACUUGGUGCAUCAACCCGC | |
| | CAGAGAGGAUCAAACUAGAUUAUGAUCAAUACUGUG | |
| | | |
| | UGAACUCAACUCUACUGGAGACCAGAACAACCACUCA GUUCCUAGCUGUCUCAAAGGGAAACUGCUCAGGGCCC | |
| | ACUACAAUCAGAGGUCAAUUCUCAAACUGCUCAGGGCCC | |
| | CCUUGUUGGACUUGUACUUAGGUCGAGGUUACAAUG | |
| | UGUCAUCUAUAGUCACUAUGACAUCCCAGGGAAUGUA | |
| | UGGGGGAACCUACCUAGUUGAAAAGCCUAAUCUGAAC | |
| | AGCAAAGGGUCAGAGUUGUCACAACUGAGCAUGUACC | |
| | GAGUGUUUGAAGUAGGUGUGAUCAGAAACCCGGGUU | |
| | UGGGGGCUCCGGUGUUCCAUAUGACAAACUAUUUUG | |
| | AGCAACCAGUCAGUAAUGGUCUCGGCAACUGUAUGGU | |
| | GGCUUUGGGGGAGCUCAAACUCGCAGCCCUUUGUCAC GGGGACGAUUCUAUCAUAAUUCCCUAUCAGGGAUCAG | |
| | GGGAAGGUGUCAGCUUCCAGCUCGUCAAGCUGGGUGU | |
| | CUGGAAAUCCCCAACCGACAUGCAAUCCUGGGUCCCC | |
| | UUAUCAACGGAUGAUCCAGUGGUAGACAGGCUUUACC | |
| | UCUCAUCUCACAGAGGUGUCAUCGCUGACAAUCAAGC | |
| | AAAAUGGGCUGUCCCGACAACACGAACAGAUGACAAG | |
| | UUGCGAAUGGAGACAUGCUUCCAGCAGGCGUGUAAA | |
| | GGUAAAAUCCAAGCACUCUGCGAGAAUCCCGAGUGGG | |
| | | |
| | UACCAUUGAAGGAUAACAGGAUUCCUUCAUACGGGG | |
| | UCCUGUCUGUUGAUCUGAGUCUGACGGUUGAGCUUA | |
| | | |

| | MeV Nucleic Acid Sequences | |
|----------------------------------|--|---------------|
| Description | Sequence | SEQ ID NO: |
| | AAUCUAGCCUUAGGCGUAAUCAACACAUUGGAGUGG | |
| | AUACCGAGAUUCAAGGUUAGUCCCAACCUCUUCACUG | |
| | UCCCAAUUAAGGAAGCAGGCGAAGACUGCCAUGCCCC | |
| | AACAUACCUACCUGCGGAGGUGGACGGUGAUGUCAAA CUCAGUUCCAACCUGGUGAUUCUACCUGGUCAAGAUC | |
| | UCCAAUAUGUUUUGGCAACCUACGAUACCUCCAGGU | |
| | UGAGCAUGCUGUGGUUUAUUACGUUUACAGCCCAAGC | |
| | CGCUCAUUUUCUUACUUUUAUCCUUUUAGGUUGCCUA | |
| | UAAAGGGGGUCCCAAUCGAACUACAAGUGGAAUGCU | |
| | UCACAUGGGAUCAAAAACUCUGGUGCCGUCACUUCUG UGUGCUUGCGGACUCAGAAUCCGGUGGACUUAUCACU | |
| | CACUCUGGGAUGGUGGGCAUGGGAGUCAGCUGCACAG | |
| | CUACCCGGGAAGAUGGAACCAAUCGCAGAUAAUGAUA | |
| | AUAGGCUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCU | |
| | UGGGCCUCCCCCAGCCCCUCCUCCCCUUCCUGCACCC | |
| | GUACCCCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCG | |
| | ССААААААААААААААААААААААААААААААААААА | |
| | AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA | |
| C_H_MEASLES_D8 | UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC | 78 |
| Sequence, NT (5' JTR, ORF, 3' | UCACUAUAGGGAAAUAAGAGAGAAAAGAAGAGUAAG AAGAAAUAUAAGAGCCACCAUGUCACCACAACGAGAC | |
| JTR, ORF, 3 | CGGAUAAAUGCCUUCUACAAAGACAACCCCCAUCCUA | |
| Sequence Length: | AGGGAAGUAGGAUAGUUAUUAACAGAGAACAUCUUA | |
| 2065 | UGAUUGAUAGACCUUAUGUUUUGCUGGCUGUUCUAU | |
| | UCGUCAUGUUUCUGAGCUUGAUCGGGUUGCUAGCCAU | |
| | UGCAGGCAUUAGACUUCAUCGGGCAGCCAUCUACACC | |
| | GCAGAGAUCCAUAAAAGCCUCAGCACCAAUCUGGAUG UAACUAACUCAAUCGAGCAUCAGGUUAAGGACGUGCU | |
| | GACACCACUCAAUCGAGCAUCAGGUUAAGGACGUGCU GACACCACUCUUCAAGAUCAUCGGUGAUGAAGUGGGC | |
| | UUGAGGACACCUCAGAGAUUCACUGACCUAGUGAAGU | |
| | UCAUCUCUGACAAGAUUAAAUUCCUUAAUCCGGACAG | |
| | GGAAUACGACUUCAGAGAUCUCACUUGGUGUAUCAAC | |
| | CCGCCAGAGAGAAUCAAAUUGGAUUAUGAUCAAUAC | |
| | UGUGCAGAUGUGGCUGCUGAAGAACUCAUGAAUGCA | |
| | UUGGUGAACUCAACUCUACUGGAGACCAGGGCAACCA | |
| | AUCAGUUCCUAGCUGUCUCAAAGGGAAACUGCUCAGG GCCCACUACAAUCAGAGGCCAAUUCUCAAACAUGUCG | |
| | CUGUCCCUGUUGGACUUGUAUUUAAGUCGAGGUUAC | |
| | AAUGUGUCAUCUAUAGUCACUAUGACAUCCCAGGGAA | |
| | UGUACGGGGGAACUUACCUAGUGGAAAAGCCUAAUC | |
| | UGAGCAGCAAAGGGUCAGAGUUGUCACAACUGAGCA | |
| | UGCACCGAGUGUUUGAAGUAGGUGUUAUCAGAAAUC CGGGUUUGGGGGCUCCGGUAUUCCAUAUGACAAACUA | |
| | UCUUGAGCAACCAGUCAGUAAUGAUUUCAGCAACUAC | |
| | AUGGUGGCUUUGGGGGAGCUCAAGUUCGCAGCCCUCU | |
| | GUCACAGGGAAGAUUCUAUCACAAUUCCCUAUCAGGG | |
| | AUCAGGGAAAGGUGUCAGCUUCCAGCUUGUCAAGCUA | |
| | GGUGUCUGGAAAUCCCCAACCGACAUGCAAUCCUGGG | |
| | UCCCCCUAUCAACGGAUGAUCCAGUGAUAGACAGGCU UUACCUCUCAUCUCA | |
| | CAAGCAAAAUGGGCUGUCCCGACAACACGGACAAU | |
| | ACAAGUUGCGAAUGGAGACAUGCUUCCAGCAGGCGUG | |
| | UAAGGGUAAAAUCCAAGCACUUUGCGAGAAUCCCGAG | |
| | UGGACACCAUUGAAGGAUAACAGGAUUCCUUCAUACG | |
| | GGGUCUUGUCUGUUGAUCUGAGUCUGACAGUUGAGC | |
| | UUAAAAUCAAAAUUGUUUCAGGAUUCGGGCCAUUGA | |
| | UCACACACGGUUCAGGGAUGGACCUAUACAAAUCCAA | |
| | CCACAACAAUAUGUAUUGGCUGACUAUCCCGCCAAUG AAGAACCUGGCCUUAGGUGUAAUCAACACAUUGGAG | |
| | UGGAUACCGAGAUUCAAGGUUAGUCCCAACCUCUUCA | |
| | CUGUUCCAAUUAAGGAAGCAGGCGAGGACUGCCAUGC | |
| | CCCAACAUACCUACCUGCGGAGGUGGAUGGUGAUGUC | |
| | AAACUCAGUUCCAAUCUGGUGAUUCUACCUGGUCAAG | |
| | AUCUCCAAUAUGUUCUGGCAACCUACGAUACUUCCAG | |
| | AGUUGAACAUGCUGUAGUUUAUUACGUUUACAGCCC | |
| | AAGCCGCUCAUUUUCUUACUUUUAUCCUUUUAGGUUG CCUGUAAGGGGGGGUCCCCAUUGAAUUACAAGUGGAA | |
| | UGCUUCACAUGGGACCAAAAACUCUGGUGCCGUCACU | |
| | UCUGUGUGCUUGCGGACUCAGAAUCUGGUGGACAUA | |
| | UCACUCACUCUGGGAUGGUGGGCAUGGGAGUCAGCUG | |
| | CACAGCCACUCGGGAAGAUGGAACCAGCCGCAGAUAG | |
| | UGAUAAUAGGCUGGAGCCUCGGUGGCCAAGCUUCUUG | |
| | CCCCUUGGGCCUCCCCCAGCCCCUCCUCCCUCCUG | |

| | MeV Nucleic Acid Sequences | |
|---|--|---------------|
| Description | Sequence | SEQ II NO: |
| | CACCCGUACCCCGUGGUCUUUGAAUAAAGUCUGAGU GGGCGGC | |
| GC_H_MEASLES_D8 ORF Sequence, NT | AUGUCACCACAACGAGACCGGAUAAAUGCCUUCUACA AAGACAACCCCCCAUCCUAAGGGAAGUAGGAUAGUUAU UAACAGAGAACAUCUUAUGAUUGAUAGACCUUAUGU UUGCUGGCUGUUCUAUUCGAGGCAUUAGACUUCAU GAUCGGGUUCCAAUCGACGCAUUAGACUUCUGACAGC UCAGCACCAAUCUGGAUGAACUAACUCAUUCAAUCGAGCA UCAGGUUAAGACGGCGUGACGACACCACUCUUCAAAAUC AUCGGUGAUGAAGUGGGCUUGAGGACACCUCAGAGA UUCACUUAAUCCGGACAGGAAUACGACUUCAAGAGA UUCACUUAGUGUAUCAACCGCCCAGAGAUUCA AAUUCCUUAAUCCGGACAGGAAUACGACUUCAAGAGA UUCACUUAGUGAUGAAGUUGAGGACACCUCAGAGA UUCACUUAGUGAUCAAUACUGUGCAGAGUUGGC GAAGAACUCAUGAUCAAUCGGUGUCCU GAAGAACUCAUGAUCAAUCGUUGCCAGAUGUGUCUC AAAGGGAACUGCUCAGGGCCCACUACAAUCAG UUGACUUCAAAACAUGUCGCUGUCCUAGAGAGUUAC UUGAGAUCAGGGUUACAAUCGUGUCCUAGUGUCUC AAAGGGAAACUGCUCAGGGCCCACUACAAUCAGUGC CAAUUCUCAAAACAUGUCGCUGUCCUAGUGUCUC AAGGGAAACUGCUCAGGGCCCACUACAAUCAGUGC CUUAGACAUCCAGGGAUCUGGCGGGAACUUACCU AUUUAAGUCCAGGGUUACAGGGGCAACUUACCU AUUUAAGUCCAGGGAUGCCGGGUAUUGAAGU AGUGUUAUCAGAAAUCUGGGGGCACCUAUGAGG CUCAAGUUCGCAGACAAUCGGGUUUGGGGAACUUACCU AUGAGAUUCCAGAAAUCUGGGGCACCAGUCAGG AUUGCCACAACUGACAGGGAUGUUGGAGGU CUCAGGUUUCAGCAACUGCCUGUUGGGGAACUCCGGU AUUCCAUAUGACAAACUAUCUUGAGCAACCAGUCAGG AUGCUUUCAGCAACUGCAUGGUGUGGGAAAUUCUA UCACAAUUUCAGCAACUGCAUGGGGAAGUUCUA CUCCAGUUGUCAAGGAUGCCGGUUUGGGGAAGUUCAA CUCCAGUUGCCAGCACUGGGUCUGGGAAAUCCCCA ACCGACUCGCUGGCAAUGAGGGUGUUGAAGGAG AUCCAUUCAGCAACUGCGUUAGGGAAAUCCCCA ACCGACUGCAUCCAGGGUUUAGGGAAAUCCCCA ACCGACAUCCAACUGGGUUUACCUCUCAUCUCA | 79 |
| GC_H_MEASLES_D8 mRNA Sequence (assumes T100 tail) Sequence Length: 2126 | G*GGGAAUAAGAGAGAAAAGAAGAUAAGAAGAA UAUAAGAGCCACCAUGUCACCACACGAGACCGGAUA AAUGCCUUCUACAAAGACAACCCCCAUCCUAAGGGAA GUAGAUAGUUAUUAACAGAGAACAUCUUAUGAUUG AUAGACCUUAUUGUCUGCUGCUUCUAUUCGUCA UGUUUCUGAGCUUGAUCGGCUGCUUCUAUUCGAG GAUUCUGAGCUUGAUCGGGCAGCCAUCUACACCGCAGA GAUCCAUAAAAGCCUCAGCACCAAUCUGGAUGUAACU AACUCAAUCGAGCAUCAGGUUAAGGACGUGCUGACAC CACUCUUCAAGAUCAUCGGUGAUGAAGUUGCAU GGACACCUCAGAGAUUCACUGACCUAGUGAAGUUCAU CUCUGACAAGAUAAUCCCUUAGUGUAAGUUCAU UACGACUUCAAGAGUCACUUGACCUAGUGAAGUUCAU | 80 |
| | CAGAGAGAAUCAAUUGGAUUAUGAUCAAUACUGUG CAGAUGUGGCUGCUGAAGAACUCAUGAAUGCAUGG UGAACUCAACUC | |

CCCUGUUGGACUUGUAUUUAAGUCGAGGUUACAAUG UGUCAUCUAUAGUCACUAUGACAUCCCAGGGAAUGUA

TABLE 13-continued

| Description | Sequence | SEQ ID NO: |
|-------------|--|---------------|
| | CGGGGGAACUUACCUAGUGGAAAAGCCUAAUCUGAGC | |
| | AGCAAAGGGUCAGAGUUGUCACAACUGAGCAUGCACC | |
| | GAGUGUUUGAAGUAGGUGUUAUCAGAAAUCCGGGUU | |
| | UGGGGGCUCCGGUAUUCCAUAUGACAAACUAUCUUGA | |
| | GCAACCAGUCAGUAAUGAUUUCAGCAACUGCAUGGUG | |
| | GCUUUGGGGGAGCUCAAGUUCGCAGCCCUCUGUCACA | |
| | GGGAAGAUUCUAUCACAAUUCCCUAUCAGGGAUCAGG | |
| | GAAAGGUGUCAGCUUCCAGCUUGUCAAGCUAGGUGUC | |
| | UGGAAAUCCCCAACCGACAUGCAAUCCUGGGUCCCCC | |
| | UAUCAACGGAUGAUCCAGUGAUAGACAGGCUUUACCU | |
| | CUCAUCUCACAGAGGCGUUAUCGCUGACAAUCAAGCA | |
| | AAAUGGGCUGUCCCGACAACACGGACAGAUGACAAGU | |
| | UGCGAAUGGAGACAUGCUUCCAGCAGGCGUGUAAGG | |
| | GUAAAAUCCAAGCACUUUGCGAGAAUCCCGAGUGGAC | |
| | ACCAUUGAAGGAUAACAGGAUUCCUUCAUACGGGGUC | |
| | UUGUCUGUUGAUCUGAGUCUGACAGUUGAGCUUAAA | |
| | AUCAAAAUUGUUUCAGGAUUCGGGCCAUUGAUCACAC | |
| | ACGGUUCAGGGAUGGACCUAUACAAAUCCAACCACAA | |
| | CAAUAUGUAUUGGCUGACUAUCCCGCCAAUGAAGAAC | |
| | CUGGCCUUAGGUGUAAUCAACACAUUGGAGUGGAUA | |
| | CCGAGAUUCAAGGUUAGUCCCAACCUCUUCACUGUUC | |
| | CAAUUAAGGAAGCAGGCGAGGACUGCCAUGCCCCAAC | |
| | AUACCUACCUGCGGAGGUGGAUGGUGAUGUCAAACUC | |
| | AGUUCCAAUCUGGUGAUUCUACCUGGUCAAGAUCUCC | |
| | AAUAUGUUCUGGCAACCUACGAUACUUCCAGAGUUGA | |
| | ACAUGCUGUAGUUUAUUACGUUUACAGCCCAAGCCGC | |
| | UCAUUUUCUUACUUUUAUCCUUUUAGGUUGCCUGUA | |
| | AGGGGGGUCCCCAUUGAAUUACAAGUGGAAUGCUUC | |
| | ACAUGGGACCAAAAACUCUGGUGCCGUCACUUCUGUG | |
| | UGCUUGCGGACUCAGAAUCUGGUGGACAUAUCACUCA | |
| | CUCUGGGAUGGUGGGCAUGGGAGUCAGCUGCACAGCC | |
| | ACUCGGGAAGAUGGAACCAGCCGCAGAUAGUGAUAA | |
| | UAGGCUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCUU | |
| | GGGCCUCCCCCAGCCCUCCUCCCCUUCCUGCACCCG | |
| | UACCCCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCGG | |
| | Саадаалаалаалаалаалаалаалаалаалаалаалаа | |
| | <u>AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA</u> | |
| | AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA | |

TABLE 14

| MeV Amino Acid Sequences | | |
|---------------------------------------|--|---------------|
| Description | Sequence | SEQ ID NO: |
| GC_F_MEASLES_B3.1 ORF Sequence, AA | MGLKVNVSAVFMAVLLTLQTPAGQIHWGNLSKIGVV GIGSASYKVMTRSSHQSLVIKLMPNITLLNNCTRVEIA EYRRLRTVLEPIRDALNAMTQNIRPVQSVASSRHK RPAGVVLAGAALGVATAAQITAGIALHRSMLNSQAID NLRASLETTNQAIEAIRQAGQEMILAVQGVQVINNE LIPSMNQLSCDLIGQKLGLKLRYYTEILSLFGPSLRDP ISAEISIQALSYALGGDINKVLEKLGYSGGDLLGILESR GIKARITHVDTESYFIVLSIAYPTLSEIKGVIVHRLEGVS YNIGSQEWYTTVPKYVATQGYLISNFDESSCTFMPEG TVCSQNALYPMSPLLQECLRGSTKSCARTLVSGSFGN RFILSQGNLIANCASILCKCYTTGTINQDPDKILTYIAA DRCPVVEVNGVTIQVGSRRYPDAVYLHRIDLGPPISLE RLDVGTNLGNAIAKLEDAKELLESSDQILRSMKGLSST SIVYILIAVCLGGLIGIPTLICCCRGRCNKKGEQVGMSR PGLKPDLTGTSKSYVRSL* | 47 |
| GC_F_MEASLES_D8 ORF Sequence, AA | MGLKVNVSVIFMAVLLTLQTPTGQIHWGNLSKIGVVG VGSASYKVMTRSSHQSLVIKLMPNITLLNNCTRVGIAE YRRLLRTVLEPIRDALNAMTQNIRPVQSVASSRRHKR FAGVVLAGAALGVATAAQITAGIALHQSMLNSQAIDN LRASLETTNQAIEAIRQAGQEMILAVQGVQDYINNELI PSMNQLSCDLIGQKLGLKLRYYTEILSLFGPSLRDPIS AEISIQALSYALGGDINKVLEKLGYSGGDLLGILESRGI KARITHVDTESYFIVLSIAYPTLSEIKGVIVHRLEGVSY NIGSQEWYTTVPKYVATQGYLISNFDESSCTFMPEGT VCSQNALYPMSPLLQECLRGSTKSCARTLVSGSFGNR | 48 |

| | MeV Amino Acid Sequences | CEO ID |
|-------------------------------------|---|---------------|
| Description | Sequence | SEQ ID NO: |
| | FILSQGNLIANCASILCKCYTTGTIINQDPDKILTYIAAD HCPVVEVNGVTIQVGSRRYPDAVYLHRIDLGPPISLER LDVGTNLGNAIAKLEDAKELLESSDQILRSMKGLSSTS IVYILIAVCLGGLIGIPALICCCRGRCNKKGEQVGMSRP GLKPDLTGTSKSYVRSL* | |
| GC_H_MEASLES_B3 ORF Sequence, AA | MSPQRDRINAFYKDNPYPKGSRIVINREHLMIDRPYVL LAVLFVMFLSLIGLLAIAGIRLHRAAIYTAEIHKSLSTN LDVTNSIEHQVKDVLTPLPKIIGDEVGLRTPQRFTDLV KFISDKIKFLNPDREYDRRDLTWCINPPERIKLDYDQY CADVAAEELMNALVNSTLLETRTTTQFLAVSKGNCS GPTTIRGQFSNMSLSLLDLYLGRGYNVSSIVTMTSQG MYGGTYLVEKPNLNSKGSELSQLSMYRVPEVGVIRNP GLGAPVFHMTNYFBQPVSNGLGNCMVALGELKLAAL CHGDDSIIPYQGSGKGVSFQLVKLGVKSPTDMQSW VPLSTDDPVVDRLVLSSHEVIADNQAKWAVPTTRT DDKLRMETCFQQACKGKIQALCENPEWVPLKDNRIPS YGVLSVDLSLTVELKIKIASGFGPLITHGSGMDLYKSN CNNVYWLTIPPMRNLALGVINTLEWIPRKVSPNLFTV PIKEAGEDCHAPTYLPAEVDGDVKLSSNLVILPGQDL QYVLATYDTSRVEHAVVYVYSPSRSFSVPYPFLPIK GVPIELQVECFTWDQKLWCRHFCVLADSESGGLITHS GMVGMGVSCTATREDGTNRR* | 49 |
| GC_H_MEASLES_D8 ORF Sequence, AA | MSPQRDRINAFYKDNPHPKGSRIVINREHLMIDRPYVL LAVLFVMFLSLIGLLAIAGIRLHRAAIYTAEIHKSLSTN LDVTNSIEHQVKDVLTPLFKIIGDEVGLRTPQRFTDLV KFISDKIKFLNPDREYDFRDLTWCINPPERIKLDYDQY CADVAAEELMNALVNSTLLETRATNQFLAVSKGNCS GPTTIRGQFSNMSLSLLDLYLSRGYNVSSIVTMTSQGM YGGTYLVEKPNLSSKGSELSQLSMHRVFEVGVIRNPG LGAPVFHMTNYLEQPVSNDFSNCMVALGELKFAALC HREDSITIPYQGSCKGVSFQLVKLGVMKSPTDMQSW VPLSTDDPVIDRLYLSSHRGVIADNQAKWAVPTTRTD DKLRMETCFQQACKGKIQALCENFEWTPLKDNRIFSY GVLSVDLSLTVELKIKIVSGFGPLITHGSGMDLYKSNH NNMYWLTIPPMKNLALGVINTLEWIPRFKVSPNLFTV PIKEAGEDCHAPTYLPAEVDGDVKLSSNLVILPGQDL QVVLATYDTSRVEHAVVYVYSPSRSFSYPYPRLPV RGVPIELQVECFTWDQKLWCRHFCVLADSESGGHITH SGWCMGVSCTATREDGTSRR* | 50 |

TABLE 15

| Туре | Virus Name | GenBank Accession |
|---------------|---|-------------------|
| hemagglutinin | hemagglutinin [Measles virus strain Moraten] | AAF85673.1 |
| hemagglutinin | hemagglutinin [Measles virus strain Rubeovax] | AAF85689.1 |
| hemagglutinin | hemagglutinin [Measles virus] | AAF89824.1 |
| hemagglutinin | hemagglutinin protein [Measles virus] | CAA91369.1 |
| hemagglutinin | hemagglutinin [Measles virus] | BAJ23068.1 |
| hemagglutinin | hemagglutinin protein [Measles virus] | BAB39848.1 |
| hemagglutinin | hemagglutinin [Measles virus] | AAA50551.1 |
| hemagglutinin | RecName: Full = Hemagglutinin glycoprotein | P08362.1 |
| hemagglutinin | hemagglutinin [Measles virus] | AAB63802.1 |
| hemagglutinin | hemagglutinin [Measles virus] | AAA56650.1 |
| hemagglutinin | hemagglutinin [Measles virus] | AAA56642.1 |
| hemagglutinin | hemagglutinin [Measles virus] | AAA74936.1 |
| hemagglutinin | hemagglutinin protein [Measles virus] | BAH56665.1 |
| hemagglutinin | hemagglutinin [Measles virus] | ACC86105.1 |
| hemagglutinin | hemagglutinin [Measles virus strain Edmonston-Zagreb] | AAF85697.1 |
| hemagglutinin | hemagglutinin [Measles virus] | AAR89413.1 |
| hemagglutinin | hemagglutinin [Measles virus] | AAA56653.1 |
| hemagglutinin | RecName: Full = Hemagglutinin glycoprotein | P35971.1 |
| hemagglutinin | Hemagglutinin [Measles virus] | CAB94916.1 |
| hemagglutinin | hemagglutinin [Measles virus] | AAC03036.1 |
| hemagglutinin | hemagglutinin [Measles virus] | AAF85681.1 |
| hemagglutinin | Hemagglutinin [Measles virus] | CAB94927.1 |
| hemagglutinin | Hemagglutinin [Measles virus] | CAB94925.1 |
| hemagglutinin | hemagglutinin protein [Measles virus] | BAB39835.1 |

TABLE 15-continued

| Гуре | Virus Name | GenBank Accession |
|--------------------------------|--|--------------------------|
| hemagglutinin | Hemagglutinin [Measles virus] | CAB94931.1 |
| hemagglutinin | hemagglutinin [Measles virus genotype A] | AFO84712.1 |
| nemagglutinin | hemagglutinin [Measles virus] | AAA56639.1 |
| nemagglutinin | Hemagglutinin [Measles virus] | CAB94926.1 |
| nemagglutinin | hemagglutinin protein [Measles virus] | BAB39836.1 |
| nemagglutinin | Hemagglutinin [Measles virus] | CAB94929.1 |
| nemagglutinin | RecName: Full = Hemagglutinin glycoprotein | P06830.1 |
| nemagglutinin | Hemagglutinin [Measles virus] | CAB94928.1 |
| nemagglutinin | hemagglutinin protein [Measles virus] | BAB39837.1 AAA74935.1 |
| nemagglutinin nemagglutinin | hemagglutinin [Measles virus] hemagglutinin protein [Measles virus] | CAB43780.1 |
| iemagglutinin | hemagglutinin [Measles virus] | BAA09952.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43815.1 |
| emagglutinin | hemagglutinin [Measles virus] | AAF28390.1 |
| emagglutinin | Hemagglutinin [Measles virus] | CAB94923.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43785.1 |
| emagglutinin | hemagglutinin [Measles virus] | ABD34001.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43782.1 |
| nemagglutinin | hemagglutinin protein [Measles virus] | CAB43781.1 |
| emagglutinin | hemagglutinin [Measles virus] | BAH22353.1 |
| emagglutinin | hemagglutinin [Measles virus] | AAC35878.2 |
| emagglutinin | hemagglutinin protein [Measles virus] | AAL86996.1 |
| emagglutinin | hemagglutinin [Measles virus] | CAA76066.2 |
| nemagglutinin | hemagglutinin [Measles virus] | AAA46428.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43803.1 |
| emagglutinin | Hemagglutinin [Measles virus] | CAB94918.1 AAF72162.1 |
| nemagglutinin nemagglutinin | hemagglutinin [Measles virus] hemagglutinin [Measles virus] | AAF72162.1 AAM70154.1 |
| nemagglutinin | hemagglutinin protein [Measles virus] | CAB43776.1 |
| iemagglutinin | hemagglutinin [Measles virus genotype D4] | ACT78395.1 |
| emagglutinin | hemagglutinin [Measles virus genotype D7] | AAL02030.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43789.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43774.1 |
| emagglutinin | Hemagglutinin [Measles virus] | CAB94920.1 |
| emagglutinin | Hemagglutinin [Measles virus] | CAB94922.1 |
| nemagglutinin | hemagglutinin [Measles virus] | ABB59491.1 |
| nemagglutinin | hemagglutinin protein [Measles virus] | BAB39843.1 |
| nemagglutinin | hemagglutinin protein [Measles virus] | CAB43804.1 |
| remagglutinin | hemagglutinin [Measles virus] | AAX52048.1 |
| nemagglutinin | Hemagglutinin [Measles virus] | CAB94930.1 |
| nemagglutinin | hemagglutinin [Measles virus] | AAA74526.1 |
| nemagglutinin | hemagglutinin protein [Measles virus] | CAB43814.1 ABB59493.1 |
| nemagglutinin nemagglutinin | hemagglutinin [Measles virus] hemagglutinin [Measles virus genotype D4] | AAL02019.1 |
| nemagglutinin | Hemagglutinin [Measles virus] | CAB94919.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | AAL86997.1 |
| emagglutinin | hemagglutinin [Measles virus genotype C2] | AAL02017.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43769.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43808.1 |
| emagglutinin | hemagglutinin [Measles virus] | BAO97032.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43805.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43777.1 |
| emagglutinin | hemagglutinin [Measles virus] | AAL67793.1 |
| emagglutinin | hemagglutinin [Measles virus] | AAF89816.1 |
| emagglutinin | hemagglutinin [Measles virus genotype D4] | AAL02020.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43786.1 |
| emagglutinin | hemagglutinin protein [Measles virus strain | AEP40452.1 |
| | MVi/New Jersey.USA/45.05] | |
| emagglutinin | hemagglutinin [Measles virus] | AAA74531.1 |
| emagglutinin | hemagglutinin [Measles virus] | AAB63800.1 |
| emagglutinin emagglutinin | hemagglutinin [Measles virus] hemagglutinin [Measles virus genotype D8] | AAO21711.1 ALE27189.1 |
| iemagglutinin | hemagglutinin protein [Measles virus] | CAB43810.1 |
| iemagglutinin | hemagglutinin [Measles virus] | AAF89817.1 |
| emagglutinin | hemagglutinin [Measles virus] hemagglutinin [Measles virus genotype D6] | AAL02022.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | CAB43800.1 |
| emagglutinin | hemagglutinin protein [Measles virus] | AGA17219.1 |
| nemagglutinin | hemagglutinin protein [Measles virus] | CAB43770.1 |
| emagglutinin | hemagglutinin protein [Measles virus strain | AEP40444.1 |
| | MVI/Texas.USA/4.07] | |
| nemagglutinin | hemagglutinin [Measles virus] | AAX52047.1 |
| emagglutinin | hemagglutinin [Measles virus] | AAB63794.1 |
| nemagglutinin | hemagglutinin [Measles virus] | AAB63796.1 |
| nemagglutinin | hemagglutinin [Measles virus] | AAA74528.1 |
| nemagglutinin | hemagglutinin [Measles virus] | AAB63774.1 |
| emagglutinin | hemagglutinin [Measles virus] | AAB63795.1 |

| TypeVins NameGenBank Accessionhemagglutininhemagglutinin [Measles virus]AAA74519.1fasion proteinfasion protein [Measles virus]AAA765645.1fasion proteinfasion protein [Measles virus]AAA76665.1fasion proteinfasion protein [Measles virus]AAF8568.1fasion proteinfasion protein [Measles virus]AAF8568.1fasion proteinfasion protein [Measles virus]AA78568.1fasion proteinfasion protein [Measles virus]AA78568.1fasion proteinfasion protein [Measles virus]AA78677.1fasion proteinfasion protein [Measles virus]AA78678.1fasion proteinfasion protein [Measles virus]AA7439.4fasion proteinfasion protein [Measles virus]AA7439.4fasion proteinfasion protein [Measles virus]AA7439.4fasion proteinfasion protein [Measles virus]AA7439.4fasion proteinfasion protein [Measles virus]AA74259.1fasion p | MeV NCBI Accession Numbers (Amino Acid Sequences) | | |
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| MVi/Washington.USA/18.08/1]fusion proteinfusion protein [Measles virus]ABY21182.1fusion proteinfusion protein [Measles virus]ALE27284.1fusion proteinfusion protein [Measles virus genotype D8]ALE27184.1fusion proteinfusion protein [Measles virus genotype D8]ALE2734.1fusion proteinfusion protein [Measles virus genotype D8]ALE27314.1fusion proteinfusion protein [Measles virus genotype G3]AFY12712.1fusion proteinfusion protein [Measles virus genotype D8]ALE27368.1fusion proteinfusion protein [Measles virus genotype H1]AIG53713.1unnamed protein product [Measles virus]CAA34588.1fusion proteinfusion protein [Measles virus genotype B3.1]AIY55563.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AAL29688.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AAL29688.1fusion proteinfusion protein [Measles virus genotype B3]AAL29688.1 <t< td=""><td></td><td></td><td></td></t<> | | | |
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| fusion proteinfusion protein [Measles virus genotype D8]ALE27284.1fusion proteinfusion protein [Measles virus]ACA09725.1fusion proteinfusion protein [Measles virus genotype D8]ALE27314.1fusion proteinfusion protein [Measles virus genotype G3]AFY12712.1fusion proteinfusion protein [Measles virus genotype D8]ALE27368.1fusion proteinfusion protein glycoprotein F0; Contains: RecName: Full = Fusion glycoprotein F1; Flags: PrecursorAIG53713.1fusion proteinfusion protein [Measles virus genotype H1]AIG53713.1unnamed protein product [Measles virus genotype B3.1]AIY55563.1fusion proteinfusion protein [Measles virus genotype B3.1]AIY55563.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53701.1fusion proteinfusion protein [Measles virus g | fusion protein | | ABY21182.1 |
| fusion proteinfusion protein [Measles virus]ACA09725.1fusion proteinfusion protein [Measles virus genotype D8]ALE27314.1fusion proteinfusion protein [Measles virus genotype G3]AFY12712.1fusion proteinfusion protein [Measles virus genotype D8]ALE27368.1fusion proteinfusion protein [Measles virus genotype H1]AIG53713.1unnamed protein product [Measles virus genotype H1]AIG53713.1unnamed protein product [Measles virus]CAA34588.1fusion proteinfusion protein [Measles virus]AAIC53703.1fusion proteinfusion protein [Measles virus genotype H3]AIC53703.1fusion proteinfusion protein [Measles virus genotype H3]AGA17208.1fusion proteinfusion protein [Measles virus genotype H3]AGA3703.1fusion proteinfusion protein [Measles virus genotype H3]AGA3706.1fusion proteinfusion protein [Measles virus genotyp | | | |
| fusion proteinfusion protein [Measles virus genotype D8]ALE27314.1fusion proteinfusion protein [Measles virus genotype G3]AFY12712.1fusion proteinfusion protein [Measles virus genotype G3]ALE27368.1fusion proteinRecName: Full = Fusion glycoprotein F0; Contains: RecName: Full = Fusion glycoprotein F1; Flags: PrecursorBAG53713.1fusion proteinfusion protein [Measles virus genotype H1]AIG53713.1fusion proteinfusion protein [Measles virus genotype H1]AIG53713.1fusion proteinfusion protein [Measles virus]CAA34588.1fusion proteinfusion protein [Measles virus]CAA7688.1fusion proteinfusion protein [Measles virus genotype B3.1]AIY55563.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AGA25706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53701.1fusion proteinfusion protein [Measles virus genotype B3]ALE27092.1 | | | |
| fusion protein fusion protein fusion protein [Measles virus genotype D8] ALE27368.1 fusion protein RecName: Full = Fusion glycoprotein F0; Contains: RecName: Full = Fusion glycoprotein F1; Flags: Precursor P35973.1 fusion protein fusion protein [Measles virus genotype H1] AIG53713.1 unnamed protein product [Measles virus] CAA34588.1 fusion protein fusion protein [Measles virus] CAA34588.1 fusion protein fusion protein [Measles virus] CAA76888.1 fusion protein fusion protein [Measles virus] ADO17330.1 fusion protein fusion protein [Measles virus genotype B3] AGA17208.1 fusion protein fusion protein [Measles virus genotype H1] AIG53703.1 fusion protein fusion protein [Measles virus genotype B3] AGA17208.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H3] AIG53706.1 fusion prote | fusion protein | fusion protein [Measles virus genotype D8] | ALE27314.1 |
| fusion protein RecName: Full = Fusion glycoprotein F0; Contains: P35973.1 RecName: Full = Fusion glycoprotein F2; Contains: RecName: Full = Fusion glycoprotein F2; Contains: RecName: Full = Fusion glycoprotein F1; Flags: Precursor fusion protein fusion protein [Measles virus genotype H1] AIG53713.1 nunnamed protein product [Measles virus] CAA34588.1 fusion protein fusion protein [Measles virus] CAA76888.1 fusion protein fusion protein [Measles virus genotype B3.1] AIY55563.1 fusion protein fusion protein [Measles virus genotype H1] AIG53703.1 fusion protein fusion protein [Measles virus genotype B3] AGA17208.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H3] AIG53706.1 fusion protein fusion protein [Measles virus genotype H3] AIG53706.1 fusion protein fusion protein [Measles virus genotype H3] AIG53706.1 <td>fusion protein</td> <td>fusion protein [Measles virus genotype G3]</td> <td>AFY12712.1</td> | fusion protein | fusion protein [Measles virus genotype G3] | AFY12712.1 |
| RecName: Full = Fusion glycoprotein F2; Contains: RecName: Full = Fusion glycoprotein F1; Flags: Precursorfusion proteinfusion protein [Measles virus genotype H1]AIG53713.1 CAA34588.1fusion proteinfusion protein [Measles virus]CAA3688.1fusion proteinfusion protein [Measles virus]CAA76888.1fusion proteinfusion protein [Measles virus genotype B3.1]AIY55563.1fusion proteinfusion protein [Measles virus genotype H3]AG017330.1fusion proteinfusion protein [Measles virus genotype H3]AGA17208.1fusion proteinfusion protein [Measles virus genotype H3]AGA17208.1fusion proteinfusion protein [Measles virus genotype H3]AG253706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H3]AIG53701.1fusion proteinfusion protein [Measles virus genotype H3]ALE27092.1 | fusion protein | | ALE27368.1 |
| RecName: Full = Fusion glycoprotein F1; Flags: Precursorfusion proteinfusion protein [Measles virus genotype H1]AIG53713.1unnamed protein product [Measles virus]CAA34588.1fusion proteinfusion protein [Measles virus]CAA3688.1fusion proteinfusion protein [Measles virus]AIY55563.1fusion proteinfusion protein [Measles virus]AD017330.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AGA29688.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype B3]ALE27092.1 | fusion protein | | P35973.1 |
| fusion proteinfusion protein [Measles virus genotype H1]AIG53713.1unnamed protein product [Measles virus]CAA34588.1fusion proteinfusion protein [Measles virus]CAA7688.1fusion proteinfusion protein [Measles virus]CAA7688.1fusion proteinfusion protein [Measles virus]AD017330.1fusion proteinfusion protein [Measles virus]AD017330.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H3]AIG53701.1fusion proteinfusion protein [Measles virus genotype H3]AIE27092.1 | | | |
| unnamed protein product [Measles virus]CAA34588.1fusion proteinfusion protein [Measles virus]CAA76888.1fusion proteinfusion protein [Measles virus]CAA76888.1fusion proteinfusion protein [Measles virus]AD017330.1fusion proteinfusion protein [Measles virus]AD017330.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53701.1fusion proteinfusion protein [Measles virus genotype B3]ALE27092.1 | fusion protein | | AIG53713.1 |
| fusion proteinfusion protein [Measles virus]CAA76888.1fusion proteinfusion protein [Measles virus genotype B3.1]AIY55563.1fusion proteinfusion protein [Measles virus]ADO17330.1fusion proteinfusion protein [Measles virus genotype H1]AIG53703.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype H1]AIC53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53701.1fusion proteinfusion protein [Measles virus genotype H3]ALE27092.1 | • - | | |
| fusion proteinfusion protein [Measles virus]ADO17330.1fusion proteinfusion protein [Measles virus genotype H1]AIG53703.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53701.1fusion proteinfusion protein [Measles virus genotype H2]AIG53701.1fusion proteinfusion protein [Measles virus genotype B3]ALE27092.1 | | fusion protein [Measles virus] | CAA76888.1 |
| fusion proteinfusion protein [Measles virus genotype H1]AIG53703.1fusion proteinfusion protein [Measles virus genotype B3]AGA17208.1fusion proteinfusion protein [Measles virus]AAL29688.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53701.1fusion proteinfusion protein [Measles virus genotype B3]ALE27092.1 | | | AIY55563.1 |
| fusion protein fusion protein [Measles virus genotype B3] AGA17208.1 fusion protein fusion protein [Measles virus] AAL29688.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H1] AIG53701.1 fusion protein fusion protein [Measles virus genotype B3] ALE27092.1 | fusion protein | fusion protein [Measles virus] | |
| fusion proteinfusion protein [Measles virus]AAL29688.1fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53701.1fusion proteinfusion protein [Measles virus genotype B3]ALE27092.1 | | | |
| fusion proteinfusion protein [Measles virus genotype H1]AIG53706.1fusion proteinfusion protein [Measles virus genotype H1]AIG53701.1fusion proteinfusion protein [Measles virus genotype B3]ALE27092.1 | | | |
| fusion proteinfusion protein [Measles virus genotype H1]AIG53701.1fusion proteinfusion protein [Measles virus genotype B3]ALE27092.1 | | | |
| fusion protein [Measles virus genotype B3] ALE27092.1 | iusion protein | | |
| | | | |
| Tuston protein Tuston protein [Measles virus genotype H1] AIG53/14.1 | | | |
| | iusion protein | iusion protein [measies virus genotype H1] | AIU00714.1 |

TABLE 15-continued

| Туре | Virus Name | GenBank Accessio |
|----------------|---|--------------------------|
| fusion protein | fusion protein [Measles virus genotype H1] | AIG53694.1 |
| fusion protein | fusion protein [Measles virus genotype 111] | AIG53668.1 |
| fusion protein | fusion protein [Measles virus] | ACC86094.1 |
| iusion protein | fusion protein [Measles virus] | AIG53670.1 |
| fusion protein | fusion protein [Measles virus genotype H1] | AIG53070.1 |
| fusion protein | fusion protein [Measles virus genotype B3] | AGA17216.1 |
| fusion protein | fusion protein [Measles virus genotype B3] | AIG53671.1 |
| fusion protein | fusion protein [Measles virus strain | AEP40451.1 |
| usion protein | MVi/New Jersey.USA/45.05] | AEI 40451.1 |
| usion protein | fusion protein [Measles virus genotype H1] | AIG53684.1 |
| usion protein | fusion protein [Measles virus genotype H1] | AIG53688.1 |
| usion protein | fusion protein [Measles virus genotype B3] | AGA17214.1 |
| fusion protein | fusion protein [Measles virus genotype H1] | AIG53683.1 |
| usion protein | fusion protein [Measles virus genotype H1] | AIG53667.1 |
| usion protein | fusion protein [Measles virus genotype H1] | AIG53686.1 |
| lusion protein | fusion protein [Measles virus genotype H1] | AIG53685.1 |
| lusion protein | fusion protein [Measles virus genotype H1] | AIG53681.1 |
| • | unnamed protein product [Measles virus] | CAA34589.1 |
| lusion protein | fusion protein [Measles virus genotype H1] | AIG53678.1 |
| fusion protein | fusion protein [Measles virus genotype H1] | AIG53710.1 |
| iusion protein | fusion protein [Measles virus genotype H1] | AIG53669.1 |
| iusion protein | fusion protein [Measles virus genotype H1] | AIG53664.1 |
| fusion protein | fusion protein [Measles virus] | AAA50547.1 |
| fusion protein | fusion protein [Measles virus genotype H1] | AIG53679.1 |
| fusion protein | fusion protein [Measles virus genotype 111] | AIG53709.1 |
| fusion protein | fusion protein [Measles virus genotype H1] | AIG53672.1 |
| usion protein | fusion protein [Measles virus genotype H1] | AIG53697.1 |
| fusion protein | fusion protein [Measles virus genotype H1] | AIG53689.1 |
| • | fusion protein [Measles virus genotype H1] | AIG53676.1 |
| fusion protein | fusion protein [Measles virus genotype H1] | AIG53675.1 |
| fusion protein | | |
| fusion protein | fusion protein [Measles virus genotype H1] | AIG53663.1 |
| usion protein | fusion protein [Measles virus] | BAA19841.1 |
| fusion protein | fusion protein [Measles virus] | AAF02701.1 |
| usion protein | fusion protein [Measles virus genotype H1] | AIG53680.1 |
| fusion protein | fusion protein [Measles virus genotype H1] | AIG53674.1 |
| c protein | C protein [Measles virus strain Moraten] | AAF85670.1 |
| C protein | RecName: Full = Protein C | P03424.1 |
| C protein | C protein [Measles virus] | ACN54404.1 |
| C protein | C protein [Measles virus] | ACN54412.1 |
| C protein | RecName: Full = Protein C | P35977.1 |
| C protein | C protein [Measles virus] | AAF85678.1 |
| C protein | C protein [Measles virus] | ABD33998.1 |
| C protein | unnamed protein product [Measles virus] | CAA34586.1 |
| C protein | C protein [Measles virus] | BAJ51786.1 |
| C protein | C protein [Measles virus] | BAA33869.1 |
| C protein | virulence factor [Measles virus] | ABO69700.1 |
| C protein | C protein [Measles virus] | NP_056920.1 |
| C protein | C protein [Measles virus] | ADO17333.1 |
| C protein | C protein [Measles virus] | ACC86082.1 |
| C protein | C protein [Measles virus] | BAA33875.1 |
| C protein | C protein [Measles virus] | ABY21189.1 |
| C protein | C protein [Measles virus] | BAE98296.1 |
| C protein | C protein [Measles virus] | ADU17782.1 |
| C protein | C protein [Measles virus strain | AEP40417.1 |
| - | MVi/Virginia.USA/15.09] | |
| C protein | C protein [Measles virus] | ADU17814.1 |
| C protein | C protein [Measles virus] | ADU17798.1 |
| C protein | C protein [Measles virus genotype D4] | AFY12700.1 |
| C protein | C protein [Measles virus] | ADU17784.1 |
| C protein | C protein [Measles virus strain | AEP40465.1 |
| | MVi/California.USA/16.03] | |
| C protein | C protein [Measles virus] | ABB71643.1 |
| C protein | C protein [Measles virus] | AEI91027.1 |
| C protein | C protein [Measles virus] | ADU17874.1 |
| C protein | C protein [Measles virus] | ADU17903.1 |
| C protein | C protein [Measles virus] | CAA34579.1 |
| C protein | C protein [Measles virus] | ADU17790.1 |
| | C protein [Measles virus] | ADU17790.1 ADU17800.1 |
| C protein | C protein [Measles virus] | |
| C protein | C protein [Measles virus] | ABB71667.1 |
| C protein | unnamed protein product [Measles virus] | CAA34572.1 |
|] protein | C protein [Measles virus strain | AEP40433.1 |
| - | MVi/Arizona.USA/11.08/2] | |
| protein [| C protein [Measles virus] | ADU17830.1 |
| C protein | C protein [Measles virus] | ADU17947.1 |
| C protein | C protein [Measles virus] | ADU17818.1 |
| c protein | 1 L J | |

TABLE 15-continued

| Туре | Virus Name | GenBank Accessio |
|--|--|--------------------------|
| туре | vitus ivalle | Gendank Accessio |
| a . : | MVi/New Jersey,USA/45.05] | |
| C protein | C protein [Measles virus strain MV//Terres LISA/4.07] | AEP40441.1 |
| C protein | MVi/Texas.USA/4.07] C protein [Measles virus] | ADU17864.1 |
| C protein | C protein [Measles virus] | ADU17838.1 |
| C protein | C protein [Measles virus] | ADU17881.1 |
| C protein | C protein [Measles virus strain | AEP40425.1 |
| | MVi/Washington.USA/18.08/1] | |
| C protein | C protein [Measles virus] | ADU17927.1 |
| C protein | C protein [Measles virus] | ADU17953.1 |
| C protein | C protein [Measles virus] | ADU17889.1 |
| C protein | C protein [Measles virus] | ADU17963.1 |
| C protein | C protein [Measles virus] | ADU17893.1 |
| C protein | C protein [Measles virus] | ADU17820.1 |
| C protein | C protein [Measles virus] | ABB71651.1 |
| C protein | C protein [Measles virus] | ADU17786.1 |
| C protein | C protein [Measles virus] C protein [Measles virus] | ADU17862.1 ADU17923.1 |
| C protein C protein | C protein [Measles virus] C protein [Measles virus] | ADU17923.1 ADU17959.1 |
| C protein | C protein [Measles virus] | ADU17959.1 ADU17951.1 |
| C protein | C protein [Measles virus] | ADU179916.1 |
| C protein | C protein [Measles virus] | ADU17957.1 |
| C protein | C protein [Measles virus] | ADU17925.1 |
| C protein | C protein [Measles virus] | ADU17901.1 |
| C protein | C protein [Measles virus] | ADU17887.1 |
| C protein | C protein [Measles virus] | ADU17832.1 |
| C protein | C protein [Measles virus] | ADU17891.1 |
| C protein | C protein [Measles virus] | ADU17961.1 |
| C protein | C protein [Measles virus] | ADU17872.1 |
| C protein | C protein [Measles virus] | ADU17929.1 |
| C protein | C protein [Measles virus] | ADU17908.1 |
| C protein | C protein [Measles virus] | ADU17910.1 |
| C protein | C protein [Measles virus] | ADU17921.1 |
| C protein | C protein [Measles virus] | ADU17824.1 |
| C protein | C protein [Measles virus strain MVi/Pennsylvania.USA/20.09] | AEP40473.1 |
| C protein | C protein [Measles virus] | ADU17828.1 |
| C protein | C protein [Measles virus] | ADU17812.1 |
| C protein | C protein [Measles virus genotype D8] | AFY12692.1 |
| C protein | nonstructural C protein [Measles virus] | ABA59559.1 |
| C protein | RecName: Full = Protein C | Q00794.1 |
| C protein | nonstructural C protein [Measles virus] | ADO17934.1 |
| C protein | nonstructural C protein [Measles virus] | ACJ66773.1 |
| C protein | C protein [Measles virus genotype G3] | AFY12708.1 |
| C protein | RecName: Full = Protein C | P26035.1 |
| C protein | C protein [Measles virus] | BAA84128.1 |
| nucleoprotein | RecName: Full = Nucleoprotein; AltName: | Q77M43.1 |
| | Full = Nucleocapsid protein; | |
| | Short = NP; Short = Protein N | |
| nucleoprotein | nucleocapsid protein [Measles virus strain Rubeovax] | AAF85683.1 |
| nucleoprotein | RecName: Full = Nucleoprotein; AltName: | Q89933.1 |
| | Full = Nucleocapsid protein; Short = NP; Short = Protein N | |
| nucleoprotein | short = NP; Short = Protein N mucleocapsid protein [Measles virus strain AIK-C] | AAF85659.1 |
| nucleoprotein | nucleoprotein [Measles virus] | ABI54102.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAA56643.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAC03050.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAA18990.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAA56640.1 |
| nucleoprotein | RecName: Full = Nucleoprotein; AltName: | P35972.1 |
| | Full = Nucleocapsid protein; | |
| | Short = NP; Short = Protein N | |
| nucleoprotein | RecName: Full=Nucleoprotein; AltName: | P10050.1 |
| | Full = Nucleocapsid protein; | |
| | Short = NP; Short = Protein N | |
| nucleoprotein | N protein [Measles virus] | BAB60956.1 |
| nucleoprotein | RecName: Full = Nucleoprotein; AltName: | BIAAA7.1 |
| | Full = Nucleocapsid protein; | |
| | Short = NP; Short = Protein N | |
| nucleoprotein | nucleoprotein [Measles virus] | AAA18991.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46894.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46871.1 |
| | pucieoprotein (Menciec surgia) | CAB46872.1 |
| nucleoprotein | nucleoprotein [Measles virus] | |
| nucleoprotein nucleoprotein | nucleoprotein [Measles virus] | ABU49606.1 |
| nucleoprotein nucleoprotein nucleoprotein nucleoprotein | | |

| MeV NCBI Accession Numbers (Amino Acid Sequences) | | |
|--|---|--------------------------|
| Туре | Virus Name | GenBank Accession |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46892.1 |
| nucleoprotein | unnamed protein product [Measles virus] | CAA34584.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAA18997.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46863.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AEF30352.1 |
| nucleoprotein nucleoprotein | nucleoprotein [Measles virus] nucleocapsid protein [Measles virus] | ABI54103.1 AAA46433.1 |
| nucleoprotein | mucleoprotein [Measles virus] | CAB46902.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46873.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46906.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAA74547.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAA74537.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46862.1 |
| nucleoprotein | nucleocapsid protein [Measles virus] | BAA09961.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAO15875.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAO15871.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46882.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB60124.1 |
| nucleoprotein | nucleoprotein [Measles virus] | ABI54104.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46869.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46880.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAA74541.1 |
| nucleoprotein | nucleocapsid protein [Measles virus strain | AEP40446.1 |
| | MVi/New Jersey.USA/45.05] | ADIE 4110.1 |
| nucleoprotein | nucleoprotein [Measles virus] nucleoprotein [Measles virus] | ABI54110.1 CAB46903.1 |
| nucleoprotein nucleoprotein | nucleoprotein [Measles virus] | CAB46899.1 |
| nucleoprotein | mucleoprotein [Measles virus] | CAB46901.1 |
| nucleoprotein | mucleocapsid protein [Measles virus] | ABB71640.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB60113.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB60114.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB60116.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46895.1 |
| nucleoprotein | nucleoprotein Measles virus | CAB60121.1 |
| nucleoprotein | nucleoprotein [Measles virus] | ABI54111.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46889.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46898.1 |
| nucleoprotein | nucleoprotein [Measles virus genotype B3] | ALE27083.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB60118.1 |
| nucleoprotein | nucleocapsid protein [Measles virus] | CAA34570.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAC29443.1 |
| nucleoprotein | nucleocapsid protein [Measles virus strain MVi/Washington.USA/18.08/1] | AEP40422.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAO15872.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46874.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAA74550.1 |
| nucleoprotein | nucleocapsid protein [Measles virus] | ABB71648.1 |
| nucleoprotein nucleoprotein | nucleoprotein [Measles virus] nucleoprotein [Measles virus] | CAB46900.1 BAH22440.1 |
| nucleoprotein | nucleocapsid protein [Measles virus] | AAA46432.1 |
| nucleoprotein | nucleocapsid protein [Measles virus] | BAA33867.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAA74539.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB60115.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB60123.1 |
| nucleoprotein | nucleocapsid protein [Measles virus] | ABB71664.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB60125.1 |
| nucleoprotein | nucleoprotein Measles virus | AAA74546.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46886.1 |
| nucleoprotein | nucleoprotein [Measles virus] | BAH22350.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB46867.1 |
| nucleoprotein | nucleocapsid protein [Measles virus] | BAA09954.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAO15873.1 |
| nucleoprotein | nucleocapsid protein [Measles virus] | AEP95735.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAL37726.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAA74549.1 |
| nucleoprotein | RecName: Full = Nucleoprotein; AltName: Full = Nucleocapsid protein; | P26030.1 |
| | Short = NP; Short = Protein N | |
| nucleoprotein | nucleoprotein [Measles virus ETH55/99] | AAK07777.1 |
| nucleoprotein | nucleoprotein [Measles virus genotype B3] | AGA17238.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AEF30351.1 |
| nucleoprotein | nucleoprotein [Measles virus genotype B3] | AGA17242.1 |
| | nucleoprotein [Measles virus ETH54/98] | AAK07776.1 |
| nucleoprotein | | |
| nucleoprotein | nucleoprotein [Measles virus] | AAA74548.1 |
| nucleoprotein nucleoprotein nucleoprotein nucleoprotein | | |

TABLE 15-continued

| Туре | Virus Name | GenBank Accession |
|------------------------|---|------------------------------|
| nucleoprotein | nucleoprotein [Measles virus] | AAA19223.1 |
| nucleoprotein | nucleoprotein [Measles virus genotype B3] | AGA17241.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAB60122.1 |
| nucleoprotein | nucleoprotein [Measles virus] | CAC34599.1 |
| nucleoprotein | nucleoprotein [Measles virus] | AAC03042.1 |
| nucleoprotein | mucleoprotein [Measles virus] | CAC34604.1 |
| nucleoprotein | mucleoprotein [Measles virus] | AAA74544.1 |
| nucleoprotein | mucleocapsid protein [Measles virus] | NP 056918.1 |
| V Protein | RecName: Full = Non-structural protein V | Q9IC37.1 |
| V Protein | RecName: Full = Non-structural protein V | Q9EMA9.1 |
| V Protein | V protein [Measles virus] | ACN54411.1 |
| V Protein | V protein [Measles virus] | ACN54403.1 |
| V Protein | V protein [Measles virus] | AEP95742.1 |
| V Protein | V protein [Measles virus strain | AEP40416.1 |
| v 110tem | MVi/Virginia.USA/15.09] | ALA 40410.1 |
| V Protein | V protein [Measles virus] | ADU17801.1 |
| V Protein | V protein [Measles virus] | ADU17801.1 ADU17849.1 |
| V Protein V Protein | V protein [Measles virus] | ABB71642.1 |
| V Protein | | |
| V Protein | V protein [Measles virus genotype D8] | AFY12693.1 |
| V Protein | V protein [Measles virus] | YP_003873249.2 AEP40432.1 |
| v Protein | V protein [Measles virus strain | AEP40432.1 |
| IZ Durata las | MVi/Arizona.USA/11.08/2] | D2 (0)(1) |
| V Protein | RecName: Full = Non-structural protein V | P26036.1 |
| V Protein | V protein [Measles virus strain | AEP40464.1 |
| VD 4 1 | MVi/California.USA/16.03] | |
| V Protein | V protein [Measles virus strain | AEP40456.1 |
| | MVi/California.USA/8.04] | |
| V Protein | V protein [Measles virus] | ABY21188.1 |
| V Protein | V protein [Measles virus strain | AEP40424.1 |
| | MVi/Washington.USA/18.08/1] | |
| V Protein | V protein [Measles virus] | BAH96581.1 |
| V Protein | V protein [Measles virus] | ABB71666.1 |
| V Protein | RecName: Full = Non-structural protein V | P60168.1 |
| V Protein | V protein [Measles virus] | BAH96589.1 |
| V Protein | V protein [Measles virus] | ADU17954.1 |
| V Protein | V protein [Measles virus strain | AEP40400.1 |
| | MVi/New York.USA/26.09/3] | |
| V Protein | V protein [Measles virus] | ABY21196.1 |
| V Protein | virulence factor [Measles virus] | ABO69701.1 |
| V Protein | V protein [Measles virus] | ABB71650.1 |
| V Protein | V protein [Measles virus] | ACC86086.1 |
| V Protein | V protein [Measles virus genotype D4] | AFY12702.1 |
| V Protein | V protein [Measles virus strain | AEP40448.1 |
| | MVi/New Jersey.USA/45.05] | |
| V Protein | V protein [Measles virus] | BAE98295.1 |
| V Protein | V protein [Measles virus] | ACC86083.1 |
| V Protein | V protein [Measles virus] | ACU5139.1 |
| V Protein | V protein [Measles virus] | ADO17334.1 |
| V Protein | V protein [Measles virus] | ADU17930.1 |
| V Protein | V protein [Measles virus genotype G3] | AFY12710.1 |
| V Protein | V protein [Measles virus genotype 05] | AEP40472.1 |
| , Hotelli | | ALI 40472.1 |
| 17 D 4 1 | MVi/Pennsylvania.USA/20.09] | A DI 11 2000 1 |
| V Protein | phosphoprotein [Measles virus] | ADU17839.1 |
| V Protein | V protein [Measles virus] | ADU17894.1 |
| V Protein | V protein [Measles virus] | ACN50010.1 |
| V Protein | V protein [Measles virus] | ADU17892.1 |
| | unnamed protein product [Measles virus] | CAA34585.1 |
| V Protein | V protein [Measles virus] | ABD33997.1 |

TABLE 16

| Name | Sequence | SEQ ID NO: |
|--------------------------------|--|---------------|
| | Flagellin Nucleic Acid Sequences | |
| NT (5' UTR, ORF, 3' UTR) | TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACTCACTAT AGGGAAATAAGAGAGAAAAGAAGAGAGTAAGAAGAAATATAAG AGCCACCATGGCACAAGTCATTAATACAAACAGCCTGTCGCTG TTGACCCAGAATAACCTGAACAAATCCCAGTCCGCACTGGGGCA CTGCTATCGAGGCGTTGGCTCTCCGGTATCCAACAGCGG AAAGACGATGCGGCAGGCCAGGC | 51 |

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TABLE 16-continued

| Name | Sequence | SEQ ID NO: |
|--|---|---------------|
| | Sequence | |
| ORF Sequence, NT | CTTCTTGCCCCTGGGCCTCCCCCCAGCCCCTCCTCCCCCCTCCTG CACCCGTACCCCCGTGGTCTTTGAATAAAGTCTGAGTGGGGGGGC ATGGCACAAGTCATTAATACAAACAGCCTGTCGCTGTTGACCC AGAATAACCTGAACAAATCCCAGTCCGCACTGGGCACTGCTAT CGACGGTTGTCTTCCGGTCTGCGTATCAACGGCGACTGCTAT CGACGGCAGGACAGCAGGCGTTGCAACCGTTTACCGCGAACA TCAAAGGTCTGACTCAGGCTTCCCGTAACGCATTACCGCGAACA ACGACCTGCAGCCGTGGCGTGAACGAACACAC AACAACCTGCAGGCCGTGAACGACTCCAGCCTGAACGACAT CTCAATGCCAGCCTGTGCCTGAACCGCGTCAGCTGCGGA ATGGTACTAACTCCAGTCTGACCTCGACTCCAGGCTGAA ATCACCCAGCGCCTGAACGAAATCCAACCTGGCAGGA CTCAGTTCAACGGCGGTGAAAGTCCTGGCGCGGAGACAACACCCT GACCATCCAGGTGGTGCAACGACGGTGAAACTACCGGCAGA CTCAGTTCAACGGCGTGAAAGTCCTGGCGCGGGAGAACACCCCT GACCATCCAGGTGGTGCCAACGACGGGAGAACACCCCT GACCATCCAGGTGGTGCCAACGACGGGAGAACACCCCT GACCATCCAGGTGGTGCCAACGCCGGAAAGAACTGCTGTAAC CGTTGATAAAGAATCAGCTCTAAAACACTGGGACTGGTAAAC CGTTGATAAAGAATCACCTATAAAAATGGTACAGATCGCTGTAAC GCCCAGAGCATACTGGGCTGATATCAAATTGATACA GCCCAGAGCATACTGGGGCTGATACCAAGGACGTGGTGTCA ATACTTATTAGATGTATAAACTACCAAGAGAGTTAATATTGATAC GACTGATAAAACTCCGTTGGCAACTGCGGAAGCTACAGCTAT CGGGGAACGGCCCATATAACCACACGTGCGGAAGCTACAGCTAT CGGGGAACGGCCCATATAACCCACAACTACGACAACTACGCTTAT CGGGGAACGGCCCATATAACCCACAACTACGGCTGAACTAC CAAAGAGGGGTGTTACTGGCGCCGATAAGGCTAATTGCGGCTACA CAAAGAGGGGCTTACTGGCGCCGATAAGGACAATACTAGCCTT GTAAAACTATCGTTGGAGGATAAAACGGTAAGGTAA | 52 |
| mRNA Sequence (assumes T100 tail) | TACTGCGT G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAUAUAA GAGCCACCAUGGCACAAGUCAUUAAUACAAACAGCCUGUCGC UGUUGACCCAGAAUAACCUGAACAAAUCCCAGUCCGCACUGG GCACUGCUAUCGAGCGUUUGUCUUCCGGUCUGCGUAUCAACA | 53 |

GCGCGAAAGACGAUGCGGCAGGACAGGCGAUUGCUAACCGUU UUACCGCGAACAUCAAAGGUCUGACUCAGGCUUCCCGUAACG

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TABLE 16-continued

| SEQ ID NO: |
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| Name | Sequence | SEQ ID NO: |
|--|---|---------------|
| | CGCAAAACGUCCUCUCUUUACUGCGUUGAUAAUAGGCUGGAG CCUCGGUGGCCAUGCUUCUUGCCCCUUGGGCCUCCCCCAGC CCCUCCUCCCCUUCCUGCACCCGUACCCCCGUGGUCUUUGAA UAAAGUCUGAGUGGGCGGC | |
| ORF Sequence, NT | AUGGCACAAGUCAUUAAUACAAACAGCCUGUCGCUGUUGACC CAGAAUAACCUGAACAAAUCCCAGUCCGCACUGGCACUGCU AUCGAGCGUUUGUCUUCCGGUCUGCGUAUCAACAGCGCGAAA GACGAUGCGCCAGGACAGGCGUUCCCGUAACGCUAACGAC GGUAUCUCCAUUGCGCAGACCACUGAAGGCCGCCUGAACGAC GGUAUCUCCAUUGCGCAGACCACUGAAGGCCGCCUGAACGAA AUCAAAAGACACACCACUGAAGCUCCCGUGAACGCUAACGAC GGUAUCUCCAUUGCGCAGACCCAUGAAGCCGCUCAACGAC CAGGCUGAAUGCACACCCAGGCGUGAACUGGCGGUUCAG UCUGCGAAUGGUACUAACGCCUGAACUCGACCUCCACUCCAUC CAGGCUGAAUCACCCAGGCCUGAACGAAAUCGACCGUGAA AUCACACACCCUGACCAUCCAGGUUGAGCUCAACGCCGUGAA ACUAUCGAUAUGACUAACGGCCUGAAAGUCCUGGCGCAG GACAACACCCUGACCAUCCAGGUUGAUGACGCUCUAAAAACCU CGGACUUGAUAAGCUUAAUGUCCAAGAUGCCUACACCCCGGA AGAACUGCUGUAACGCUUGAUAAAAUCAGCUCUUAAAAAGG GUACAGAUCCUUUUACAGCCCAGGGGUUACUGGGCUGAU AUCAAAUUUAAAGAUGUCCAAGAUGCUAUAUAAAAGG CUGCAAUUGGCGGUGGUGCAACGGGGUUACUGGGGCUGAU AUCAAAUUUAAAGAUGGUCAUAUUUUGAUGAGAUGUUAAAAGG CGGGCCUUCUGCUGGUGUUAUUAUAUCGACUGUUAUAAAGG CUGCAACUGCGGAAGCUACAGCUAUUUUGAUGAAACUCCG UUGGCAACUGCGGAAGCUACAGCUAUUUUGAUGAAACUCCG UUGGCAACUGCGGAAGCUACAGCUAUUUGAGGAACGGCCACU AUAACAAUGGGGUUACUAGGCCUAUUUGAGGAACGGCCACU AUAACCACCACAACUAGCUAUUUGAUGAGAACGGCUAU GGUGCUUCUGCUGGGUACAACUACUUGUGCACAGGGGU UUGGCAACUGCGGAAGCUACAGCUUUGUGAGCAGGGGU UUGGCAACUGCGGUAACAGCUAUUGCUGAGCAGGGGU UUGGCAACUGCGGAAUUACUGAACUACUACUACUAACUACU GUUUGAGGAUAAAACCGGUAAGGUUAUUGAGGUGGCUAUG CAGGAAAAGGGCGAAUUACUGCAACUACUUAUAAA GAUGGUCUCCGCUUAAAACCGUUAUGAGAACUACUUAUACA GAAAACAGGGGGACGAAUUACUGCAACUACUUAUACA GAACAGCGGUGAAAUUACUGCAACUGCUAAACCACUAUUACA GAACAGGGGGUAAAAUCUGAAACUGGAACCACUUAAACA GAACAGGGGUGAAAUUCUGAAGCUUUGUAACACUACUUAUACA GAACACGCGUUAAAAGCGUUAAAGACUUGCUACGAUAACAUUACA GAACAGCGGUGAACUUAAAGGGUUAAUACAGAUAACAUAACUUCA GAACACCACUUCCAACUGGGCACUUAGCACAGAUAACCUGAAACUUCA GAACAGCGGUGAACUUAAAGGUUAAUACGGUUAAAACCUG UCUUCUGCCCGUAGCCGUAUCGAACCGGUUCGAAACCGUUUCA AACUCCACCAUUCGACCGGCAAUACCGUAAAUACCGGAAUCCGGAAACCUGCACAGCUUC GAAGCCUCCAUCAGACGUAUCGGCGAAUACCGUAAAUACCUG GAACCUCCACAUUCUGGCGCGCAGAUUCCGCACAGGUUCGCAAACCUGGCC GAAGUCUCCACACAUUCUGCGCGCACAGCUUCGCACAGGUUCGCAAACCUGCACAGCUUCGACCGAGAUUCCGCCGAAAACCUACGUAAACCUGAAACCUGAAACCUGAACCUGCCCUUACGACAACCUGAAAC | 82 |
| mRNA Sequence (assumes T100 tail) | G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAAUAUAA GAGCCACCAUGGCACAGUCAUUAAUACAAACAGCCUGUCGC UGUUGACCCAGGAUAACCUGAACAAAUCCCAGUCCGCACUGG GCACUGCUAUCGAGCGUUUGCUCCGUUCGCGUAUCGAACA GCGCGAAAGAUCAAAGGUCUGACUCAGGCUUCCCGUAUCAACA GCGCGAACAUCAAAGGUCUGACUCAGGCUUCCCGUAUCAACG CUAACGACGUUAUCUCCAUUGGCAGACACUGAAGGGCGC UGAACGAAUCAACAACACCUGCAGCGUGUGCGUGACUGG CUCAUCCAGUCUGCAUUGCAACUCAGGCUGACUCAG ACUCCAUCCAGGCUGAAUCAACUCCCAGGUUGCGUGAACUGG ACCGUUCAGUCUGCGAAUGGUACUAACUCCCAGGUUGACUGA ACCGUGUAUCCGGCCAGACUCAGUUCAACGGCCGUGAAAGUCC UGGCGCAGGACUUCGAUUCAACGGCCUGAAAGUCC UGGCGCAGGACUACGUUCAACGGCGUGAACGACC ACGGUGAAACUAUCGAUUGAUUUAAUGUCAACGGCGUGAAAGUCC UGCCGUCAGUCUGCGUAUGAUUGAUUUAAUGUCAACGGCCUAC AACACUGGGACUUCGUUGAUCAACGGCCAAGAAUACUGU AAAACUGGACUUGGGUUGAUCAACGGCGGGUUACUGG GCCGGUGUAUCCGAUUCGGUGGUGCAACGGGGGUUACUGG GGCGGAUAUCCAAUUUGACUUAAUGACAACUACUUAU AUAAAGCUGCAAUUGGCGGUGGUCCAACGGGGGUUACUGG GGCCGAUAUCCAAUUUGGCGUGGUCAACGGGGGUUACUGG GGCCGAUAUCAAAUUUAAAGAGGUCAAUACUAUUUAAAGAG UUAAAGCCGGUGCUUCUGCGGGGGUCAACGCGGUGAAA AACUCCGUUGGCAACUGCGGAAGCUACAGCUAUAU AACCAACUGCCAACGCGGGCCAAGACCUUGUAA AACUCCGUUGGCAACUGCGGAAGCUACAGCUUGUAA AACUCCGUUGGCACCGCGAACACGCUGUGAAA AACUCCGUUGGCACCGCCCAAAUACUUGGGGAAC GGCCACUAUAACCCACAACUGCGGGCCCAAGACUGCUGGUA AACUUCGGUGCGCCCAAACGGUCAACUUGCUGGAGA AACUUCGUUGGAAAAACGGUAAACUAGCUUGUAA AACUUCGGUGACGGUUCAAACGGUUAAUUCGGGCGCUACA UAUAAGGGUGAUAAAACGGUAAACUAGCUUGUGA AACUUCAGAAACAGGGCGAUAACGGACCAUUGCUGGAA AACUUCAGAAACAGGGGUUAAAACGGUUAAUUGAGAGUUGAU AACUUCAGAACAGGGGUUCAAACUGAGCUUGGA AACUUCAGAACAGGGGUUAAAACGGUAACUAGCUUGUGA AACUUCAGAACAGGCGUUGAAAAUUGAUGCUGCUGACAACACU AACUUCAGAACAGGCGUUGAAAAUUGAUGCUGCUGGC ACAGGUUGAUAACCCCUGGCAGAAAAUUGAUGCUGCCU ACCGUUGAAAACCCACUGCGUUAAAACGGUUAAUACAGA UAAGACUGAAAACCGGCUGAAAAUUGAUGCUGCCUGGC ACAGGUUAACCCACUGGCCUGGC | 83 |

| Name | Sequence | SEQ ID NO: |
|------|--|---------------|
| | UAACCUGUCUUCUGCCCGUAGCCGUAUCGAAGAUUCCGACUA | |
| | CGCAACCGAAGUCUCCAACAUGUCUCGCGCGCAGAUUCUGCA | |
| | GCAGGCCGGUACCUCCGUUCUGGCGCAGGCGAACCAGGUUCC | |
| | GCAAAACGUCCUCUUUUACUGCGUUGAUAAUAGGCUGGAGC | |
| | CUCGGUGGCCAUGCUUCUUGCCCCUUGGGCCUCCCCCAGCC | |
| | CCUCCUCCCUUCCUGCACCCGUACCCCCGUGGUCUUUGAAU | |
| | AAAGUCUGAGUGGGCGGCAAAAAAAAAAAAAAAAAAAAA | |
| | ААААААААААААААААААААААААААААААААААААААА | |
| | ААААААААААААААААААААААААААААААААААААААА | |

TABLE 17

| | Flagellin Amino Acid Sequences | |
|--------------------|---|---------------|
| Name | Sequence | SEQ ID NO: |
| ORF | MAQVINTNSLSLLTQNNLNKSQSALGTAIERLSSGLRINSAKDDAA | 54 |
| Sequence, | GQAIANRFTANIKGLTQASRNANDGISIAQTTEGALNEINNNLQRV | |
| AA | ${\tt RELAVQSANGTNSQSDLDSIQAEITQRLNEIDRVSGQTQFNGVKVL}$ | |
| | AQDNTLTIQVGANDGETIDIDLKEISSKTLGLDKLNVQDAYTPKET | |
| | AVTVDKTTYKNGTDPITAQSNTDIQTAIGGGATGVTGADIKFKDG | |
| | QYYLDVKGGASAGVYKATYDETTKKVNIDTTDKTPLATAEATAI RGTATITHNQIAEVTKEGVDTTTVAAQLAAAGVTGADKDNTSLV | |
| | KLSFEDKNGKVIDGGYAVKMGDDFYAATYDEKTGAITAKTTTYT | |
| | DGTGVAQTGAVKFGGANGKSEVVTATDGKTYLASDLDKHNFRT | |
| | GGELKEVNTDKTENPLOKIDAALAOVDTLRSDLGAVONRFNSAIT | |
| | NLGNTVNNLSSARSRIEDSDYATEVSNMSRAQILQQAGTSVLAQA | |
| | NQVPQNVLSLLR | |
| Flagellin- | MAQVINTNSLSLLTQNNLNKSQSALGTAIERLSSGLRINSAKDDAA | 55 |
| GS linker- | GQAIANRFTANI KGLTQASRNANDGISIAQTTEGALNEINNNLQRV | |
| circumsporozoite | RELAVQSANSTNSQSDLDSIQAEITQRLNEIDRVSGQTQFNGVKVL | |
| protein | AQDNTLTIQVGANDGETIDIDLKQINSQTLGLDTLNVQQKYKVSD | |
| (CSP) | ${\tt TAATVTGYADTTIALDNSTFKASATGLGGTDQKIDGDLKFDDTTG$ | |
| | KYYAKVTVTGGTGKDGYYEVSVDKTNGEVTLAGGATSPLTGGLP | |
| | ATATEDVKNVQVANADLTEAKAALTAAGVTGTASVVKMSYTDN | |
| | ${\tt NGKTIDGGLAVKVGDDYYSATQNKDGSISINTTKYTADDGTSKTA}$ | |
| | LNKLGGADGKTEVVSIGGKTYAASKAEGHNFKAQPDLAEAAATT | |
| | TENPLQKIDAALAQVDTLRSDLGAVQNRFNSAITNLGNTVNNLTS | |
| | ARSRIEDSDYATEVSNMSRAQILQQAGTSVLAQANQVPQNVLSLL | |
| | RGGGGSGGGGSMMAPDPNANPNANPNANPNANPNANPNANPNA | |
| | NPNANPNANPNANPNANPNANPNANPNANPNANPNANPN | |
| | ANPNANPNKNNQGNGQGHNMPNDPNRNVDENANANNAVKNNN | |
| | NEEPSDKHIEQYLKKIKNSISTEWSPCSVTCGNGIQVRIKPGSANKP KDELDYENDIEKKICKMEKCSSVFNVVNS | |
| | | 56 |
| Flagellin- RPVT | MMAP DP NANPNANP NANPNANPNANPNANP NANPNANPNANP | 20 |
| linker- | QCNGQGHNMPNDPNRNVDENANANANANANANANANANANANANANANANANANANA | |
| | QUAGQUARIANI ND FININY DEMANANINY KAMINI EFSDART EQT LKKIKNSISTEWSPCSVTCGNGIQVRIKPGSANKPKDELDYENDIEK | |
| protein | KICKMEKCSSVFNVVNSRPVT <u>MAQVINTNSLSLLTQNNLNKSQSA</u> | |
| (CSP) | LGTAIERLSSGLRINSAKDDAAGQAIANRFTANIKGLTQASRNAND | |
| (002) | GISIAQTTEGALNEINNNLQRVRELAVQSANSTNSQSDLDSIQAEIT | |
| | QRLNEIDRVSGQTQFNGVKVLAQDNTLTIQVGANDGETIDIDLKQI | |
| | NSQTLGLDTLNVQQKYKVSDTAATVTGYADTTIALDNSTFKASAT | |
| | GLGGTDQKIDGDLKFDDTTGKYYAKVTVTGGTGKDGYYEVSVD | |
| | KTNGEVTLAGGATSPLTGGLPATATEDVKNVQVANADLTEAKAA | |
| | LTAAGVTGTASVVKMSYTDNNGKTIDGGLAVKVGDDYYSATQN | |
| | KDGSISINTTKYTADDGTSKTALNKLGGADGKTEVVSIGGKTYAA | |
| | SKAEGHNFKAQPDLAEAAATTTENPLQKIDAALAQVDTLRSDLG | |
| | $\underline{AVQNRFNSAITNLGNTVNNLTSARSRIEDSDYATEVSNMSRAQILQ}$ | |
| | QAGTSVLAQANQVPQNVLSLLR | |

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TABLE 18

| Human Metaphe | umovirus Mutant Amino Acid Sequences | |
|---------------------------------------|--|------------------|
| Strain | Sequence | SEQ ID NO: |
| HMPV_SC_DSCAV1_4MMV | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGFSLIKTELDLTKSALRELKTVSADQLAREEQIEDPGSGSFVLG AIALGVAAAAAVTAGVAICKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LAFAVRELKDFVSKNLTRALNKNKCDIDDLKMAVSFSOFNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGIL CGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWY CQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYFC KVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQ DADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFNVALDQVFE NIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKK PTGAPPELSGVTNNGFIPHN | 85 |
| HMPV_SC_DSTRIC_4MMV | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAICKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRKKGFGIL CGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWY CQNAGSTVYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC KVSTGRHPISNVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQ DADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPE <u>HQMH</u> VALDQVFE NIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKK | 86 |
| HMPV_SC_DM_Krarup_T74LD185P | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSFSQFNRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | 87 |
| HMPV_SC_TM_Krarup_T74LD185PD454N | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVRQFS DNAGITPAISLDMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNVACLLREDQGMVC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHFISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPENQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIKKTKKP TGAPPELSGVTNNGFIPHN | 88 |
| HMPV_SC_4M_Krarup_T74LS170LD185P | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIEN <u>PGSGS</u> FVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTINEAVSTLGNGVRV LATAVRELKDFVLKNLTRAINKNKCDIPDLKMAVSFSQFNRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDFIKFPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIKKTKKP TGAPPELSGVTNNGFIPHN | 89 |
| HMPV_SC_5M_Krarup_T74LS170LD185PD454N | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVLKNLTRAINKNKCDIPDLKMAVSFSOFNRRFLNVVROFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDFIKFPENOFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | 90 |
| HMPV_SC_DM_Krarup_E51PT74L | MSWKVVIIFSLLITPOHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTL <u>P</u> VG DVENLTCSDGPSLIKTELDL <u>L</u> KSALRELKTVSADQLAREEQIENP <u>GSGS</u> FVLG | 91 |

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TABLE 18-continued

| Human Metapneum | ovirus Mutant Amino Acid Sequences | |
|---|--|------------------|
| Strain | Sequence | SEQ ID NO: |
| | AI AGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVPCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | |
| HMPV_SC_TM_Krarup_E51PT74LD454N | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLPVG DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENP <u>GSGS</u> FVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDIKFPENJGPQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | 92 |
| HMPV_SC_StabilizeAlpha_T74L | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENP <u>GSGS</u> FVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSPSQFNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | 93 |
| HMPV_SC_StabilizeAlpha_V55L | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DLENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLMVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNEVGIIKQLNKGCSVITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVITLIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | 94 |
| HMPV_SC_StabilizeAlpha_S170L | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVLKNLTRAINKNKCDIDDLKMAVSFSQFNRFFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVVQLSKVEGEQHVIKGRPVSSSFDFIKFPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | 95 |
| HMPV_SC_StabilizeAlpha_T174W | MSWKVVIIFSLLITPOHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLWRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDIKFPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | 96 |
| HMPV_SC_4M_StabilizeAlpha_V55LT74LS170LT174 | MSWKVVIIFSLLITPOHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DLENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENP <u>GSGS</u> FVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVLKNLWRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS | 97 |

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TABLE 18-continued

| Human M | Metapneumovirus Mutant Amino Acid Sequences | |
|---------------------------|---|------------------|
| Strain | Sequence | SEQ ID NO: |
| | DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | |
| HMPV_ProlineStab_E51P | MSWKVVIIPSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLPVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP | 98 |
| HMPV_ProlineStab_D185P | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDI <u>P</u> DLKMAVSFSQFNRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP | 99 |
| HMPV_ProlineStab_D183P | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENP <u>GSGS</u> FVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKC <u>P</u> IDDLKMAVSFSQFNRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | 100 |
| HMPV_ProlineStab_E131P | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEQQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | 101 |
| HMPV_ProlineStab_D447P | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPG <u>SGS</u> FVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFPPIKF <u>P</u> EDQPQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | 102 |
| HMPV_TrimerRepulsionD454N | MSWKVVIIFSLLITPOHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENP <u>GSGS</u> FVLG AIALGVAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC | 103 |

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TABLE 18-continued

| Human M | Metapneumovirus Mutant Amino Acid Sequences | |
|---------------------------|--|------------------|
| Strain | Sequence | SEQ ID NO: |
| | QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMYALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPE <u>NO</u> FQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP TGAPPELSGVTNNGFIPHN | |
| HMPV_TrimerRepulsionE453N | MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENP <u>GSGS</u> FVLG AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRFLNVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSPDPIKFPQDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP | 104 |
| HMPV_StabilizeAlphaF196W | MSWKVVIIPSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AIALGVAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQMRRFLMVVRQFS DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKGFGILI GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD ADTVTIDNTVYQLSXVEGEQHVIKGRPVSSSFDPIKPPEDQFQVALDQVFENI ENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTKKP | 105 |

TABLE 19

| Strain | Nucleic Acid Sequence | SEQ II NO: |
|---------------------|---|------------------|
| | Human Metapneumovirus Mutant Nucleic Acid Sequences | |
| HMPV SC DSCAV1 4MMV | ATGAGCTGGAAGGTGGTCATCATCTTCAG | GCCTGCTGATCA 106 |
| | CACCTCAGCACGGCCTGAAAGAGAGCTAC | CCTGGAAGAGT |
| | CCTGCAGCACCATCACAGAGGGCTACCTC | STCTGTGCTGAG |
| | AACCGGCTGGTACACCAACGTGTTCACAC | CTGGAAGTGGGC |
| | GACGTCGAGAATCTGACATGCTCTGATGC | GCCCTAGCCTGA |
| | TCAAGACCGAGCTGGATCTGACCAAGAG | CGCCCTGAGAG |
| | AACTCAAGACCGTGTCTGCCGATCAGCTC | GGCCAGAGAGGA |
| | ACAGATCGAGAATCCTGGCAGCGGCAGC | ITTGTGCTGGGA |
| | GCCATTGCTCTTGGAGTGGCTGCTGCTGC | CAGCTGTTACAG |
| | CAGGCGTGGCCATCTGCAAGACCATCAGA | ACTGGAAAGCG |
| | AAGTGACCGCCATCAACAACGCCCTGAAC | GAAGACAAACG |
| | AGGCCGTCAGCACTCGGCAATGGCGT | TAGAGTGCTGGC |
| | CTTTGCCGTGCGCGAGCTGAAGGACTTCC | GTGTCCAAGAAC |
| | CTGACACGGGCCCTGAACAAGAACAAGTC | GCGACATCGAC |
| | GACCTGAAGATGGCCGTGTCCTTTAGCC | AGTTCAACCGGC |
| | GGTTTCTGAACGTCGTGCGGCAGTTTAGC | CGACAACGCCGG |
| | AATCACACCAGCCATCAGCCTGGACCTGA | ATGACAGATGCT |
| | GAGCTGGCTAGAGCCGTGCCTAACATGCC | CTACATCTGCCG |
| | GCCAGATCAAGCTGATGCTCGAGAATAGA | AGCCATGGTCCG |
| | ACGGAAAGGCTTCGGCATTCTGTGTGGCC | GTGTACGGCAGC |
| | AGCGTGATCTATATGGTGCAGCTGCCTAT | TCTTCGGCGTGA |
| | TCGACACCCCTGCTGGATTGTGAAGGCC | CGCTCCTAGCTG |
| | TAGCGAGAAGAAGGGCAATTACGCCTGCC | CTGCTGAGAGA |
| | GGACCAAGGCTGGTATTGTCAGAACGCCC | GCAGCACCGTG |
| | TACTACCCTAACGAGAAGGACTGCGAGAG | CAAGAGGCGAC |
| | CACGTGTTCTGTGATACCGCCGCTGGAA | TCAATGTGGCCG |
| | AGCAGAGCAAAGAGTGCAACATCAACATC | CAGCACCACCA |
| | ACTATCCCTGCAAGGTGTCCACCGGCAG | GCACCCTATTTC |
| | TATGGTGGCTCTGTCTCCTCTGGGAGCCC | CTGGTGGCTTGTT |
| | ATAAGGGCGTGTCCTGTAGCATCGGCAG | CAACAGAGTGG |
| | GCATCATCAAGCAGCTGAACAAGGGCTG | CAGCTACATCAC |
| | CAACCAGGACGCCGATACCGTGACCATCC | GACAACACCGTG |
| | TATCAGCTGAGCAAGGTGGAAGGCGAACA | AGCACGTGATC |
| | AAGGGCAGACCTGTGTCCAGCAGCTTCGA | ACCCTATCAAGT |

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TABLE 19-continued

| train | Nucleic Acid Sequence | SEQ ID NO: |
|----------------------------|---|---------------|
| | TCCCTGAGGATCAGTTCAACGTGGCCCTGGACCAGGTGTT | |
| | CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC | |
| | AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC | |
| | TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC | |
| | CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC | |
| | AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG | |
| | ACCAACAATGGCTTCATCCCTCACAAC | |
| MPV_SC_DSTRIC_4MMV | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA | 107 |
| | CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT | |
| | CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG | |
| | AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA | |
| | TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG | |
| | AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA | |
| | ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA | |
| | GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG | |
| | CAGGCGTGGCCATCTGCAAGACCATCAGACTGGAAAGCG | |
| | AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG | |
| | AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC | |
| | CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC | |
| | GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC | |
| | GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG | |
| | AATCACCAGCCATCAGCCTGGACCTGATGACAGATGCT | |
| | GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG | |
| | GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG | |
| | ACGGAAAGGCTTCGGCATTCTGTGTGGCGTGTACGGCAGC | |
| | AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA | |
| | TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA | |
| | GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG | |
| | TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC | |
| | CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG | |
| | AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA | |
| | ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC | |
| | TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT | |
| | ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC | |
| | CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG | |
| | TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC | |
| | AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT | |
| | TCCCTGAGCACCAGTGGCATGTGGCCCTGGACCAGGTGTT | |
| | CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC | |
| | AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC | |
| | TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC | |
| | CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG | |
| | ACCAACAATGGCTTCATCCCTCACAAC | |
| | | |
| MPV_SC_DM_Krarup_T74LD185P | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT | 108 |
| | CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG | |
| | AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC | |
| | | |
| | GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA | |
| | GACGTCGAGAATCTGACATGCTCTGATGGCUCTAGUCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGAGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGAG CAGATCGAGAATCCTGGCAGCGGCGGCGGCTGTGTGCTGGGAG CCATTGCTCTTGGAGTGGCGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGGG CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG CCATTGCTCTGGGATGGCTGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCAACGGACTGGAAAGCGA AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA GGCCGTCAGCACACTCGGCATGGCCGTTAGAGTGCTGGCC ACAGCCGTGCGCGGAGCTGAAGGACTTCGTGTCCAAGAAACC | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGAGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGAGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGAGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGAA CAGATCGAGAATCCTGGCAGCGGCAGCTTGTGCTGGAGAG CCATTGCTCTTGGAGTGGCTGCTGCAGCGCGTGTACAGC AGCGTGGCCATCGCTAAGACCATCAGACTGGAAGACGA AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA GGCCGTCAGCACACTCGGCATGGCGTTAGAGTGCTGGC ACAGCCGTCGGCGAGCTGAAGAGACTTCGTGTCCAAGAACC TGACACGGCCCATTAACAAGAACAAGTGCGACACCCCTGA CCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG TTTCTGAAGATGGCCGTGTCCTTTAGCCAGCTCAACCGGCG TTTCTGAAGATGGCCGTGCCTTAAGCAGCACCGCGGA TTCCTGAACGTCGTGCCGGCCTGATGGCGCAGAGATGCTGA GCTGGCTAGAGCCGTGCCTGATGCCTACGCGCGGC CAGATCAAGCCGTGCCTGACATCGCCTGACCCAGGCCGGC | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGGCGCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGAGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGAGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGGCGCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGAGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGAGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGGGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGAA CAGATCGAGAATCCTGGCAGCGGCAGCTTGTGCGGAGAG CCATTGCTCTTGGAGTGGCTGCTGCGCAGCTGTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAACGA GGCCGTCAGCACACTCGGCATGGCGTTAGAGTGGCGC ACAGCCGTCGGCGAGCTGAAGAGACTTCGTGTCCAAGAACC TGACACGGCCATTAACAACGACGCCGTTAAGAGCGCAGC CCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG TTTCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG TTTCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG CCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG CCTGAAGATGGCCGTGCCTTAACAAGGCCGCAGA TTCCGACCAGCATCAGCCTGGACCTGATGCCAAGATGCTGA GCTGGCTAAGCCGTGCCTGACAGCCTGACGCCGGC CAGATCAAGCTGATGCTGAGAATAGAGCCATGGTCCGAC GGAAAGGCTCGGCATCTGCAGTGACGGCGGCGCGCG ACCACCCTGCTGGATTGTGAAGGCCGTCTCAGGCGGCAGCA CGTGATCTATATGGTGCAGCTGCCTGCTGCTGAGAGAGGGCA | |

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TABLE 19-continued

| | TABLE 19-continued | |
|----------------------------------|---|---------------|
| Strain | Nucleic Acid Sequence | SEQ ID NO: |
| | ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA AGGGCGTGTCCTGTAGCATCGGCAGCAACAAGAGGGGCAT CATCAAGCAGCTGTAACAAGGGCTGCAGCTACATCACCAAC CAGGACGCCGATACCGTGACCATCGACAACACCGTGATCA AGCTGAGCAAGGTGGAAGCGAACACACCGTGATCAAGG GCAGACCTGTGTCCAGGCGGCCCTGGACCAGGTGTTCGAG AACATCGAGAATTCCCAGGTGGCCCTGGACCAGGTCTCGAC GAATCCTGTCTAGCCCGGCTCGGGCACCAGGCTTCAAC GAATCCTGTCAGCCGACCAGGGAACACCGGCTTCAT CATCGTGATCATCCTGATCGCCGTGCGCGCGCCCTGG ATCCTGGTGCCATCTTCATCATGAGAAGACACCCGAC | |
| | AGCCCACCGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC | |
| HMPV_SC_TM_Krarup_T74LD185PD454N | ATGAGCTGGAAGGTGGTCATCATCTTCAGCTGCTGCTATCA CACCTCAGCACGGCCGAAAGAGAGGCACCTGGTGTGGAAGAGT CCTGCAGGACACATCACAGAGGGCTACCTGGTGTGGAGAGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTGGAGGC GACGTCGAGAATCTGGCATGCTCTGATGGCCCTGGAGAGAGA | 109 |
| HMPV_SC_4M_Krarup_T74LS170LD185P | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCTGAAAGAGAGAGACTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGGTGGTGGGG AACCGGCTGGACATCTGACACGGCTCTGGAAGAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCAGG TCAAGACCGAGCTGGCATCTGCTCAAGAGCGCCCTGAGAGAGA | 110 |

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TABLE 19-continued

| Strain | Nucleic Acid Sequence | SEQ ID NO: |
|---------------------------------------|---|---------------|
| | CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG | |
| | ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG | |
| | CGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGGA | |
| | CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTAC | |
| | TACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCAC | |
| | GTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAGC | |
| | AGAGCAAAGAGTGCAACATCAACATCAGCACCACCAACT | |
| | ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT | |
| | GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA | |
| | AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT | |
| | CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC | |
| | CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG | |
| | GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC | |
| | TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG | |
| | AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA | |
| | GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT | |
| | CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG | |
| | ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA | |
| | AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA | |
| | CAATGGCTTCATCCCTCACAAC | |
| HMPV_SC_5M_Krarup_T74LS170LD185PD454N | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA | 111 |
| | CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT | |
| | CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG | |
| | AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC | |
| | GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA | |
| | TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA | |
| | ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA | |
| | CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG | |
| | CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC | |
| | AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA | |
| | AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA | |
| | GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC | |
| | ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAACC | |
| | TGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTGA | |
| | CCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCGG | |
| | TTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGAA | |
| | TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA | |
| | GCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGGC | |
| | CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC | |
| | GGAAAGGCTTCCGCATTCTGATTGGCGTGTACGGCAGCAG | |
| | CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG | |
| | ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG | |
| | CGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGGA | |
| | CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTAC | |
| | TACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCAC | |
| | GTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAGC | |
| | AGAGCAAAGAGTGCAACATCAACATCAGCACCACCAACT | |
| | ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT | |
| | | |

HMPV_SC_DM_Krarup_E51PT74L

ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACACTGCCTGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG ${\tt CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC}$ AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA ${\tt GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC}$ ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC

CAATGGCTTCATCCCTCACAAC

GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC TGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA

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Strain

TABLE 19-continued

SEO ID Nucleic Acid Sequence NO: TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA GAATCCTGTCTAGCGCCGAGAAAGGGAAACACCGGCTTCAT CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC HMPV_SC_TM_Krarup_E51PT74LD454N ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 113 CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACACTGCCTGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA ${\tt CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG}$ CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC TGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 114

HMPV_SC_StabilizeAlpha_T74L

CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA

Nucleic Acid Sequence

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Strain

TABLE 19-continued

ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA AGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC HMPV_SC_StabilizeAlpha_V55L ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 115 CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC GACCTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA TCGACACCCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG ACCAACAATGGCTTCATCCCTCACAAC

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SEO ID

NO:

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TABLE 19-continued

| | TABLE 19-continued | |
|------------------------------|--|--------------|
| Strain | Nucleic Acid Sequence | SEQ I NO: |
| HMPV_SC_StabilizeAlpha_S170L | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCTGAAAGAGGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGGTGGCTGAG AACCGGCTGTACACCAACAGGTCTCACACTGGAAGTGGC GACGTCGAGAATCTGACAAGGCCCCTGAGCCAGCCGGG CACGTCGAGACTGGACTG | 116 |
| | CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG ACCAACAATGGCTTCATCCCTCACAAC | |
| HMPV_SC_StabilizeAlpha_T174W | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGGTGGGAGGG GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCGG GACGTCGAGAATCTGGCCAGCGGCAGCTGGGAGGGA AACTCAAGACCGTGTCTGGCGAGCGGCGCGCGAGAGGA ACTCAAGACCGTGTCTGGCGAGCGGCGCGCGGAGGGA GCCATTGCTCTGGAGTGGCGCGCGCGCGCGGCGGCTGTACAG GCCATGGCCCTCGGCAAGGAGCATTGGGCTGGCG AAGTGACCGCCATCACAACGACCCTGAAGAAGCAAACG AAGTGACCGCCATCACAACGACCCTGAAGAAGCAAACG CACGCCGTGGCCATCGGCAACGACGTGAAGACCAACG CACGCCGTGGCCGCGCGCGCGCTGTGCGCACGCGC CACAGCCGTGGCGCGGCGGCGGCTGTAGAGGCGTCCGGC GGTTTCTGAACGTCGTGCGCGCGCGGCAGTTAGCGGCACATCGGC GACCTGAAGATGGCCGTGCCTGAACAACGCCGGG GGTTCTGAACGTCGTGCGCGCGGCAGTTAGCGCACACGGC GACCTGGACGGCCATCAGCCTGGAACGACACGCGG GGTTCCGAACGTCGTGGCGCGGCCGTTAGCCGACACGCGG CCCAGATCAAGCTGGGCGCGCTGCTAACATGCCTGCACGCGG GCCAGATCAAGCTGGGCGCGCTGCTAACATGCCTGCGCGCG ACCGGAAAGGCTTCGGCAGCTGGACCATGGTCCG ACGGGAACGCCTGGCAGCTGGACCTGGTCCGGCAGCTGGCACGCGG CCCAGATCAGCCTGGCAGCTGCTACATCGCCGG CGCGGAACGGCTGGCGACTTGGCGTGCCTACCTGCCG ACGGGAACGCCTGGCAGCTGCCTATCTTCGGCGGCG CCCCAGCCCGCGCGGCGCCCTCCTGGCGGCGCGCCCCTACCTGCCG ACGGAAAGGCTTGGGCAGCTGCCTACCTTCGGCGGCGCCC ACGGAAAGGCTGGGAATTGCGCAGCCGCGCCCCCAGCTG TACGACACCCCGCGCGGCGCG | 117 |

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TABLE 19-continued

| Strain | Nucleic Acid Sequence | SEQ II NO: |
|--|---|---------------|
| | TCCCTGAGGATCAGTTCCAGGTGGCCTGGACCAGGTGT CGAGAACATCGAGAATCCCAGGCCTGGTGGACCAGTCC AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGGTCATCCTGATCGCCGTGCTGGGCAGCTC CATGATCCTGGTGTCCATCTTCATCATGAAGAAGAC AAGAACCCCACCGGCGCTCCTCCAGAACTGACGGAGTG ACCAACAATGGCTTCATCCTCACAAC | |
| HMPV_SC_4M_StabilizeAlpha_V55LT74LS170LT174W | CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGGCTGAG AACCGGCTGGTACACCACGGGCTGCACAGGGGG CACCTCCGAGAATCTGACAGCGGCCCTGAGAGA ACTCAAGACCGTGTCTGCCGCAAGAGGGGGG CATGCTCTTGGAGTGGCTGCTGCGCGCAGAGAGAGA CAGATCCTGGCAGGGGCGCGGGCGGGGGGGGGG | 118 |
| HMPV_ProlineStab_E51P | CAATGGCTTCATCCTCACAAC ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGTGGTGAG AACCGGCTGGTACACCAGAGGGCTACCTGTCTGGGCTGAG GACGTCGAGAATCTGACAGAGGGCTACCTGTCTGGGCG GACGTCGAGATCTGACAGACGTCTGATGGCCCTGAGAG AACTCAAGACCGAGCTGGTCTGACCAAGAGCGCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCGCAGCGCTGGGCCAGAGAGGA ACAGATCGAGAATCCTGGCGCAGCGCTGGAGCGTTAGACTGGCA GCCATTGCTCTGGAGTGCTGCTGCTGCCGGCAGTACAG CAGGCGTCGCCATCACACAGCGCTCGAGACGTACAG CAGGCGTCGCCATCACACAGCGCTTGGTGCCAGCG AGTGACCGCCATCACACAGCGCTGAGAGAGCAAACG AGGCCGTCGGCCAGCTGAAGGACTTCGTGCTGGC CACAGCCGTCGCCAGCTGAAGGACTTCGTGCCAGAAC CTGACAGCGGCCAGCTGAAGGACTTCGTGCCAGAAC GACCTGAAGATGGCCGTGTCCTTTAGCAGGTCAACGGC GACTTGGACACCTCGGCGACGTTGACGCCGCAGACGGC GACTGGCTAGGCCGTGCCCTACACTGGCCGGC CCAGACCGCGCCGCGCGCCCCTACACGCCG GGCTACGACCAGCCGTGCCCTACACTGGCCG CCCGGAACGCGTCGGCAGTTCAGGCCGCCGC AGGGGGAACATCAGCCGGCAGTTGGAAGGCCGCG AGCGGAAAGACTGCGGCATTGTGAAGGCCACCTACGCCG AGGCGGAACATCAGCCGGCAGTTGGAAGGCCGCCTAGCTGGC AGGCGGAACACTGGCAGTTGGCAGCCCCTACCTGCGGGAAC AGGCCAAGGCGGCAGTTGGAAGGCCGCCCTACCTGGCGGC AGCCTGAAGACTGGGCATTGGCAGCCGCCTACCTCGGCGGC AGCCGGAAAGACGCGGCAGTTGGAAGGCCGCCTCACGCG AGCCAGACAAGAAGGCAATTGCCCGCCGCGCAGACCGGC AGCCAGACCAAGGCGGCATTGCGAGACAAAGGCGACC CACGGCAAAGAAGAGGCATTCGCGGCGCAGACACAAGGCGAC CACGGCAACGCTGGGAATTGCCCGCGCGCAGACCGGC CACGGCAACGCGGCGAGATTGCGAGACCAAAGGCGCACCGTG TACCACCCTGGGAATGGCAGCTGCCGCGCAGACCGGC CACGGCAACGACGGCATTGCCGCGCGCGCAGACCGGC CACGGCAAGGCAATACACCGCGCGCAGCACCGGC CACGGCAACGAGCGCAATCAACCACAAGGCGCACCGCG CACGGCAAAGAGCCGCCGCGCGCGCAGACCGGC CACGGCAACAAGAGCCGCCGCGCGCGCAGACCGGC CACGGCAACAAGAGCCGCCGCGCGCGCAGACCGGC CACGGCAACAAGAGCCGCCGCGCGCGCGCACCGCG CACGGCAACAAGAGCCGCCGCGCGCGCGCACCGCG CACGGCAACAAGAGCCGCCGCGCGCGCGCCGCCGCCGCCG | 119 |

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TABLE 19-continued

| | 19-continued | |
|------------------------|--|--------------|
| Strain | Nucleic Acid Sequence | SEQ I NO: |
| | ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC | |
| | TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT | |
| | ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG | |
| | GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC | |
| | | |
| | TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT | |
| | TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT | |
| | CGAGAACATCGAGAATTCCCCAGGCTCTGGTGGACCAGTCC | |
| | AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC | |
| | TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC | |
| | CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC | |
| | AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG | |
| | ACCAACAATGGCTTCATCCCTCACAAC | |
| IMPV ProlineStab D185P | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA | 120 |
| | CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT | |
| | CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG | |
| | AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC | |
| | GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA | |
| | TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG | |
| | AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA | |
| | ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA | |
| | GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG | |
| | CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG | |
| | AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG | |
| | AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC | |
| | CTGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTG | |
| | ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG | |
| | GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA | |
| | ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG | |
| | AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG | |
| | CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA | |
| | CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA | |
| | GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC | |
| | GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA | |
| | GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG | |
| | ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA | |
| | CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA | |
| | CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG | |
| | CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC | |
| | TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT | |
| | GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA | |
| | AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT | |
| | CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC | |
| | AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG | |
| | GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC | |
| | TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG | |
| | AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA | |
| | GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT | |
| | CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG | |
| | ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA | |
| | AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA | |
| | CAATGGCTTCATCCCTCACAAC | |
| HMPV_ProlineStab_D183P | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA | 121 |
| | CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT | |
| | CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG | |
| | AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC | |
| | GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA | |
| | TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG | |
| | AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA | |
| | ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA | |
| | GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG | |
| | CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG | |
| | AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG | |
| | | |
| | CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC | |
| | CTGACACGGGCCATTAACAAGAACAAGTGCCCTATCGACG | |
| | ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG | |
| | CTTTCTC3 ACCTCCTCCCCC3 CTTTTACCC3 C3 ACCCCCC3 | |
| | GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA | |
| | ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG | |
| | | |

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| | TABLE 19-continued | CDO 11 |
|------------------------|--|---------------|
| Strain | Nucleic Acid Sequence | SEQ II NO: |
| | | |
| | GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA GCGAGAAGAAGGGCCAATTACGCCTGCCTGCTGAGAGAGG | |
| | ACCAAGGCIGGTATIGTCAGAACGCCGGCAGCACCGIGTA CTACCCTAACGAGAGGACIGCGAGACAAGAGGCGACCA | |
| | CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG | |
| | CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC | |
| | TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA | |
| | AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT | |
| | CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC | |
| | CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG | |
| | GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC | |
| | TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA | |
| | GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT | |
| | CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG | |
| | ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA | |
| | CAATGGCTTCATCCCTCACAAC | |
| HMPV_ProlineStab_E131P | | 122 |
| | CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG | |
| | AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC | |
| | GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA | |
| | TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA | |
| | ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA | |
| | GCCATTGCTCTTGGAGTGGCTGCTGCAGCTGTTACAG | |
| | | |
| | AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC | |
| | ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC | |
| | TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG | |
| | ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA | |
| | ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG | |
| | AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG | |
| | CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA | |
| | GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC | |
| | GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA | |
| | GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG | |
| | ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA | |
| | CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG | |
| | CAGAGCAAAGAGTGCAACATCAACATCAGCACCAACA | |
| | TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA | |
| | AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT | |
| | CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC | |
| | CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG | |
| | GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCCC | |
| | TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG | |
| | AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT | |
| | CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG | |
| | ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA | |
| | AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC | |
| HMPV_ProlineStab_D447P | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA | 123 |
| - | | |
| | CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC | |
| | GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA | |
| | TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG | |
| | AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGA | |
| | ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG | |
| | CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG | |
| | AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG | |

AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC

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TABLE 19-continued

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| | TABLE 19-continued | |
|--------------------------|--|---------------|
| Strain | Nucleic Acid Sequence | SEQ ID NO: |
| | CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC | |
| | GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC | |
| | GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG | |
| | AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT | |
| | GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG | |
| | | |
| | ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACCGCAGC AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA | |
| | TCGACACCCCTGCTGGATTGTGAAGGCCGCCTCCTAGCTG | |
| | TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCGAGAGA | |
| | GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG | |
| | TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC | |
| | CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG | |
| | AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA | |
| | ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC | |
| | TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT | |
| | ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG | |
| | | |
| | CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG | |
| | TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC AAGGGCAGACCTGTGTCCAGCAGCTTCCCCACCTATCAAGT | |
| | TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT | |
| | CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC | |
| | AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC | |
| | TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC | |
| | CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC | |
| | AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG | |
| | ACCAACAATGGCTTCATCCCTCACAAC | |
| MPV_TrimerRepulsionD454N | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA | 124 |
| | CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT | |
| | CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG | |
| | AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC | |
| | GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA | |
| | | |
| | AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA | |
| | GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCGCAGCTGTTACAG | |
| | CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG | |
| | AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG | |
| | AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC | |
| | CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC | |
| | CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC | |
| | GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC | |
| | GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG | |
| | AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT | |
| | GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG | |
| | GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG | |
| | ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC | |
| | AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG | |
| | TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA | |
| | GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG | |
| | TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGGCGAC | |
| | CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG | |
| | AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA | |
| | ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC | |
| | TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT | |
| | ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG | |
| | GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC | |
| | CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG | |
| | TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC | |
| | AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT | |
| | TCCCTGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTT CCACAACCAGTGCACAGTTCCCAGGTGGCCCTGGACCAGGTGTT | |
| | CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC | |
| | AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC | |
| | CATGATCCTGGTGTCCATCTTCATCATCATCAGAAGAAGACC | |
| | AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG | |
| | ACCAACAATGGCTTCATCCCTCACAAC | |
| MDV TrimerPepulcionE452N | RTCR COTCCR R COTCCT CR TCR TCTTCR COCTCCTCR TCR | 195 |
| MPV_TrimerRepulsionE453N | ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT | 125 |
| | CCTGCAGCACCATCACAGAGGGCTACCTGTCTGGCAGAGG | |
| | | |

CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG

Nucleic Acid Sequence

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SEO ID

NO:

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Strain

TABLE 19-continued

AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCGAGAAGAAGGGGCAATTACGCCTGCCTGCTGAGAGA GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT TCCCTCAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT CGAGAACATCGAGAATTCCCCAGGCTCTGGTGGACCAGTCC AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG ACCAACAATGGCTTCATCCCTCACAAC HMPV_StabilizeAlphaF196W ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 126 CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT CCTGCAGCACCATCACAGAGGGGCTACCTGTCTGTGCTGAG AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC GACCTGAAGATGGCCGTGTCCTTTAGCCAGTGGAACCGGC GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA TCGACACCCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG ACCAACAATGGCTTCATCCCTCACAAC

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TABLE 19-continued

| 11101 | LE 19-continued | |
|---------------------|--|---------------|
| Strain | Nucleic Acid Sequence | SEQ II NO: |
| Human Metap | neumovirus mRNA Sequences | |
| Muman Metap | neumovirus mRNA Sequences AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAAGAGGUCUCUGGUGCU GAGAACCGGCUGGUACACCAAGAGGUUCACACUGGAAGA GUCCUGCAGCACCAUCACAAGGUUUCACACUGGAAGU GGGCGACGUCGAGAAUCUGACAUGUCUGGUGCUGCUG GAGAACCGGCUGGAUCUGACACUGGAUCAGCUGCCAG GAGAGAUCAAGACCGUGUCUGCCGAUCAGCUGCCAG AGAGGAACUCAAGACCGUGUCUGCCGAUCAGCUGCUGCA GCUGUUACAAGACCGUGUCUUGGAAGACCAUUCAGA GCUGUUACAGCAGGCGUGGCCUUCUGCAAGACCAUUCAGA GUGUGGAAGUGAAGU | 127 |
| IMPV_SC_DSURIC_4MMV | CCAUGAUCCUGGUGUCCAUCUUCAUCAUCAUGAUGAGAAGA CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG UGACCAACAAUGGCUUCAUCCUCACAAC AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAUA GUCCUCCAGCACGACGCUGAAAGAGGCUACCUGUGGAGA GUCCUGCAGCACCAUCACAAGAGGGCUACCUGUGUGGUG GAGAACCGGCUGGUACACAAGAGGGCUCUGAUGGCCUG GAGAACCGGCUGGUACACCACGUGUUCACACUGGAAGA GUCCUGAGACACAUCACAAGAGGGCUACUGAUGACCACUGGAGAA GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCAG GAGAACAGAUCAAGACCGUGUCUGCCAGUCGCUGCUGCUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUCUGCUGCUGCUG UGCUGGGAGCCAUUGCUCUUGGAAGACCAUCAGA GCUGUUACAGCAGGCGUGGCCAUCUGCAAGACCAUCAGA GCUGUUACAGCAGGCGUGGCCAUCUGCAAGACCAUCAGA GCUGUUACAGCAGGCGUCAGCACCAUCGGCAAGCCUUG UGCUGGAGCAAUGCCGUCAGCAGCGCCAUUG AGAGUACUGGCCACAGCCGUCGCGCAUCUGCUAAC GUGUCCAAGAACCUGACAGCCGUCAGCAAGACCAUCAGA AUGCCAACAACGGCGUCAGCACACUCGGCAAUGAGCUU GUGUCCAAGAACCUGACACGCGGCAGCUUAACAAGAACAAG UGCGACAACGGCCGUUCAGAACGUGUGGGGCAUUUC GUGUCCAAGAACCUGACCAGCCGUGCCGU | 128 |

| Strain | Nucleic Acid Sequence | SEQ ID NO: |
|----------------------------------|--|---------------|
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC UGAGCACCAGUGGCAUGUGGCCCUGGACCAGGUGUUCGA GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA CAGAAUCCUGUCUACCCGAGAAAGGGAAACACCGGCUU CAUCAUCGUGAUCAUCCUGAUCAUCAUCAUCAUCAUCAGAGAA CAGAACCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU GACCAACAAUGGCUUCAUCCUCACAAC | |
| HMPV_SC_DM_Krarup_U74LD185P | AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAAGA GUCCUGCAGCACCGCCUGAAAGAGAGCUACCUGGUGGAAGA GUCCUGCAGCACCAUCACAAGAGGGCUACCUGUCUGUGCU GAGAACCGGCUGGUACACCAACGUGUCUCACACUGGAAGU GGGCGACGUCGAGAAUCUGCUCAACGUGCCCUAG CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAACAUCGCCCAG GAGAGAACAGAUCGAGAUCUGCCGAUCACCUGCCAG GCUGUUACAGACGGUGGCCAUCGCUAAGACCAUCAGA CUGGUACAGAGCGUGGCCAUCGCUAAGACCAUCAGA CUGGUACAGAGCGUGGCCAUCGCUAAGACCCUGGAA GCUGUUACAGCAGCGUCAGCACCCUGGAAGACCAUCAGA CUGGAAAGCUGACCGCCAUCACACACCCCUGAAG AAGACAAACGAGGCCGUCAGCACAUCAACAACGCCUUGAA GCUGUCCAGAAACCUGACACGCGCGAGCUGAAGACCUUC GUGUCCAAGAACCUGACACGCGCGAGCUGAAGACCUC GUGUCCAAGAACCUGACACCACCAGCCGUGACCAUCAACAAG UGCGACAUCCCUGACACACCAGCCGUGACGCUGCUGUUA AGCGUACAUCCUGACCUGA | 129 |
| HMPV_SC_UM_Krarup_U74LD185PD454N | UGACCAACAAUGGCUUCAUCCCUCACAAC AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAAGAGGCUACCUGGUGGU GAGAACCGGCUGGACACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUG GAGAACCGACCAUCGCUGGAUCUGCUCAGAGGCCCUG GAGAGACUCAAGACCGAGCUGGCUCAGAGCGCGGCGU GAGAGAACCAAAUCCGAGCUGGCUCAGAGCGCGGCGU UGCUGGGAGCCAUUGCUCUUGGAUCUGCUCAGGCAGCUGCCAG AGAGAACCAAAUCGAGAAUCCUGGCAGCGGCGCUGCUGCAG CUGUUACAGCAGGCGUGGCCAUCGACAACAGCCCUCGGCAGCUGCUGCUGCUGCUGCGGGAGCCUCGCCAGGCAGCUGGCAUCAACAACAACCACCUCGGCAAUCGCUAGAAAGCAUCAGA CUGGAAAGCGAAGUGACCGCCCUCGCUAAGACACCCUCGGA AGACAAACGAGGCGUCGCCAUCAACAACGACCUCGUG UGCUGGCGCCCGCCGCAGCUGGCAAUGGCGUU AGAGCAAACCGAGCCUCAGCACACUCGGCAAUGGCGUU GUGUCCAAGAACCUGACAGGGCCAUUAACAACAACGACCUUC GUGUCCAAGAACCUGACCGGCCAUUAACAAGAACAAG CUGGACAUCCCUGACCUGA | 130 |

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TABLE 19-continued

| TABLI | E 19-continued | |
|--------------------------------------|--|------------|
| Strain | Nucleic Acid Sequence | SEQ NO: |
| | AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA | |
| | UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA | |
| | GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG | |
| | AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG | |
| | AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA | |
| | AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC | |
| | UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC | |
| | GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC | |
| | AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG | |
| | CUGACCAAGGUGGAAGGCGAACAGCACGUGUUCAGGG | |
| | CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC | |
| | UGAGAACCAGUUCCAGGUGGCCCUGGACCAGGUGUUCGA | |
| | GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA | |
| | CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU | |
| | CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC | |
| | CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC | |
| | CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU GACCAACAAUGGCUUCAUCCCUCACAAC | |
| | GALLAACAOGEOULAULEULALAAL | |
| MPV_SC_4M_Krarup_U74LS170LD185P | AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU | 131 |
| | CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA | |
| | GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU | |
| | GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU | |
| | GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG | |
| | CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG | |
| | AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG | |
| | UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA | |
| | GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA | |
| | CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG | |
| | AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU | |
| | AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC | |
| | GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAACAA | |
| | GUGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAG | |
| | CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU UAGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGA | |
| | CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA | |
| | CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA | |
| | GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC | |
| | UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG | |
| | CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG | |
| | AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG | |
| | CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA | |
| | GAAGGACUGCGAGCAGCACCGUGUACUACCCUAACGA | |
| | AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGGGGGGAGCAAAG | |
| | AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA | |
| | AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC | |
| | UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC | |
| | GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC | |
| | AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG | |
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG | |
| | CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG | |
| | CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC | |
| | UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG | |
| | AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA | |
| | ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU | |
| | UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA | |
| | CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG | |
| | UGACCAACAAUGGCUUCAUCCCUCACAAC | |
| | | |
| MPV_SC_5M_Krarup_U74LS170LD185PD454N | | 13 |
| | CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU | |
| | GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU | |
| | GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG | |
| | CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCCU | |
| | GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG | |
| | AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG | |

AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG ${\tt AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU}$ AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAACAA

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TABLE 19-continued

| Strain | Nucleic Acid Sequence | SEQ I NO: |
|--------------------------------|---|--------------|
| | GUGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAG | |
| | CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU | |
| | UAGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGA | |
| | CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA | |
| | CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA | |
| | GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC | |
| | UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG | |
| | CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG | |
| | AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG | |
| | CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA | |
| | UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA | |
| | GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG | |
| | AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG | |
| | AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA | |
| | AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC | |
| | UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC | |
| | GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC | |
| | AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG | |
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG | |
| | CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG | |
| | CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC | |
| | UGAGAACCAGUUCCAGGUGGCCCUGGACCAGGUGUUCGA | |
| | GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA | |
| | CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU | |
| | CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC | |
| | CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC | |
| | CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU | |
| | GACCAACAAUGGCUUCAUCCCUCACAAC | |
| | | 100 |
| MPV_SC_DM_Krarup_E51PU74L | AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU | 133 |
| | CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA | |
| | GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU | |
| | GAGAACCGGCUGGUACACCAACGUGUUCACACUGCCUGU | |
| | GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG | |
| | CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU | |
| | GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG | |
| | AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG | |
| | UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA | |
| | GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA | |
| | CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG | |
| | AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU | |
| | AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC | |
| | GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG | |
| | UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC | |
| | CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU | |
| | AGCGACAACGCCGGGAAUCACACCAGCCAUCAGCCUGGAC | |
| | CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC | |
| | AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG | |
| | AUGCCUACAUCUGCCGGCCAGAUCUAGCUGGCGUCCGAG | |
| | | |
| | GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC | |
| | AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA | |
| | UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC | |
| | AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA | |
| | UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA | |
| | GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG | |
| | AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG | |
| | AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA | |
| | AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC | |
| | UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC | |
| | GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC | |
| | AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG | |
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG | |
| | CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG | |
| | CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC | |
| | UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG | |
| | AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA | |
| | ACAGAAUCCUGUCUAGCCCCAGGCUCUGGUGGACCAGUCCA | |
| | UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGCAGCU | |
| | | |
| | CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA | |
| | CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG | |
| | UGACCAACAAUGGCUUCAUCCCUCACAAC | |
| MPV SC UM Krarup E51PU74LD454N | AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU | 134 |

HMPV_SC_UM_Krarup_E51PU74LD454N

AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU GAGAACCGGCUGGUACACCAACGUGUUCACACUGCCUGU GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG

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TABLE 19-continued

SEO ID Strain Nucleic Acid Sequence NO: CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC UGAGAACCAGUUCCAGGUGGCCCUGGACCAGGUGUUCGA GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU GACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_SUabilizeAlpha_U74L AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 135 CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU

| Strain | Nucleic Acid Sequence | SEQ I NO: |
|------------------------------|---|--------------|
| | ± | |
| | CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG | |
| | UGACCAACAAUGGCUUCAUCCCUCACAAC | |
| HMPV_SC_SUabilizeAlpha_V55L | AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU | 136 |
| | CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA | |
| | GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU | |
| | GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU | |
| | GGGCGACCUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG | |
| | | |
| | GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG | |
| | UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA | |
| | GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA | |
| | CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG | |
| | AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU | |
| | AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC | |
| | GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG | |
| | UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC | |
| | | |
| | AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC | |
| | AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG | |
| | AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU | |
| | GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC | |
| | AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA | |
| | UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC | |
| | AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA | |
| | UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA | |
| | GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCA | |
| | AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCCUGCA | |
| | AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC | |
| | UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC | |
| | GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC | |
| | AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG | |
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG | |
| | CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG | |
| | | |
| | UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA | |
| | ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCCGGCU | |
| | UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU | |
| | CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA | |
| | CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG | |
| | UGACCAACAAUGGCUUCAUCCCUCACAAC | |
| IMPV_SC_SUabilizeAlpha_S170L | AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU | 137 |
| | CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA | |
| | GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU | |
| | GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU | |
| | GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU | |
| | GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG | |
| | AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG | |
| | UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA | |
| | GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA | |
| | CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG | |
| | AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU | |
| | AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC | |
| | GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAACAA GUGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAG | |
| | CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU | |
| | UAGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGA | |
| | CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA | |
| | CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA | |
| | GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC | |
| | UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG | |
| | | |
| | AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG CAAUUACGCCUGCCUGAGAGAGGACCAAGGCUGGUA | |
| | UUGUCAGAACGCCGGCAGCACCGUGAGAGCACCAAGGCUGGUA | |
| | GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG | |
| | AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG | |
| | AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG | |
| | AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA | |
| | | |

| TABLE | 19-continued |
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| | .9-continued | |
|--|--|---------------|
| Strain | Nucleic Acid Sequence | SEQ ID NO: |
| | GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACAG GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCGAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCG UGAGGAUCAGUUCCAGGUGGACCUGGUCGACCAGUGUUCG AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA ACAGAUCCUGUCUAGCCGAGAAGGAAACACCGGCU UCAUCAUCGUGAUCAUCCUGAUCGCUGGGCAGCU UCAUCAUCGUGAUCAUCCUGAUCAUCAUCAUCAAGAAGA CCAAGAAUCCCGCGCCUCUCAUCAUUAUCAAGAAGA CCAAGAACCCCGCCGCGCUCCUCCAGAACUGAGCGGAG UGACCAACAAUGGCUUCAUCCUCACAAC | |
| HMPV_SC_SUabilizeAlpha_U174W | AUGAGCUGGAAGGUGGUCAUCAUCAUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGUGUGU GAGAACCGGCUGGIACACCACGUGUUCACACUGGUGU GGGCACCGUCGAGAUCUGACAUGUCUGAUGGCCUAG CCUGAUCAAGACCGAGCUGACUGACCUGAUCUGAU | 138 |
| HMPV_SC_4M_SUabilizeAlpha_V55LU74LS170LU174W | | 139 |

Nucleic Acid Sequence

CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA

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SEO ID

NO:

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Strain

HMPV ProlineSUab E51P

TABLE 19-continued

UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG UGACCAACAAUGGCUUCAUCCCUCACAAC AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 140 CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU GAGAACCGGCUGGUACACCAACGUGUUCACACUGCCUGU GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG UGACCAACAAUGGCUUCAUCCCUCACAAC AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU

HMPV_ProlineSUab_D185P

CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGGCUACCUGUCUGUGCU GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU

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| TABLE | 19-continued |
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| Strain | Nucleic Acid Sequence | SEQ II NO: |
|-----------------------|--|---------------|
| | AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG | |
| | UGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAGC CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU | |
| | AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC | |
| | CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC | |
| | AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG | |
| | AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU | |
| | GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA | |
| | UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGAGGGC | |
| | AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA | |
| | UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA | |
| | GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG | |
| | AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG | |
| | AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC | |
| | UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC | |
| | GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC | |
| | AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG | |
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG | |
| | | |
| | CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG | |
| | AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA | |
| | ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU | |
| | UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU | |
| | CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA | |
| | CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG UGACCAACAAUGGCUUCAUCCCUCACAAC | |
| MDV BrolinsClab D192D | AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU | 142 |
| MPV_ProlineSUab_D183P | CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGCAGAAGA | 142 |
| | GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU | |
| | GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU | |
| | GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG | |
| | CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU | |
| | GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG | |
| | AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA | |
| | GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA | |
| | CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG | |
| | AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU | |
| | AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC | |
| | GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG | |
| | UGCCCUAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU | |
| | AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC | |
| | CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC | |
| | AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG | |
| | AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU | |
| | GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC | |
| | AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC | |
| | AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA | |
| | UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA | |
| | GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG | |
| | AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG | |
| | AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA | |
| | AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC | |
| | GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC | |
| | AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG | |
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG | |
| | CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG | |
| | | |
| | UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA | |
| | AGAACAUCGAGAAUUCCCCAGGCUCUGGUGGACCAGUCCA | |
| | UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU | |
| | CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA | |
| | CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG | |
| | UGACCAACAAUGGCUUCAUCCCUCACAAC | |
| MPV_ProlineSUab_E131P | AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU | 143 |

AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU CACACCUCAGCACGGCCUGAAAGAAGCUACCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU

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TABLE 19-continued

| TZ | ABLE 19-continued | |
|-----------------------|---|--------------|
| Strain | Nucleic Acid Sequence | SEQ I NO: |
| | GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU | |
| | GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG | |
| | CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG | |
| | AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG | |
| | UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA | |
| | GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA | |
| | CUGCCUAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG | |
| | AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU | |
| | AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC | |
| | GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC | |
| | CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGCGCAGUUU | |
| | AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC | |
| | CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC | |
| | AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG | |
| | AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU | |
| | GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC | |
| | AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA | |
| | UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC | |
| | AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA | |
| | GAAGGACUGCGAGACAAGAGCGACCACGUGUUCUGUG | |
| | AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG | |
| | AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA | |
| | AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC | |
| | UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC | |
| | GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC | |
| | AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG | |
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG | |
| | CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC | |
| | UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG | |
| | AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA | |
| | ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU | |
| | UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU | |
| | CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA | |
| | CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG UGACCAACAAUGGCUUCAUCCCUCACAAC | |
| MPV_ProlineSUab_D447P | AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU | 144 |
| MPV_PIOTINESGAD_D447P | CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA | 144 |
| | GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU | |
| | GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU | |
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| | CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU | |
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| | AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG | |
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| | CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU | |
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| | UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC | |
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| | CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC | |
| | AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG | |
| | AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC | |
| | GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA | |
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| | AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA | |
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| | AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC | |
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| | | |
| | | |
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| | AAGCAGCUGAACAAGGGCUGCAGCUACAUCACAACCAA GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG | |
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG | |
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG | |

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TABLE 19-continued

SEO ID Nucleic Acid Sequence Strain NO: ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_UrimerRepulsionD454N AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 145 CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC UGAGAACCAGUUCCAGGUGGCCCUGGACCAGGUGUUCGA GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU GACCAACAAUGGCUUCAUCCCUCACAAC HMPV UrimerRepulsionE453N AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 146 CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA

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TABLE 19-continued

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| | UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC | |
| | GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC | |
| | AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG | |
| | GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG | |
| | CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG | |
| | CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC | |
| | UCAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCGA | |
| | GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA | |
| | CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU | |
| | CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC | |
| | CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC | |
| | CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU | |
| | GACCAACAAUGGCUUCAUCCCUCACAAC | |
| IMPV SUabilizeAlphaF196W | AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU | 147 |
| | CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA | |
| | GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU | |
| | GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU | |
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| | AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG | |
| | UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA | |
| | GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA | |
| | CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG | |
| | AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU | |
| | AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC | |
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| | UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG | |
| | CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG | |
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| | | |
| | | |
| | | |
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| | CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA | |
| | CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG | |
| | UGACCAACAAUGGCUUCAUCCCUCACAAC | |

EQUIVALENTS

Those skilled in the art will recognize, or be able to ⁵⁵ ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the disclosure

described herein. Such equivalents are intended to be encompassed by the following claims.

All references, including patent documents, disclosed herein are incorporated by reference in their entirety.

<160> NUMBER OF SEQ ID NOS: 147

<210> SEQ ID NO 1 <211> LENGTH: 1620 <212> TYPE: DNA <213> ORGANISM: Human metapneumovirus

SEQUENCE LISTING

403

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| aaatgtgaca | ttgetgatet | gaagatggct | gtcagcttca | gtcaattcaa | cagaagattt | 600 |
| ctaaatgttg | tgeggeagtt | ttcagacaat | gcagggataa | caccagcaat | atcattggac | 660 |
| ctgatgactg | atgetgagtt | ggccagagct | gtatcataca | tgccaacatc | tgcagggcag | 720 |
| ataaaactga | tgttggagaa | ccgcgcaatg | gtaaggagaa | aaggatttgg | aatcctgata | 780 |
| ggggtetaeg | gaagetetgt | gatttacatg | gttcaattgc | cgatctttgg | tgtcatagat | 840 |
| acaccttgtt | ggatcatcaa | ggcageteee | tettgeteag | aaaaaacgg | gaattatget | 900 |
| tgeeteetaa | gagaggatca | agggtggtat | tgtaaaaatg | caggatetae | tgtttactac | 960 |
| ccaaatgaaa | aagactgcga | aacaagaggt | gatcatgttt | tttgtgacac | agcagcaggg | 1020 |
| atcaatgttg | ctgagcaatc | aagagaatgc | aacatcaaca | tatctactac | caactaccca | 1080 |
| tgcaaagtca | gcacaggaag | acaccctata | agcatggttg | cactatcacc | teteggtget | 1140 |
| | | | | | | 1 |

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| tgcaaagtca | gcacaggaag | acaccctatc | agcatggttg | cactatcacc | teteggtget | 1140 |
| ttggtagett | gctacaaagg | ggttagetge | tcgactggca | gtaatcaggt | tggaataatc | 1200 |
| aaacaactac | ctaaaggctg | ctcatacata | actaaccagg | acgcagacac | tgtaacaatt | 1260 |
| gacaacactg | tgtatcaact | aagcaaagtt | gagggtgaac | agcatgtaat | aaaagggaga | 1320 |
| ccagtttcaa | gcagttttga | tccaatcagg | tttcctgagg | atcagttcaa | tgttgegett | 1380 |
| gatcaagtet | ttgaaagcat | tgaaaacagt | caagcactag | tggaccagtc | aaacaaaatt | 1440 |
| ctgaacagtg | cagaaaaagg | aaacactggt | ttcattattg | taataattt | gattgctgtt | 1500 |
| cttgggttaa | ccatgatttc | agtgagcatc | atcatcataa | tcaaaaaaac | aaggaagccc | 1560 |
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| ttaattgcag ttggactget eetataetge aagg | ccagaa gcacaccagt cacactaagt | 1690 |
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| Thr Leu Glu Val Gly Asp Val Glu Asn L 50 55 | eu Thr Cys Ser Asp Gly Pro 60 | |
| Ser Leu Ile Lys Thr Glu Leu Asp Leu T 65 70 | hr Lys Ser Ala Leu Arg Glu 75 80 | |
| Leu Lys Thr Val Ser Ala Asp Gln Leu A 85 9 | - | |
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| Ile Lys Leu Met Leu Glu Asn Arg Ala M 245 2 | et Val Arg Arg Lys Gly Phe 50 255 | |
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| Pro Asn Glu Lys Asp Cys Glu Thr Arg G | ly Asp His Val Phe Cys Asp | |
| | | |

| | | | | | | | | | | | | con | tin | ued | |
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| | | | | 325 | | | | | 330 | | | | | 335 | |
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| Asn | Ile | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Суз | Lys | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Сүз |
| Tyr 385 | Lys | Gly | Val | Ser | Cys 390 | Ser | Ile | Gly | Ser | Asn 395 | | Val | Gly | Ile | Ile 400 |
| ГЛа | Gln | Leu | Asn | Lys 405 | Gly | Суз | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr | Val | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly |
| Glu | Gln | His 435 | Val | Ile | Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| Ile | Lys 450 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Asn | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Asn | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lys 515 | ГАЗ | Thr | Lys | Гла | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| His | Gly | Leu | Lys 20 | Glu | Ser | Tyr | Leu | Glu 25 | Glu | Ser | Cys | Ser | Thr 30 | Ile | Thr |
| Glu | Gly | Tyr 35 | Leu | Ser | Val | Leu | Arg 40 | Thr | Gly | Trp | Tyr | Thr 45 | Asn | Val | Phe |
| Thr | Leu 50 | Glu | Val | Gly | Asp | Val 55 | Glu | Asn | Leu | Thr | 60 СЛа | Thr | Asp | Gly | Pro |
| Ser 65 | Leu | Ile | Lys | Thr | Glu 70 | Leu | Asp | Leu | Thr | Lys 75 | Ser | Ala | Leu | Arg | Glu 80 |
| Leu | Lys | Thr | Val | Ser 85 | Ala | Asp | Gln | Leu | Ala 90 | Arg | Glu | Glu | Gln | Ile 95 | Glu |
| Asn | Pro | Arg | Gln 100 | Ser | Arg | Phe | Val | Leu 105 | Gly | Ala | Ile | Ala | Leu 110 | Gly | Val |
| Ala | Thr | Ala 115 | Ala | Ala | Val | Thr | Ala 120 | Gly | Ile | Ala | Ile | Ala 125 | | Thr | Ile |
| Arg | Leu 130 | | Ser | Glu | Val | Asn 135 | | Ile | Lys | Gly | Ala 140 | | | Gln | Thr |
| | | Ala | Val | Ser | Thr | | Gly | Asn | Gly | | Arg | Val | Leu | Ala | |
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413

| Ala V | /al | Arg | Glu | Leu 165 | Lys | Glu | Phe | Val | Ser 170 | Lys | Asn | Leu | Thr | Ser 175 | Ala |
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| Phe S | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser |
| Asp I 2 | \sn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp |
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| Ile I | ya | Leu | Met | Leu 245 | Glu | Asn | Arg | Ala | Met 250 | Val | Arg | Arg | Lys | Gly 255 | Phe |
| Gly I | lle | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu I | ?ro | Ile 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Суя | Trp | Ile 285 | Ile | Lys | Ala |
| Ala H | 2ro 290 | Ser | СЛа | Ser | Glu | Lys 295 | Asn | Gly | Asn | Tyr | Ala 300 | Суз | Leu | Leu | Arg |
| Glu <i>X</i> 305 | /sp | Gln | Gly | Trp | Tyr 310 | Cys | Lys | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro A | \sn | Glu | Lys | Asp 325 | Сув | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Сув 335 | Asp |
| Thr A | \la | Ala | Gly 340 | Ile | Asn | Val | Ala | Glu 345 | Gln | Ser | Arg | Glu | Cys 350 | Asn | Ile |
| Asn 1 | lle | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Суз | Lys | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro 1 | [le 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Суз |
| Tyr I 385 | уз | Gly | Val | Ser | Сув 390 | Ser | Ile | Gly | Ser | Asn 395 | Trp | Val | Gly | Ile | Ile 400 |
| Lүз (| Jln | Leu | Pro | Lys 405 | Gly | Cys | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Аар |
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| Glu (| Jln | His 435 | Val | Ile | Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| Ile I 4 | јув 150 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Asn | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 8 465 | Ser | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | ГЛа | Ile 480 |
| Leu A | \sn | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Val 495 | Ile |
| Leu V | /al | Ala | Val 500 | Leu | Gly | Leu | Thr | Met 505 | Ile | Ser | Val | Ser | Ile 510 | Ile | Ile |
| Ile I | lle | Lys 515 | ГЛЗ | Thr | Arg | Lys | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Asn |
| Gly V | 7al 530 | Thr | Asn | Gly | Gly | Phe 535 | Ile | Pro | His | Ser | | | | | |
| 2010- | | ю т т | | 7 | | | | | | | | | | | |
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| Thr | Leu 50 | Glu | Val | Gly | Asp | Val 55 | Glu | Asn | Leu | Thr | Сүз 60 | Thr | Asp | Gly | Pro |
| Ser 65 | Leu | Ile | гуа | Thr | Glu 70 | Leu | Aab | Leu | Thr | Lys 75 | Ser | Ala | Leu | Arg | Glu 80 |
| Leu | Lys | Thr | Val | Ser 85 | Ala | Asp | Gln | Leu | Ala 90 | Arg | Glu | Glu | Gln | Ile 95 | Glu |
| Asn | Pro | Arg | Gln 100 | Ser | Arg | Phe | Val | Leu 105 | Gly | Ala | Ile | Ala | Leu 110 | Gly | Val |
| Ala | Thr | Ala 115 | Ala | Ala | Val | Thr | Ala 120 | Gly | Ile | Ala | Ile | Ala 125 | Гуз | Thr | Ile |
| Arg | Leu 130 | Glu | Ser | Glu | Val | Asn 135 | Ala | Ile | Lys | Gly | Ala 140 | Leu | Lys | Thr | Thr |
| Asn 145 | Glu | Ala | Val | Ser | Thr 150 | Leu | Gly | Asn | Gly | Val 155 | Arg | Val | Leu | Ala | Thr 160 |
| Ala | Val | Arg | Glu | Leu 165 | Гла | Glu | Phe | Val | Ser 170 | Lys | Asn | Leu | Thr | Ser 175 | Ala |
| Ile | Asn | Гуз | Asn 180 | ГЛа | Cys | Aab | Ile | Ala 185 | Asp | Leu | ГАз | Met | Ala 190 | Val | Ser |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser |
| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Asn | Asp |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Ser | Tyr | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 |
| Ile | Lys | Leu | Met | Leu 245 | Glu | Asn | Arg | Ala | Met 250 | Val | Arg | Arg | Lys | G1y 255 | Phe |
| Gly | Ile | Leu | 11e 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu | Pro | Ile 275 | Phe | Gly | Val | Ile | Asn 280 | Thr | Pro | Суя | Trp | Ile 285 | Ile | Lys | Ala |
| Ala | Pro 290 | Ser | Сүз | Ser | Glu | Lys 295 | Asp | Gly | Asn | Tyr | Ala 300 | Сув | Leu | Leu | Arg |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Сув | гла | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro | Asn | Glu | Lys | Asp 325 | Суз | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Сув 335 | Asp |
| Thr | Ala | Ala | Gly 340 | Ile | Asn | Val | Ala | Glu 345 | Gln | Ser | Arg | Glu | Сув 350 | Asn | Ile |
| Asn | Ile | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Сув | Lys | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Суз |
| Tyr 385 | Lys | Gly | Val | Ser | Суз 390 | Ser | Thr | Gly | Ser | Asn 395 | Gln | Val | Gly | Ile | Ile 400 |
| Lys | Gln | Leu | Pro | Lys 405 | Gly | Cys | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
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417

| Thr | Val | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly |
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| Ile | Arg 450 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Asn | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Ser | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Lys | Ile 480 |
| Leu | Asn | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Leu | Thr | Met 505 | Ile | Ser | Val | Ser | Ile 510 | Ile | Ile |
| Ile | Ile | Lys 515 | Гла | Thr | Arg | Lys | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Asn |
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| Ala | Val | Thr | Leu 20 | Сүз | Phe | Ala | Ser | Ser 25 | Gln | Asn | Ile | Thr | Glu 30 | Glu | Phe |
| Tyr | Gln | Ser 35 | Thr | Суз | Ser | Ala | Val 40 | Ser | Lys | Gly | Tyr | Leu 45 | Ser | Ala | Leu |
| Arg | Thr 50 | Gly | Trp | Tyr | Thr | Ser 55 | Val | Ile | Thr | Ile | Glu 60 | Leu | Ser | Asn | Ile |
| Lys 65 | Glu | Asn | ГЛа | Сүз | Asn 70 | Gly | Thr | Asp | Ala | Lys 75 | Val | Гуа | Leu | Ile | Lys 80 |
| Gln | Glu | Leu | Aab | Lys 85 | Tyr | Гла | Asn | Ala | Val 90 | Thr | Glu | Leu | Gln | Leu 95 | Leu |
| Met | Gln | Ser | Thr 100 | Pro | Ala | Ala | Asn | Asn 105 | Arg | Ala | Arg | Arg | Glu 110 | Leu | Pro |
| Arg | Phe | Met 115 | Asn | Tyr | Thr | Leu | Asn 120 | Asn | Thr | Lys | Asn | Thr 125 | Asn | Val | Thr |
| Leu | Ser 130 | Гуз | Гүз | Arg | Гуз | Arg 135 | Arg | Phe | Leu | Gly | Phe 140 | Leu | Leu | Gly | Val |
| Gly 145 | Ser | Ala | Ile | Ala | Ser 150 | Gly | Ile | Ala | Val | Ser 155 | ГЛа | Val | Leu | His | Leu 160 |
| Glu | Gly | Glu | Val | Asn 165 | - | Ile | Lys | Ser | Ala 170 | Leu | Leu | Ser | Thr | Asn 175 | Lys |
| Ala | Val | Val | Ser 180 | Leu | Ser | Asn | Gly | Val 185 | Ser | Val | Leu | Thr | Ser 190 | Lys | Val |
| Leu | Asp | Leu 195 | Гүз | Asn | Tyr | Ile | Asp 200 | Гуа | Gln | Leu | Leu | Pro 205 | Ile | Val | Asn |
| ГЛа | Gln 210 | Ser | СЛа | Ser | Ile | Ser 215 | Asn | Ile | Glu | Thr | Val 220 | Ile | Glu | Phe | Gln |
| Gln 225 | Lys | Asn | Asn | Arg | Leu 230 | Leu | Glu | Ile | Thr | Arg 235 | Glu | Phe | Ser | Val | Asn 240 |
| Ala | Gly | Val | Thr | Thr 245 | Pro | Val | Ser | Thr | Tyr 250 | Met | Leu | Thr | Asn | Ser 255 | Glu |
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| Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro 305 310 315 320 |
| Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg 325 330 335 |
| Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe 340 345 350 |
| Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp 355 360 365 |
| Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Ile 370 375 380 |
| Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr 385 390 395 400 |
| Asp Val Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys 405 410 415 |
| Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile 420 425 430 |
| Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp 435 440 445 |
| Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly 450 455 460 |
| Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro 465 470 475 480 |
| Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn 485 490 495 |
| Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu 500 505 510 |
| Leu His Asn Val Asn Ala Gly Lys Ser Thr Thr Asn Ile Met Ile Thr 515 520 525 |
| Thr Ile Ile Val Ile Ile Val Ile Leu Leu Ser Leu Ile Ala Val 530 535 540 |
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| aactettgtg gtgaccaaca gatcaagcaa tacaagaggt tattggatag actgatcatt 240 |
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421

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| tacaatatee aaaatagaga atggtatate eetetteeea geeatateat gaegaaaggg | 960 |
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| ctagatteta ttggaagttg geateaatet ageaetaeaa teatagttat tttgataatg | 1500 |
| atgattatat tgtttataat taatataaca ataattacaa ttgcaattaa gtattacaga | 1560 |
| attcaaaaga gaaatcgagt ggatcaaaat gataagccgt atgtattaac aaacaag | 1617 |
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| atggaatact ggaagcacac caaccacgga aaggatgctg gtaatgagct ggagacatcc | 60 |
| acagecaete atggeaacaa geteaceaae aagataacat atatattgtg gaegataaee | 120 |
| ctggtgttat tatcaatagt cttcatcata gtgctaacta attccatcaa aagtgaaaag | 180 |
| gcccgcgaat cattgctaca agacataaat aatgagttta tggaagttac agaaaagatc | 240 |
| caagtggcat cggataatac taatgatcta atacagtcag gagtgaatac aaggettett | 300 |
| acaatteaga gteatgteea gaattatata eeaatateat tgacacaaca aatateggat | 360 |
| cttaggaaat tcattagtga aattacaatt agaaatgata atcaagaagt gccaccacaa | 420 |
| agaataacac atgatgtggg tataaaacct ttaaatccag atgatttetg gagatgeaeg | 480 |
| tetggtette catetttgat gaaaacteea aaaataagat taatgeeggg accaggatta | 540 |
| ttagetatge caacgactgt tgatggetgt gteagaacee egteettagt gataaatgat | 600 |
| | |
| ctgatttatg cttacacctc aaatctaatt actcgaggtt gccaggatat agggaaatca | 660 |
| etgatttatg ettacaeete aaatetaatt aetegaggtt geeaggatat agggaaatea tateaagtat taeagatagg gataataaet gtaaaeteag aettggtaee tgaettaaat | |
| | 660 |
| tatcaagtat tacagatagg gataataact gtaaactcag acttggtacc tgacttaaat | 660 720 |

423

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gcatcatcag gcatagaaga tattgtactt gatattgtca attatgatgg ctcaatctcg 900 acaacaagat ttaagaataa taatataagt tttgatcaac catatgoggo attataccoa 960 tetgttggae cagggatata etacaaagge aaaataatat ttetegggta tggaggtett 1020 gaacateeaa taaatgagaa tgeaatetge aacacaaetg ggtgteetgg gaaaacaeag 1080 agagactgta atcaagcatc tcatagtcca tggttttcag atagaaggat ggtcaactct 1140 1200 ataattgttg ttgacaaggg cttgaactca gttccaaaat tgaaggtatg gacgatatct atgagacaaa attactgggg gtcagaagga agattacttc tactaggtaa caagatctac 1260 atatacacaa gatetacaag tiggcacage aagttacaat taggaataat igacattact 1320 gactacagtg atataaggat aaaatggaca tggcataatg tgctatcaag accaggaaac 1380 aatqaatqte catqqqqaca tteatqteeq qatqqatqta taacqqqaqt atataceqat 1440 gcatateeac teaateeeac aggaageatt gtateatetg teatattgga eteacaaaaa 1500 togagagtea acceagteat aacttactea acageaaceg aaagggtaaa egagetgget 1560 atoogaaaca aaacactoto agotgggtao acaacaacaa gotgoattao acactataac 1620 1680 aaaqqqtatt qttttcatat aqtaqaaata aatcataaaa qcttaaacac atttcaaccc

aaagggtatt gttttcatat agtagaaata aatcataaaa gcttaaacac atttcaacce 1680 atgttgttca aaacagagat tccaaaaagc tgcagt 1716

<210> SEQ ID NO 11 <211> LENGTH: 1716 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 11

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| atcatcgtgg tggacaaggg cctgaacagc gtgcccaagc tgaaagtgtg gacaatcagc | 1200 |
| atgegeeaga actactgggg cagegaggge agaettetge tgetgggaaa caagatetae | 1260 |
| atetacaeee ggteeaceag etggeacage aaaetgeage tgggaateat egacateaee | 1320 |
| gactacageg acateeggat caagtggaee tggeacaaeg tgetgageag aceeggeaae | 1380 |
| aatgagtgee ettggggeea cagetgeeee gatggatgta teaceggegt gtacacegae | 1440 |
| geetaceeee tgaateetae eggeteeate gtgteeageg tgateetgga cageeagaaa | 1500 |
| agcagagtga accocgtgat cacatacagc accgccaccg agagagtgaa cgaactggcc | 1560 |
| atcagaaaca agaccetgag egeeggetae accaecaeaa getgeateae acaetaeaae | 1620 |
| aagggetaet getteeaeat egtggaaate aaceaeaagt eeetgaaeae etteeageee | 1680 |
| atgetgttea agaeegagat eeccaagage tgetee | 1716 |
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| gacatcacca agotgcagca cgtggggcgtg ctcgtgaaca gococcaaggg catgaagatc | 120 |
| agecagaact tegagacacg ctacetgate etgageetga teeecaagat egaggacage | 180 |
| aacagetgeg gegaceagea gateaageag taeaagegge tgetggaeag aetgateate | 240 |
| cccctgtacg acggcctgcg gctgcagaaa gacgtgatcg tgaccaacca ggaaagcaac | 300 |
| gagaacaccg acccccggac cgagagatto ttoggoggog tgatoggcac aatogoootg | 360 |
| ggagtggeca caagegeeca gattacagee getgtggeee tggtggaage caageaggee | 420 |
| agaagegaca tegagaaget gaaagaggee ateegggaca eeaacaagge egtgeagage | 480 |
| gtgcagtcca gcgtgggcaa tctgatcgtg gccatcaagt ccgtgcagga ctacgtgaac | 540 |
| aaagaaateg tgeeetetat egeeeggetg ggetgtgaag etgeeggaet geagetggge | 600 |
| attgocotga cacagoacta cagogagotg accaacatot toggogacaa catoggoago | 660 |
| ctgcaggaaa agggcattaa gctgcaggga atcgccagcc tgtaccgcac caacatcacc | 720 |
| gagatettea ceaccageae egtggataag taegaeatet aegaeetget gtteaeegag | 780 |
| agcatcaaag tgegegtgat egaegtggae etgaaegaet aeageateae eetgeaagtg | 840 |
| cggctgcccc tgctgaccag actgctgaac acccagatet acaaggtgga cagcatetee | 900 |
| tacaacatoo agaacegega gtggtacato estetgecea gecacattat gaceaaggge | 960 |
| gcetttetgg geggageega egtgaaagag tgeategagg eetteageag etacatetge | 1020 |
| cccagegaee etggettegt getgaaceae gagatggaaa getgeetgag eggeaacate | 1080 |
| agecagtgee ceagaaeeae egtgaeetee gaeategtge ceagataege ettegtgaat | 1140 |
| ggeggegtgg tggecaactg catcaccacc acctgtacct gcaacggeat eggeaacegg | 1200 |
| atcaaccage etcoegatea gggegtgaag attateacee acaaagagtg taacaceate | 1260 |
| ggcatcaacg gcatgctgtt caataccaac aaagagggca cootggcott ctacaccooc | 1320 |
| gacgatatca cootgaacaa otoogtggot otggaccooa togacatoto catogagotg | 1380 |
| aacaaggeea agagegaeet ggaagagtee aaagagtgga teeggeggag caaccagaag | 1440 |
| ctggacteta teggeagetg geaceagage ageaceacea teategtgat eetgattatg | 1500 |
| | |

| 1 | 2 | 7 |
|---|---|---|
| | - | 1 |

| -continue | |
|-----------|--|
| | |

| atgattatcc tgttcatca | at caacattacc atcatcacta | tegecattaa gtactacegg | 1560 |
|--|------------------------------------|-----------------------|------|
| atccagaaac ggaaccgg | gt ggaccagaat gacaagcoot | acgtgctgac aaacaag | 1617 |
| <210> SEQ ID NO 13 <211> LENGTH: 539 <212> TYPE: PRT <213> ORGANISM: Huma | an parainfluenza virus 3 | | |
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| Met Pro Ile Ser Ile | Leu Leu Ile Ile Thr Thr | Met Ile Met Ala Ser | |
| 1 5 | 10 | 15 | |
| His Cys Gln Ile Asp | Ile Thr Lys Leu Gln His | Val Gly Val Leu Val | |
| 20 | 25 | 30 | |
| Asn Ser Pro Lys Gly | Met Lys Ile Ser Gln Asn | Phe Glu Thr Arg Tyr | |
| 35 | 40 | 45 | |
| Leu Ile Leu Ser Leu | Ile Pro Lys Ile Glu Asp | Ser Asn Ser Cys Gly | |
| 50 | 55 | 60 | |
| Asp Gln Gln Ile Lys | Gln Tyr Lys Arg Leu Leu | Asp Arg Leu Ile Ile | |
| 65 | 70 | 80 | |
| Pro Leu Tyr Asp Gly | Leu Arg Leu Gln Lys Asp | Val Ile Val Thr Asn | |
| 85 | 90 | 95 | |
| Gln Glu Ser Asn Glu | Asn Thr Asp Pro Arg Thr | Glu Arg Phe Phe Gly | |
| 100 | 105 | 110 | |
| Gly Val Ile Gly Thr | Ile Ala Leu Gly Val Ala | Thr Ser Ala Gln Ile | |
| 115 | 120 | 125 | |
| Thr Ala Ala Val Ala | Leu Val Glu Ala Lys Gln | Ala Arg Ser Asp Ile | |
| 130 | 135 | 140 | |
| Glu Lys Leu Lys Glu 145 | Ala Ile Arg Asp Thr Asn 150 155 | | |
| Val Gln Ser Ser Val | Gly Asn Leu Ile Val Ala | Ile Lys Ser Val Gln | |
| 165 | 170 | 175 | |
| Asp Tyr Val Asn Lys | Glu Ile Val Pro Ser Ile | Ala Arg Leu Gly Cys | |
| 180 | 185 | 190 | |
| Glu Ala Ala Gly Leu | Gln Leu Gly Ile Ala Leu | Thr Gln His Tyr Ser | |
| 195 | 200 | 205 | |
| Glu Leu Thr Asn Ile | Phe Gly Asp Asn Ile Gly | Ser Leu Gln Glu Lys | |
| 210 | 215 | 220 | |
| Gly Ile Lys Leu Gln | Gly Ile Ala Ser Leu Tyr | Arg Thr Asn Ile Thr | |
| 225 | 230 235 | 240 | |
| Glu Ile Phe Thr Thr | Ser Thr Val Asp Lys Tyr | Asp Ile Tyr Asp Leu | |
| 245 | 250 | 255 | |
| Leu Phe Thr Glu Ser | Ile Lys Val Arg Val Ile | Asp Val Asp Leu Asn | |
| 260 | 265 | 270 | |
| Asp Tyr Ser Ile Thr | Leu Gln Val Arg Leu Pro | Leu Leu Thr Arg Leu | |
| 275 | 280 | 285 | |
| Leu Asn Thr Gln Ile | Tyr Lys Val Asp Ser Ile | Ser Tyr Asn Ile Gln | |
| 290 | 295 | 300 | |
| Asn Arg Glu Trp Tyr | Ile Pro Leu Pro Ser His | Ile Met Thr Lys Gly | |
| 305 | 310 315 | 320 | |
| Ala Phe Leu Gly Gly | Ala Asp Val Lys Glu Cys | Ile Glu Ala Phe Ser | |
| 325 | 330 | 335 | |
| Ser Tyr Ile Cys Pro | Ser Asp Pro Gly Phe Val | Leu Asn His Glu Met | |
| 340 | 345 | 350 | |

| | | | | | | | | | ~1 | Cys | Deve | | | | | |
|--|---|--|---|--|--|---|---|--|---|--|---|---|--|---|--|--|
| Glu | Ser | Cys 355 | Leu | Ser | Gly | Asn | Ile 360 | Ser | GIn | - | PIO | Arg 365 | Thr | Thr | Val | |
| Thr | Ser 370 | Asp | Ile | Val | Pro | Arg 375 | | Ala | Phe | Val | Asn 380 | Gly | Gly | Val | Val | |
| Ala 385 | Asn | Cys | Ile | Thr | Thr 390 | Thr | Сув | Thr | Cys | Asn 395 | Gly | Ile | Gly | Asn | Arg 400 | |
| Ile | Asn | Gln | Pro | Pro 405 | Asp | Gln | Gly | Val | Lys 410 | Ile | Ile | Thr | His | Lys 415 | Glu | |
| СЛа | Asn | Thr | Ile 420 | Gly | Ile | Asn | Gly | Met 425 | Leu | Phe | Asn | Thr | Asn 430 | ГÀа | Glu | |
| Gly | Thr | Leu 435 | Ala | Phe | Tyr | Thr | Pro 440 | Asp | Asp | Ile | Thr | Leu 445 | Asn | Asn | Ser | |
| Val | Ala 450 | Leu | Asp | Pro | Ile | Asp 455 | Ile | Ser | Ile | Glu | Leu 460 | Asn | Lys | Ala | Lys | |
| Ser 465 | Asp | Leu | Glu | Glu | Ser 470 | Lys | Glu | Trp | Ile | Arg 475 | Arg | Ser | Asn | Gln | Lys 480 | |
| Leu | Asp | Ser | Ile | Gly 485 | Ser | Trp | His | Gln | Ser 490 | Ser | Thr | Thr | Ile | Ile 495 | Val | |
| | | Ile | 500 | | | | | 505 | | | | | 510 | | | |
| Thr | Ile | Ala 515 | Ile | Lys | Tyr | Tyr | Arg 520 | Ile | Gln | Lys | Arg | Asn 525 | Arg | Val | Asp | |
| | Asn | Asp | Lys | Pro | Tyr | Val 535 | Leu | Thr | Asn | Lys | | | | | | |
| <21(<21) | 530)> SI L> LI | EQ II ENGTH | H: 51 | | | | | | | | | | | | | |
| <210 <211 <212 | 530)> SI L> LI 2> TY | | H: 57 PRT | 72 | an pa | araiı | nflue | enza | viru | 15 3 | | | | | | |
| <210 <211 <212 <213 <400 | 530)> SH 1> LH 2> T? 3> OH 0> SH | ENGTI YPE : | H: 57 PRT ISM: NCE: | 72 Huma 14 | | | | | | | Asp | Ala | Gly | Asn | Glu | |
| <21(<211 <212 <213 <40(Met 1 | 530)> SH L> LH 2> T 3> OF 0> SH Glu | ength YPE : RGANI EQUEI | H: 57 PRT ISM: NCE: Trp | 72 Huma 14 Lys 5 | His | Thr | Asn | His | Gly 10 | Lys | _ | | Asn | 15 | | |
| <210 <211 <212 <213 <400 Met 1 Leu | 530)> SH L> LH 2> T 3> OF 0> SH Glu Glu | ENGTH YPE: RGANI EQUEN Tyr Thr Ile | H: 57 PRT ISM: NCE: Trp Ser 20 | 72 Huma 14 Lys 5 Thr | His Ala | Thr Thr | Asn His Thr | His Gly 25 | Gly 10 Asn | Lys Lys | Leu | Thr Ser | Asn 30 | 15 Lys | Ile | |
| <210 <211 <212 <213 <400 Met 1 Leu Thr | 530)> SH L> LH 2> TY 3> OF Glu Glu Tyr Ile | ENGTH YPE : RGANI EQUEN Tyr Thr | H: 57 PRT ISM: NCE: Trp Ser 20 Leu | 72 Huma 14 Lys 5 Thr Trp | His Ala Thr | Thr Thr Ile Ser | Asn His Thr 40 | His Gly 25 Leu | Gly 10 Asn Val | Lys Lys Leu | Leu Leu Lys | Thr Ser 45 | Asn 30 Ile | 15 Lys Val | Ile Phe | |
| <210 <211 <212 <213 <400 Met 1 Leu Thr Ile Leu | 530 530 530 54 54 50 530 530 530 530 530 530 530 | ENGTH YPE: RGANI EQUEN Tyr Thr Ile 35 | H: 57 PRT ISM: NCE: Trp Ser 20 Leu Leu | 72 Huma 14 Lys 5 Thr Trp Thr | His Ala Thr Asn Asn | Thr Thr Ile Ser 55 | Asn His Thr 40 Ile | His Gly 25 Leu Lys | Gly 10 Asn Val Ser | Lys Lys Leu Glu Glu | Leu Leu Lys 60 | Thr Ser 45 Ala | Asn 30 Ile Arg | 15 Lys Val Glu | Ile Phe Ser Ile | |
| <210 <211 <212 <213 <400 Met 1 Leu Thr Ile Leu 65 | 530)> SH 1> LL 2> TY 3> OF Glu Glu Glu Tyr Ile 50 Leu | ENGTH YPE: RGAN EQUEN Tyr Thr Ile 35 Val | H: 5 ⁻ PRT ISM: ISM: Trp Ser 20 Leu Leu Asp | 72 Huma 14 Lys 5 Thr Thr Thr Ile Asp | His Ala Thr Asn 70 | Thr Thr Ile Ser 55 Asn | Asn His Thr 40 Ile Glu | His Gly 25 Leu Lys Phe | Gly 10 Asn Val Ser Met Leu | Lys Lys Leu Glu 75 | Leu Leu Lys 60 Val | Thr Ser 45 Ala Thr | Asn 30 Ile Arg Glu | 15 Lys Val Glu Lys Val | Ile Phe Ser Ile 80 | |
| <210 <211 <212 <212 <213 Leu Leu Ile Leu 65 Gln | 530 SI SI SI SI SI SI SI SI SI SI SI SI SI | ENGTH YPE: CRGANI EQUEN Tyr Thr Ile 35 Val Gln | H: 57 PRT ISM: ISM: ICE: Trp Ser 20 Leu Leu Asp Ser Leu | Huma 14 Lys 5 Thr Trp Thr Ile Asp 85 | His Ala Thr Asn Asn 70 Asn | Thr Thr Ile Ser 55 Asn Thr | Asn His Thr 40 Ile Glu Asn | His Gly 25 Leu Lys Phe Asp His | Gly 10 Asn Val Ser Met Leu 90 | Lys Lys Glu Glu 75 | Leu Leu Lys 60 Val Gln | Thr Ser 45 Ala Thr Ser | Asn 30 Ile Arg Glu Gly Ile | 15 Lys Val Glu Lys Val 95 | Ile Phe Ser Ile 80 Asn | |
| <210 <211 <212 <213 <400 Met 1 Leu Thr Ile Leu 65 Gln Thr | 530 SI SI SI SI SI SI Glu Glu Glu Tyr Ile 50 Leu Val Arg | ENGTH IPE:: CQAN: SQUEN TYT Thr Ile 35 Val Gln Ala Leu Thr | H: 57 PRT ISM: NCE: Trp Ser 20 Leu Leu Asp Ser Leu 100 | 72 Huma 14 Lys 5 Thr Thr Ile 85 Thr | His Ala Thr Asn 70 Asn Ile | Thr Thr Ile Ser 55 Asn Thr Gln | Asn His Thr 40 Ile Glu Asn Ser Asp | His Gly 25 Leu Lys Phe Asp His 105 | Gly 10 Asn Val Ser Met Leu 90 Val | Lys Lys Glu 75 Ile Gln | Leu Leu Lys 60 Val Gln Asn | Thr Ser 45 Ala Thr Ser Tyr Ile | Asn 30 Ile Arg Glu Gly Ile 110 | 15 Lys Val Glu Lys Val 95 Pro | Ile Phe Ser Ile 80 Asn Ile | |
| <210 <211 <212 <213 <400 Met 1 Leu Thr Ile Leu 65 Gln Thr Ser | 530 SI SI SI SI SI SI SI Glu Glu Glu Tyr Ile So Leu Val Arg Leu Ile | ENGTH IPE: CQAN: EQUEN Tyr Thr Ile 35 Val Gln Ala Leu | H: 57 PRT ISM: NCE: Trp Ser 20 Leu Leu Asp Ser Leu 100 Gln | 72 Huma 14 Lys 5 Thr Thr Thr Ile 85 Thr Gln | His Ala Thr Asn 70 Asn Ile Ile | Thr Thr Ile Ser Ssr Thr Gln Ser Gln | Asn His Thr 40 Ile Glu Asn Ser Asp 120 | His Gly 25 Leu Lys Phe Asp His 105 Leu | Gly 10 Asn Val Ser Met Leu 90 Val Arg | Lys Lys Glu Glu 75 Ile Gln Lys | Leu Leu Lys 60 Val Gln Asn Phe Gln | Thr Ser 45 Ala Thr Ser Tyr Ile 125 | Asn 30 Ile Arg Glu Glu Gly Ile 110 Ser | 15 Lys Val Glu Lys Val 95 Pro Glu | Ile Phe Ser Ile 80 Asn Ile Ile | |
| <210 <211 <212 <212 <400 Met 1 Leu Thr Ile 65 Gln Thr Ser Thr Asp | 530 SI SI SI SI SI SI SI Glu Glu Tyr Ile 50 Leu Val Arg Leu Ile 130 | ENGTH YPE: CQNE EQUEN Tyr Thr Ille 35 Val Gln Ala Leu Thr 115 | H: 57 PRT ISM: ISM: ISM: Trp Ser 20 Leu Leu Leu Ser Leu 100 Gln Asn | 12 Huma 14 Lys 5 Thr Thr Thr Ile 85 Thr Gln Asp | His Ala Thr Asn Asn Asn Ile Ile Asn Pro | Thr Thr Ile Ser Thr Gln Ser Gln 135 | Asn His Thr 40 Ile Glu Asn Ser Asp 120 Glu | His Gly 25 Leu Lys Phe Asp His 105 Leu Val | Gly 10 Asn Val Ser Met Leu 90 Val Arg Pro | Lys Lys Glu Glu Glu Glu Lys Pro Asp | Leu Leu Lys 60 Val Gln Asn Phe Gln 140 | Thr Ser 45 Ala Thr Ser Tyr Ile 125 Arg | Asn 30 Ile Arg Glu Glu Ile 110 Ser Ile | 15 Lys Val Glu Lys Val 95 Pro Glu Thr | Ile Phe Ser Ile Asn Ile His | |
| <210 <211 <212 <213 <400 Met 1 Leu Thr Ile 65 Gln Thr Ser Thr Thr Asp 145 | 530 SI SI SI SI SI SI SI SI SI SI | ENGTH IPE: CQAN: SQUEN Tyr Thr Thr Ile 35 Val Gln Ala Leu Thr 115 Arg | H: 57 PRT ISM: VCE: Trp 20 Leu Leu Asp Ser Leu 100 Gln Asn Ile | 72 Huma 14 Lys 5 Thr Thr Thr Ile Asp 85 Thr Gln Asp Lys Ser | His Ala Thr Asn Asn Ile Ile Asn Pro 150 | Thr Thr Ile Ser Ssr Thr Gln Ser Gln 135 Leu | Asn His Thr 40 Ile Glu Asn Ser Asp 120 Glu Asn | His Gly 25 Leu Lys Phe Asp His 105 Leu Val | Gly 10 Asn Val Ser Met Leu 90 Val Arg Pro Asp | Lys Lys Glu Glu Glu Gln Lys Pro Asp 155 | Leu Leu Lys 60 Val Gln Asn Phe Gln 140 Phe | Thr Ser 45 Ala Thr Ser Tyr Ile 125 Arg Trp | Asn 30 Ile Arg Glu Glu Gly Ile 110 Ser Ile Arg | 15 Lys Val Glu Lys Val 95 Pro Glu Thr Cys Met | Ile Phe Ser Ile 80 Asn Ile Ile His Thr | |
| <210 <211 <212 <213 <400 Met 1 Leu Thr Ile 65 Gln Thr Ser Thr Asp 145 Ser | 530 SI SI SI SI SI SI SI SI SI SI | ENGTH YPE:: CQNET SQUEE Tyr Thr Ille 35 Val Gln Ala Leu Thr 115 Arg Gly | H: 57 PRT ISM: ISM: NCE: Trp Ser 20 Leu Leu Leu Ser 100 Gln Asn Ile Pro | 12 Huma 14 Lys 5 Thr Thr Thr Ile 85 Thr Gln Asp Lys Ser 165 | His Ala Thr Asn Asn Asn Ile Ile Asn Pro 150 Leu | Thr Thr Ile Ser Shr Gln Ser Gln 135 Leu Met | Asn His Thr 40 Glu Asn Ser Asp 120 Glu Asn Lys | His Gly 25 Leu Lys Phe Asp His 105 Leu Val Pro Thr | Gly 10 Asn Val Ser Leu 90 Val Arg Pro Asp Pro 170 | Lys Lys Glu Glu Glu Clu Gln Lys Pro Asp 155 Lys | Leu Leu Lys 60 Val Gln Asn Phe Gln 140 Phe Ile | Thr Ser 45 Ala Thr Ser Tyr Ile 125 Arg Trp Arg | Asn 30 Ile Arg Glu Glu Gly Ile 110 Ser Ile Arg Leu | 15 Lys Val Glu Lys Val 95 Pro Glu Thr Cys Met 175 | Ile Phe Ser Ile Asn Ile His Thr 160 Pro | |

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| Thr | Pro | Ser 195 | Leu | Val | Ile | Asn | Asp 200 | Leu | Ile | Tyr | Ala | Tyr 205 | Thr | Ser | Asn |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Leu | Ile 210 | Thr | Arg | Gly | Cys | Gln 215 | Asp | Ile | Gly | Lys | Ser 220 | Tyr | Gln | Val | Leu |
| Gln 225 | Ile | Gly | Ile | Ile | Thr 230 | Val | Asn | Ser | Asp | Leu 235 | Val | Pro | Asp | Leu | Asn 240 |
| Pro | Arg | Ile | Ser | His 245 | Thr | Phe | Asn | Ile | Asn 250 | Asp | Asn | Arg | Гуз | Ser 255 | Сүв |
| Ser | Leu | Ala | Leu 260 | Leu | Asn | Thr | Aap | Val 265 | Tyr | Gln | Leu | Суз | Ser 270 | Thr | Pro |
| Lys | Val | Asp 275 | Glu | Arg | Ser | Asp | Tyr 280 | Ala | Ser | Ser | Gly | Ile 285 | Glu | Asp | Ile |
| Val | Leu 290 | Asp | Ile | Val | Asn | Tyr 295 | Asp | Gly | Ser | Ile | Ser 300 | Thr | Thr | Arg | Phe |
| Lys 305 | Asn | Asn | Asn | Ile | Ser 310 | Phe | Asp | Gln | Pro | Tyr 315 | Ala | Ala | Leu | Tyr | Pro 320 |
| Ser | Val | Gly | Pro | Gly 325 | Ile | Tyr | Tyr | Lys | Gly 330 | Lys | Ile | Ile | Phe | Leu 335 | Gly |
| Tyr | Gly | Gly | Leu 340 | Glu | His | Pro | Ile | Asn 345 | Glu | Asn | Ala | Ile | Сув 350 | Asn | Thr |
| Thr | Gly | Суя 355 | Pro | Gly | Lys | Thr | Gln 360 | Arg | Asp | Суя | Asn | Gln 365 | Ala | Ser | His |
| Ser | Pro 370 | Trp | Phe | Ser | Asp | Arg 375 | Arg | Met | Val | Asn | Ser 380 | Ile | Ile | Val | Val |
| Asp 385 | Lys | Gly | Leu | Asn | Ser 390 | Val | Pro | Lys | Leu | Lys 395 | Val | Trp | Thr | Ile | Ser 400 |
| Met | Arg | Gln | Asn | Tyr 405 | Trp | Gly | Ser | Glu | Gly 410 | Arg | Leu | Leu | Leu | Leu 415 | Gly |
| Asn | Гла | Ile | Tyr 420 | Ile | Tyr | Thr | Arg | Ser 425 | Thr | Ser | Trp | His | Ser 430 | Lys | Leu |
| Gln | Leu | Gly 435 | Ile | Ile | Asp | Ile | Thr 440 | Asp | Tyr | Ser | Asp | 11e 445 | Arg | Ile | Lys |
| Γrp | Thr 450 | Trp | His | Asn | Val | Leu 455 | Ser | Arg | Pro | Gly | Asn 460 | Asn | Glu | САа | Pro |
| Trp 465 | Gly | His | Ser | Сүз | Pro 470 | Asp | Gly | Сүз | Ile | Thr 475 | Gly | Val | Tyr | Thr | Asp 480 |
| Ala | Tyr | Pro | Leu | Asn 485 | Pro | Thr | Gly | Ser | Ile 490 | Val | Ser | Ser | Val | Ile 495 | Leu |
| Aap | Ser | Gln | Lya 500 | Ser | Arg | Val | Asn | Pro 505 | Val | Ile | Thr | Tyr | Ser 510 | Thr | Ala |
| Thr | Glu | Arg 515 | Val | Asn | Glu | Leu | Ala 520 | Ile | Arg | Asn | Lys | Thr 525 | Leu | Ser | Ala |
| Gly | Tyr 530 | Thr | Thr | Thr | Ser | Cys 535 | Ile | Thr | His | Tyr | Asn 540 | Lys | Gly | Tyr | Суз |
| Phe 545 | His | Ile | Val | Glu | Ile 550 | Asn | His | Гла | Ser | Leu 555 | Asn | Thr | Phe | Gln | Pro 560 |
| Met | Leu | Phe | ГАа | Thr 565 | Glu | Ile | Pro | Lys | Ser 570 | Сув | Ser | | | | |
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n Arg Val Val Phe Thr Ile Leu Leu 1 5 10 15 Leu Leu Val Ala Pro Ala Tyr Ser 20 <210> SEQ ID NO 18 <211> LENGTH: 17 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polypeptide <400> SEQUENCE: 18 Met Lys Cys Leu Leu Tyr Leu Ala Phe Leu Phe Ile Gly Val Asn Cys 1 5 10 15 Ala <210> SEQ ID NO 19 <211> LENGTH: 15 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polypeptide <400> SEQUENCE: 19 Met Tr
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| | | | | -contin | nuea | | |
|------------|------------|------------|------------|------------|------------|------|--|
| gtagggeeag | attctgttaa | gtetgettgt | attgaggttg | atatacaaca | gacettettt | 120 | |
| gataaaactt | ggcctaggcc | aattgatgtt | tctaaggctg | acggtattat | ataccctcaa | 180 | |
| ggccgtacat | attetaacat | aactatcact | tatcaaggtc | ttttcccta | tcagggagac | 240 | |
| catggtgata | tgtatgttta | ctctgcagga | catgctacag | gcacaactee | acaaaagttg | 300 | |
| tttgtageta | actattetca | ggacgtcaaa | cagtttgcta | atgggtttgt | cgtccgtata | 360 | |
| ggagcagctg | ccaattccac | tggcactgtt | attattagec | catctaccag | cgctactata | 420 | |
| cgaaaaattt | accetgettt | tatgctgggt | tetteagttg | gtaatttete | agatggtaaa | 480 | |
| atgggccgct | tetteaatea | tactctagtt | ctttgeeeg | atggatgtgg | cactttactt | 540 | |
| agagetttt | attgtattet | agageetege | tctggaaatc | attgtcctgc | tggcaattee | 600 | |
| tatacttett | ttgccactta | tcacactect | gcaacagatt | gttetgatgg | caattacaat | 660 | |
| cgtaatgcca | gtetgaaete | ttttaaggag | tattttaatt | tacgtaactg | cacctttatg | 720 | |
| tacacttata | acattaccga | agatgagatt | ttagagtggt | ttggcattac | acaaactgct | 780 | |
| caaggtgttc | acctettete | ateteggtat | gttgatttgt | acggcggcaa | tatgtttcaa | 840 | |
| tttgccacct | tgeetgttta | tgatactatt | aagtattatt | ctatcattcc | tcacagtatt | 900 | |
| cgttctatcc | aaagtgatag | aaaagcttgg | gctgccttct | acgtatataa | acttcaaccg | 960 | |
| ttaactttcc | tgttggattt | ttctgttgat | ggttatatac | gcagagctat | agactgtggt | 1020 | |
| tttaatgatt | tgtcacaact | ccactgetca | tatgaateet | tcgatgttga | atctggagtt | 1080 | |
| tattcagttt | cgtctttcga | agcaaaacct | tetggeteag | ttgtggaaca | ggetgaaggt | 1140 | |
| gttgaatgtg | atttttcacc | tettetgtet | ggcacacete | ctcaggttta | taatttcaag | 1200 | |
| cgtttggttt | ttaccaattg | caattataat | cttaccaaat | tgettteact | ttttctgtg | 1260 | |
| aatgatttta | cttgtagtca | aatatctcca | gcagcaattg | ctagcaactg | ttattettea | 1320 | |
| ctgattttgg | attattttc | atacccactt | agtatgaaat | ccgatctcag | tgttagttct | 1380 | |
| gctggtccaa | tateccagtt | taattataaa | cagteettt | ctaatcccac | atgtttgatc | 1440 | |
| ttagcgactg | tteeteataa | ccttactact | attactaagc | ctcttaagta | cagctatatt | 1500 | |
| aacaagtgct | ctcgtcttct | ttctgatgat | cgtactgaag | tacctcagtt | agtgaacgct | 1560 | |
| aatcaatact | caccctgtgt | atccattgtc | ccatccactg | tgtgggaaga | cggtgattat | 1620 | |
| tataggaaac | aactatctcc | acttgaaggt | ggtggctggc | ttgttgctag | tggeteaaet | 1680 | |
| gttgccatga | ctgagcaatt | acagatgggc | tttggtatta | cagttcaata | tggtacagac | 1740 | |
| accaatagtg | tttgccccaa | gcttgaattt | gctaatgaca | caaaaattgc | ctctcaatta | 1800 | |
| ggcaattgcg | tggaatattc | cctctatggt | gtttegggee | gtggtgttt | tcagaattgc | 1860 | |
| acagetgtag | gtgttcgaca | gcagcgettt | gtttatgatg | cgtaccagaa | tttagttggc | 1920 | |
| tattattetg | atgatggcaa | ctactactgt | ctgcgtgctt | gtgttagtgt | tcctgtttct | 1980 | |
| gtcatctatg | ataaagaaac | taaaacccac | gctactctat | ttggtagtgt | tgcatgtgaa | 2040 | |
| cacatttett | ctaccatgtc | tcaatactcc | cgttctacgc | gatcaatgct | taaacggcga | 2100 | |
| gattetaeat | atggeeeet | tcagacacct | gttggttgtg | teetaggaet | tgttaattcc | 2160 | |
| tetttgtteg | tagaggactg | caagttgcct | ctcggtcaat | ctctctgtgc | tetteetgae | 2220 | |
| acacctagta | ctctcacacc | tcgcagtgtg | cgctctgtgc | caggtgaaat | gcgcttggca | 2280 | |
| tecattgett | ttaatcatcc | catteaggtt | gatcaactta | atagtagtta | ttttaaatta | 2340 | |
| agtataccca | ctaatttttc | ctttggtgtg | actcaggagt | acattcagac | aaccattcag | 2400 | |
| aaagttactg | ttgattgtaa | acagtacgtt | tgcaatggtt | tccagaagtg | tgagcaatta | 2460 | |
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| ctgcgcgagt atggccagtt ttgttccaaa ataaaccagg ctctccatgg tgccaattta | 2520 |
|---|-------------------|
| cgccaggatg attetgtacg taatttgttt gegagegtga aaagetetea ateateteet | 2580 |
| atcataccag gttttggagg tgactttaat ttgacacttc tagaacctgt ttctatatct | 2640 |
| actggcagtc gtagtgcacg tagtgctatt gaggatttgc tatttgacaa agtcactata | 2700 |
| getgateetg gttatatgea aggttaegat gattgtatge ageaaggtee ageateaget | 2760 |
| cgtgatetta tttgtgetca atatgtgget ggttataaag tattacetee tettatggat | 2820 |
| gttaatatgg aageegegta taetteatet ttgettggea geatageagg tgttggetgg | 2880 |
| actgctggct tatcctcctt tgctgctatt ccatttgcac agagtatytt ttataggtta | 2940 |
| aacggtgttg gcattactca acaggttett teagagaace aaaagettat tgeeaataag | 3000 |
| tttaatcagg ctctgggagc tatgcaaaca ggcttcacta caactaatga agcttttcgg | 3060 |
| aaggttcagg atgctgtgaa caacaatgca caggctctat ccaaattagc tagcgagcta | 3120 |
| tetaataett tiggigetat tieegeetet atiggagaea teataeaaeg tetigaigit | 3180 |
| ctcgaacagg acgeccaaat agacagaett attaatggee gtttgacaae actaaatget | 3240 |
| tttgttgcac agcagettgt tegtteegaa teagetgete ttteegetea attggetaaa | 3300 |
| gataaagtca atgagtgtgt caaggcacaa tccaagcgtt ctggattttg cggtcaaggc | 3360 |
| acacatatag tgteetttgt tgtaaatgee eetaatggee tttaetttat geatgttggt | 3420 |
| tattaceeta geaaceacat tgaggttgtt tetgettatg gtetttgega tgeagetaac | 3480 |
| cctactaatt gtatageeee tgttaatgge taetttatta aaactaataa eactaggatt | 3540 |
| gttgatgagt ggtcatatac tggctcgtcc ttctatgcac ctgagcccat cacctetet | 3600 |
| aatactaagt atgttgcacc acaggtgaca taccaaaaca tttctactaa cctccctcct | 3660 |
| cctcttctcg gcaattccac cgggattgac ttccaagatg agttggatga gtttttcaaa | 3720 |
| aatgttagca ccagtatacc taattttggt tetetaacac agattaatac tacattactc | 3780 |
| gatettaeet aegagatgtt gtetetteaa caagttgtta aageeettaa tgagtettae | 3840 |
| atagacetta aagagettgg caattataet tattacaaca aatggeegtg gtacatttgg | 3900 |
| ettggtttea ttgetggget tgttgeetta getetatgeg tettetteat aetgtgetge | 3960 |
| actggttgtg gcacaaactg tatgggaaaa cttaagtgta atcgttgttg tgatagatac | 4020 |
| gaggaatacg acctcgagcc gcataaggtt catgttcact aa | 4062 |
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| gtagggccag attetgttaa gtetgettgt attgaggttg atatacaaca gaetttettt | |
| | 120 |
| gataaaactt ggcctaggcc aattgatgtt tctaaggctg acggtattat ataccctcaa | 120 180 |
| gataaaactt ggeetaggee aattgatgtt tetaaggetg aeggtattat ataeceteaa ggeegtaeat attetaacat aaetateaet tateaaggte ttttteeeta teagggagae | |
| | 190 |
| ggeogtacat attetaacat aactateact tateaaggte ttttteeeta teagggagae | 180 240 |
| ggeegtacat attetaacat aactateaet tateaaggte tittteeeta teagggagae catggigata igiatgitta eteigeagga catgetaeag geacaaetee acaaaagiig | 180 240 300 |

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| | | | | -contir | nued | | |
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| cgaaaaattt | accetgettt | tatgctgggt | tetteagttg | gtaatttete | agatggtaaa | 480 | |
| atgggeeget | tcttcaatca | tactctagtt | cttttgeeeg | atggatgtgg | cactttactt | 540 | |
| agagetttt | attgtattct | ggagcetege | tctggaaatc | attgtcctgc | tggcaattee | 600 | |
| tatacttett | ttgccactta | tcacactect | gcaacagatt | gttetgatgg | caattacaat | 660 | |
| cgtaatgcca | gtetgaaete | ttttaaggag | tattttaatt | tacgtaactg | cacctttatg | 720 | |
| tacacttata | acattaccga | agatgagatt | ttagagtggt | ttggcattac | acaaactgct | 780 | |
| caaggtgttc | acctcttctc | atctcggtat | gttgatttgt | acggcggcaa | tatgtttcaa | 840 | |
| tttgccacct | tgcctgttta | tgatactatt | aagtattatt | ctatcattcc | tcacagtatt | 900 | |
| cgttctatcc | aaagtgatag | aaaagettgg | getgeettet | acgtatataa | acttcaaccg | 960 | |
| ttaactttcc | tgttggattt | ttetgttgat | ggttatatac | gcagagctat | agactgtggt | 1020 | |
| tttaatgatt | tgtcacaact | ccactgetca | tatgaatcct | tcgatgttga | atctggagtt | 1080 | |
| tattcagttt | cgtctttcga | agcaaaacct | tetggeteag | ttgtggaaca | ggetgaaggt | 1140 | |
| gttgaatgtg | atttttcacc | tettetgtet | ggcacacetc | ctcaggttta | taattteaag | 1200 | |
| cgtttggttt | ttaccaattg | caattataat | cttaccaaat | tgettteact | tttttctgtg | 1260 | |
| aatgatttta | cttgtagtca | aatatctcca | gcagcaattg | ctagcaactg | ttattcttca | 1320 | |
| ctgattttgg | attacttttc | atacccactt | agtatgaaat | ccgatctcag | tgttagttet | 1380 | |
| gctggtccaa | tateccagtt | taattataaa | cagteettt | ctaatcccac | atgtttgatt | 1440 | |
| ttagcgactg | tteeteataa | cettactact | attactaagc | ctcttaagta | cagctatatt | 1500 | |
| aacaagtgct | ctcgtcttct | ttetgatgat | cgtactgaag | tacctcagtt | agtgaacgct | 1560 | |
| aatcaatact | caccctgtgt | atccattgtc | ccatccactg | tgtgggaaga | cggtgattat | 1620 | |
| tataggaaac | aactatctcc | acttgaaggt | ggtggctggc | ttgttgctag | tggetcaact | 1680 | |
| gttgccatga | ctgagcaatt | acagatgggc | tttggtatta | cagttcaata | tggtacagac | 1740 | |
| accaatagtg | tttgccccaa | gettgaattt | gctaatgaca | caaaaattgc | ctctcaatta | 1800 | |
| ggcaattgcg | tggaatattc | cctctatggt | gtttcgggcc | gtggtgtttt | tcagaattgc | 1860 | |
| acagetgtag | gtgttcgaca | geagegettt | gtttatgatg | cgtaccagaa | tttagttggc | 1920 | |
| tattattetg | atgatggcaa | ctactactgt | ttgegtgett | gtgttagtgt | teetgtttet | 1980 | |
| gtcatctatg | ataaagaaac | taaaacccac | getactetat | ttggtagtgt | tgcatgtgaa | 2040 | |
| cacatttett | ctaccatgtc | tcaatactcc | egttetaege | gatcaatget | taaacggcga | 2100 | |
| gattetacat | atggeeeet | tcagacacct | gttggttgtg | teetaggaet | tgttaattee | 2160 | |
| tetttgtteg | tagaggactg | caagttgcct | cttggtcaat | ctctctgtgc | tetteetgae | 2220 | |
| acacctagta | ctctcacacc | tegeagtgtg | egetetgtte | caggtgaaat | gegettggea | 2280 | |
| tccattgett | ttaatcatcc | tattcaggtt | gatcaactta | atagtagtta | ttttaaatta | 2340 | |
| agtataccca | ctaatttttc | ctttggtgtg | actcaggagt | acattcagac | aaccattcag | 2400 | |
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| cgccaggatg | attetgtacg | taatttgttt | gcgagcgtga | aaagetetea | atcatctcct | 2580 | |
| atcataccag | gttttggagg | tgactttaat | ttgacacttc | tggaacetgt | ttctatatct | 2640 | |
| actggcagtc | gtagtgcacg | tagtgetatt | gaggatttgc | tatttgacaa | agtcactata | 2700 | |
| gctgatcctg | gttatatgca | aggttacgat | gattgcatgc | agcaaggtcc | agcatcaget | 2760 | |
| cgtgatctta | tttgtgctca | atatgtgget | ggttacaaag | tattacctcc | tettatggat | 2820 | |
| | | | | | | | |

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| teegtgeggt | cggtgcctgg | cgaaatgcgg | ctggcctcca | tegeetteaa | tcacccaatc | 180 |
| caagtggatc | agctgaatag | ctcgtatttc | aagctgtcca | tecccaegaa | cttctcgttc | 240 |
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| agcaagatca | accaggeget | gcatggaget | aacttgegee | aggacgactc | cgtgcgcaac | 420 |
| ctctttgcct | ctgtgaagtc | ateccagtec | tecccaatca | teeegggatt | cggaggggac | 480 |
| ttcaacctga | ccctcctgga | gcccgtgtcg | atcagcaccg | gtagcagatc | ggegegetea | 540 |
| gccattgaag | atettetgtt | cgacaaggtc | accategeeg | ateegggeta | catgcaggga | 600 |
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| gtggccgggt | acaaagtgct | geeteetetg | atggatgtga | acatggaggc | cgcttatact | 720 |
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| -cont | inued |
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| -0011 | . mueu |

| | | | | -cont li | iuea | | |
|--------------------------|----------------------|------------------------------|------------|--------------------------|------------|-------------|--|
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| cttcaacaag | tggtcaaggc | cctgaacgag | agetacateg | acctgaagga | gctgggcaac | 1740 | |
| tatacctact | acaacaagtg | gccggacaag | attgaggaga | ttctgtcgaa | aatctaccac | 1800 | |
| attgaaaacg | agategeeag | aatcaagaag | cttatcggcg | aagee | | 1845 | |
| <220> FEAT <223> OTHE | URE: R INFORMATIO | icial Sequer ON: Synthet: | | ectide | | | |
| <400> SEQU | ENCE: 23 | | | | | | |
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| | | | | tgtccaaggc | | 180 | |
| | | | | cctaccaggg | | 240 | |
| | | | | gccacgccac | | 300 | |
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| Thr Val Ile Ile 130 | Ser Pro Ser Thr Ser Ala Thr 135 | Ile Arg Lys Ile Tyr 140 | |
| Pro Ala Phe Met 145 | Leu Gly Ser Ser Val Gly Asn 150 155 | Phe Ser Asp Gly Lys 160 | |
| | Phe Asn His Thr Leu Val Leu 165 170 | Leu Pro Asp Gly Cys 175 | |
| Gly Thr Leu Leu 180 | Arg Ala Phe Tyr Cys Ile Leu 185 | | |
| | Ala Gly Asn Ser Tyr Thr Ser 200 | | |
| Thr Pro Ala Thr | Asp Cys Ser Asp Gly Asn Tyr | Asn Arg Asn Ala Ser | |
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| Thr | Gln | Thr | Ala 260 | Gln | Gly | Val | His | Leu 265 | Phe | Ser | Ser | Arg | Tyr 270 | Val | Asp |
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| | Ala | Thr | Val | Pro 485 | | | | | | 475 | Thr | | - | | 480 |
| Leu | | | | 485 | His | Asn | Leu | Thr | Thr 490 | 475 Ile | | Гла | Pro | Leu 495 | 480 Lys |
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| Leu Tyr Glu Ile Leu 545 Val | Ser Val Val 530 Ser Ala | Tyr Pro 515 Pro Pro Met | Ile 500 Gln Ser Leu Thr | 485 Asn Leu Thr Glu 565 | His Lys Val Gly 550 Gln | Asn Cys Asn Trp 535 Gly Leu | Leu Ser Ala 520 Glu Gly Gln | Thr Arg 505 Asn Asp Trp Met | Thr 490 Leu Gln Gly Leu Gly 570 | 475 Ile Leu Tyr Asp Val 555 Phe | Thr Ser Ser Tyr 540 Ala | Lys Asp Pro 525 Tyr Ser Ile | Pro Asp 510 Cys Arg Gly Thr | Leu 495 Arg Val Lys Ser Val 575 | 480 Lys Thr Ser Gln Thr 560 Gln |
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| Ala 945 | Ala | Tyr | Thr | Ser | Ser 950 | Leu | Leu | Gly | Ser | Ile 955 | Ala | Gly | Val | Gly | Trp 960 | | |
| Thr | Ala | Gly | Leu | Ser 965 | Ser | Phe | Ala | Ala | Ile 970 | Pro | Phe | Ala | Gln | Ser 975 | Ile | | |
| Phe | Tyr | Arg | Leu 980 | Asn | Gly | Val | Gly | Ile 985 | Thr | Gln | Gln | Val | Leu 990 | Ser | Glu | | |
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| Gln | Thr 1010 | | Phe | e Thi | r Thi | Th: 10: | | an G | lu A | la Pl | | rg 020 | Lys ' | Val | Gln | | |
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| Ile | Ile 1059 | | ı Arg | g Lei | ı Asp | Va. 10 | | eu Gi | lu G | ln A | - | la 065 | Gln | Ile . | Asp | | |
| Arg | Leu 1070 | | e Asr | ı Gly | / Arç | g Lev 10' | | ır Tl | nr L | eu Ai | | la 080 | Phe ' | Val . | Ala | | |
| Gln | Gln | Leu | . Val | . Arg | g Sei | c Glu | ı Se | er A | la A | la L | eu S | er . | Ala (| Gln | Leu | | |

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| Ala | Leu 1310 | | ı Le | u Cy | ′s V | 7al | Phe 131! | | e I. | le | Leu | су | | уя 320 | Thr | Gly | Сув | 3 |
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| Met | Ile | | | Val | . Ph | ie I | Leu 1 | Leu | Met | | | eu | Leu | Thr | Pro | | r Glu | Lu |
| 1 | m - | | - | 5 | | | | - | - | 10 | | | - | | | 15 | | |
| Ser | Tyr | Val | Азр 20 | Va] | . G1 | y F | Pro I | - | Ser 25 | : Va | 1 L | уs | Ser | Ala | 1 Cys 30 | 3 I l | e Glu | LU |
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| Ser 65 | Asn | Ile | Thr | Ilε | • Th 70 | | Fyr (| Gln | Gly | ∕Le | u P 7 | | Pro | Tyr | Glr | ı Gl | y Asj 80 | _ |
| His | Gly | Asp | Met | Tyr | : Va | 11 | fyr : | Ser | Ala | ı Gl | уН | is | Ala | Thr | Gl | 7 Th: | r Th: | ır |

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| | | | | | | 400 | , | | | | | | | | | | | 50 |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------------|-------------------|------------|------------|------|--|----|
| | | | | | | | | | | | - | con | tin | ued | | | | |
| | | | | 85 | | | | | 90 | | | | | 95 | | | | |
| Pro | Gln | Lys | Leu 100 | Phe | Val | Ala | Asn | Tyr 105 | Ser | Gln | Asp | Val | Lys 110 | Gln | Phe | | | |
| Ala | Asn | Gly 115 | Phe | Val | Val | Arg | Ile 120 | Gly | Ala | Ala | Ala | Asn 125 | Ser | Thr | Gly | | | |
| Thr | Val 130 | Ile | Ile | Ser | Pro | Ser 135 | Thr | Ser | Ala | Thr | Ile 140 | Arg | Гуз | Ile | Tyr | | | |
| Pro 145 | Ala | Phe | Met | Leu | Gly 150 | Ser | Ser | Val | Gly | Asn 155 | Phe | Ser | Asp | Gly | Lys 160 | | | |
| Met | Gly | Arg | Phe | Phe 165 | Asn | His | Thr | Leu | Val 170 | Leu | Leu | Pro | Asp | Gly 175 | Суз | | | |
| Gly | Thr | Leu | Leu 180 | Arg | Ala | Phe | Tyr | Cys 185 | Ile | Leu | Glu | Pro | Arg 190 | Ser | Gly | | | |
| Asn | His | Cys 195 | Pro | Ala | Gly | Asn | Ser 200 | Tyr | Thr | Ser | Phe | Ala 205 | Thr | Tyr | His | | | |
| Thr | Pro 210 | Ala | Thr | Asp | Суз | Ser 215 | Aab | Gly | Asn | Tyr | Asn 220 | Arg | Asn | Ala | Ser | | | |
| Leu 225 | Asn | Ser | Phe | ГАз | Glu 230 | Tyr | Phe | Asn | Leu | Arg 235 | Asn | Суз | Thr | Phe | Met 240 | | | |
| Tyr | Thr | Tyr | Asn | Ile 245 | Thr | Glu | Asp | Glu | Ile 250 | Leu | Glu | Trp | Phe | Gly 255 | Ile | | | |
| Thr | Gln | Thr | Ala 260 | Gln | Gly | Val | His | Leu 265 | Phe | Ser | Ser | Arg | Tyr 270 | Val | Asp | | | |
| Leu | Tyr | Gly 275 | Gly | Asn | Met | Phe | Gln 280 | Phe | Ala | Thr | Leu | Pro 285 | Val | Tyr | Asp | | | |
| Thr | Ile 290 | Lys | Tyr | Tyr | Ser | Ile 295 | Ile | Pro | His | Ser | Ile 300 | Arg | Ser | Ile | Gln | | | |
| Ser 305 | Asp | Arg | Lys | Ala | Trp 310 | Ala | Ala | Phe | Tyr | Val 315 | Tyr | Lys | Leu | Gln | Pro 320 | | | |
| Leu | Thr | Phe | Leu | Leu 325 | Asp | Phe | Ser | Val | Asp 330 | Gly | Tyr | Ile | Arg | Arg 335 | Ala | | | |
| Ile | Asp | Сув | Gly 340 | Phe | Asn | Aab | Leu | Ser 345 | Gln | Leu | His | Суз | Ser 350 | Tyr | Glu | | | |
| Ser | Phe | Asp 355 | Val | Glu | Ser | Gly | Val 360 | Tyr | Ser | Val | Ser | Ser 365 | Phe | Glu | Ala | | | |
| Lys | Pro 370 | Ser | Gly | Ser | Val | Val 375 | Glu | Gln | Ala | Glu | Gly 380 | Val | Glu | Сүз | Asp | | | |
| Phe 385 | Ser | Pro | Leu | Leu | Ser 390 | Gly | Thr | Pro | Pro | Gln 395 | Val | Tyr | Asn | Phe | Lys 400 | | | |
| Arg | Leu | Val | Phe | Thr 405 | Asn | Сув | Asn | Tyr | Asn 410 | Leu | Thr | Lys | Leu | Leu 415 | Ser | | | |
| Leu | Phe | Ser | Val 420 | Asn | Asp | Phe | Thr | Сув 425 | Ser | Gln | Ile | Ser | Pro 430 | Ala | Ala | | | |
| Ile | Ala | Ser 435 | Asn | Суз | Tyr | Ser | Ser 440 | Leu | Ile | Leu | Asp | Tyr 445 | Phe | Ser | Tyr | | | |
| Pro | Leu 450 | Ser | Met | Гла | Ser | Asp 455 | Leu | Ser | Val | Ser | Ser 460 | Ala | Gly | Pro | Ile | | | |
| Ser 465 | Gln | Phe | Asn | Tyr | Lys 470 | Gln | Ser | Phe | Ser | Asn 475 | Pro | Thr | Сув | Leu | Ile 480 | | | |
| Leu | Ala | Thr | Val | Pro 485 | His | Asn | Leu | Thr | Thr 490 | Ile | Thr | Lys | Pro | Leu 495 | Lys | | | |
| Tyr | Ser | Tyr | Ile 500 | Asn | Гуз | Суз | Ser | Arg 505 | Leu | Leu | Ser | Asp | Asp 510 | Arg | Thr | | | |
| | | | | | | | | | | | | | | | | | | |

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| Glu | Val | Pro 515 | Gln | Leu | Val | Asn | Ala 520 | Asn | Gln | Tyr | Ser | Pro 525 | Cys | Val | Ser |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Ile | Val 530 | Pro | Ser | Thr | Val | Trp 535 | Glu | Asp | Gly | Asp | Tyr 540 | Tyr | Arg | Lys | Gln |
| Leu 545 | Ser | Pro | Leu | Glu | Gly 550 | Gly | Gly | Trp | Leu | Val 555 | Ala | Ser | Gly | Ser | Thr 560 |
| Val | Ala | Met | Thr | Glu 565 | Gln | Leu | Gln | Met | Gly 570 | Phe | Gly | Ile | Thr | Val 575 | Gln |
| Tyr | Gly | Thr | Asp 580 | Thr | Asn | Ser | Val | Cys 585 | Pro | Lys | Leu | Glu | Phe 590 | Ala | Asn |
| Asp | Thr | Lys 595 | Ile | Ala | Ser | Gln | Leu 600 | Gly | Asn | Суа | Val | Glu 605 | Tyr | Ser | Leu |
| Tyr | Gly 610 | Val | Ser | Gly | Arg | Gly 615 | Val | Phe | Gln | Asn | Cys 620 | Thr | Ala | Val | Gly |
| Val 625 | Arg | Gln | Gln | Arg | Phe 630 | Val | Tyr | Asp | Ala | Tyr 635 | Gln | Asn | Leu | Val | Gly 640 |
| Tyr | Tyr | Ser | Aab | Asp 645 | Gly | Asn | Tyr | Tyr | Cys 650 | Leu | Arg | Ala | Сув | Val 655 | Ser |
| Val | Pro | Val | Ser 660 | Val | Ile | Tyr | Asp | Lys 665 | Glu | Thr | Lys | Thr | His 670 | Ala | Thr |
| Leu | Phe | Gly 675 | Ser | Val | Ala | Сув | Glu 680 | His | Ile | Ser | Ser | Thr 685 | Met | Ser | Gln |
| Tyr | Ser 690 | Arg | Ser | Thr | Arg | Ser 695 | Met | Leu | Lys | Arg | Arg 700 | Asp | Ser | Thr | Tyr |
| Gly 705 | Pro | Leu | Gln | Thr | Pro 710 | Val | Gly | Суз | Val | Leu 715 | Gly | Leu | Val | Asn | Ser 720 |
| Ser | Leu | Phe | Val | Glu 725 | Asp | Сүя | Lys | Leu | Pro 730 | Leu | Gly | Gln | Ser | Leu 735 | Cys |
| Ala | Leu | Pro | Asp 740 | Thr | Pro | Ser | Thr | Leu 745 | Thr | Pro | Arg | Ser | Val 750 | Arg | Ser |
| Val | Pro | Gly 755 | Glu | Met | Arg | Leu | Ala 760 | Ser | Ile | Ala | Phe | Asn 765 | His | Pro | Ile |
| Gln | Val 770 | Asp | Gln | Leu | Asn | Ser 775 | Ser | Tyr | Phe | Lys | Leu 780 | Ser | Ile | Pro | Thr |
| Asn 785 | Phe | Ser | Phe | Gly | Val 790 | Thr | Gln | Glu | Tyr | Ile 795 | Gln | Thr | Thr | Ile | Gln 800 |
| Lys | Val | Thr | Val | Asp 805 | Сув | Lys | Gln | Tyr | Val 810 | Сув | Asn | Gly | Phe | Gln 815 | Lys |
| СЛа | Glu | Gln | Leu 820 | Leu | Arg | Glu | Tyr | Gly 825 | Gln | Phe | СЛа | Ser | Lуа 830 | Ile | Asn |
| Gln | Ala | Leu 835 | His | Gly | Ala | Asn | Leu 840 | Arg | Gln | Asp | Asp | Ser 845 | Val | Arg | Asn |
| Leu | Phe 850 | Ala | Ser | Val | Lys | Ser 855 | Ser | Gln | Ser | Ser | Pro 860 | Ile | Ile | Pro | Gly |
| Phe 865 | Gly | Gly | Asp | Phe | Asn 870 | Leu | Thr | Leu | Leu | Glu 875 | Pro | Val | Ser | Ile | Ser 880 |
| Thr | Gly | Ser | Arg | Ser 885 | Ala | Arg | Ser | Ala | 11e 890 | Glu | Asp | Leu | Leu | Phe 895 | Asp |
| Lys | Val | Thr | Ile 900 | Ala | Asp | Pro | Gly | Tyr 905 | Met | Gln | Gly | Tyr | Asp 910 | Asp | Cys |
| Met | Gln | Gln 915 | Gly | Pro | Ala | Ser | Ala 920 | Arg | Asp | Leu | Ile | Сув 925 | Ala | Gln | Tyr |

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| Val Ala Gly Tyr Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu 930 935 940 |
|--|
| Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp 945 950 955 960 |
| Thr Ala Gly Leu Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile 965 970 975 |
| Phe Tyr Arg Leu Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu 980 985 990 |
| Asn Gln Lys Leu Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met 995 1000 1005 |
| Gln Thr Gly Phe Thr Thr Asn Glu Ala Phe Gln Lys Val Gln 1010 1015 1020 |
| Asp Ala Val Asn Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser 1025 1030 1035 |
| Glu Leu Ser Asn Thr Phe Gly Ala Ile Ser Ala Ser Ile Gly Asp 1040 1045 1050 |
| Ile Ile Gln Arg Leu Asp Val Leu Glu Gln Asp Ala Gln Ile Asp 1055 1060 1065 |
| Arg Leu Ile Asn Gly Arg Leu Thr Thr Leu Asn Ala Phe Val Ala 1070 1075 1080 |
| Gln Gln Leu Val Arg Ser Glu Ser Ala Ala Leu Ser Ala Gln Leu 1085 1090 1095 |
| Ala Lys Asp Lys Val Asn Glu Cys Val Lys Ala Gln Ser Lys Arg 1100 1105 1110 |
| Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val Ser Phe Val Val 1115 1120 1125 |
| Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly Tyr Tyr Pro 1130 1135 1140 |
| Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys Asp Ala 1145 1150 1155 |
| Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe Ile 1160 1165 1170 |
| Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly 1175 1180 1185 |
| Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys 1190 1195 1200 |
| Tyr Val Ala Pro Gln Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu 1205 1210 1215 |
| Pro Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp 1220 1225 1230 |
| Glu Leu Asp Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn 1235 1240 1245 |
| Phe Gly Ser Leu Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr 1250 1255 1260 |
| Tyr Glu Met Leu Ser Leu Gln Gln Val Val Lys Ala Leu Asn Glu 1265 1270 1275 |
| Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn 1280 1285 1290 |
| Lys Trp Pro Trp Tyr Ile Trp Leu Gly Phe Ile Ala Gly Leu Val 1295 1300 1305 |
| |

Ala Leu Ala Leu Cys Val Phe Phe Ile Leu Cys Cys Thr Gly Cys 1310 1315 Leu Lys Cys Asn Arg Cys Cys Asp

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|--------------------------|---------------------------------|--------------------------------|-------------|------------|---------------|--------------|------------|------------|----------------|------------|------------|-------------|-------------------|------------|------------|
| | 132 | 5 | | | | 133 | 30 | | | | 1. | 335 | | | |
| Arg | Tyr 134 | | u Glu | u Ty: | r Asj | p Lei 134 | | lu P: | ro H: | is Ly | | al 1 350 | His ' | Val H | His |
| <21 <21 <21 <21 | L> L) 2> T 3> O) 3> F) | ENGTI YPE : RGAN EATU | ISM: RE: | 15 Art: | ific: TION | | _ | | P 0 1yj | pept | ide | | | | |
| < 40 |)> SI | EQUE | NCE: | 26 | | | | | | | | | | | |
| Met 1 | Ile | His | Ser | Val 5 | Phe | Leu | Leu | Met | Phe 10 | Leu | Leu | Thr | Pro | Thr 15 | Glu |
| Ser | Asp | Cys | Lys 20 | Leu | Pro | Leu | Gly | Gln 25 | Ser | Leu | Суз | Ala | Leu 30 | Pro | Asp |
| Thr | Pro | Ser 35 | Thr | Leu | Thr | Pro | Arg 40 | Ser | Val | Arg | Ser | Val 45 | Pro | Gly | Glu |
| Met | Arg 50 | Leu | Ala | Ser | Ile | Ala 55 | Phe | Asn | His | Pro | Ile 60 | Gln | Val | Aab | Gln |
| Leu 65 | Asn | Ser | Ser | Tyr | Phe 70 | Lys | Leu | Ser | Ile | Pro 75 | Thr | Asn | Phe | Ser | Phe 80 |
| Gly | Val | Thr | Gln | Glu 85 | Tyr | Ile | Gln | Thr | Thr 90 | Ile | Gln | Гла | Val | Thr 95 | Val |
| Asp | Сув | Гуз | Gln 100 | Tyr | Val | Суя | Asn | Gly 105 | Phe | Gln | Lys | Сув | Glu 110 | Gln | Leu |
| Leu | Arg | Glu 115 | Tyr | Gly | Gln | Phe | Cys 120 | Ser | Lys | Ile | Asn | Gln 125 | Ala | Leu | His |
| Gly | Ala 130 | Asn | Leu | Arg | Gln | Asp 135 | Asp | Ser | Val | Arg | Asn 140 | Leu | Phe | Ala | Ser |
| Val 145 | Гла | Ser | Ser | Gln | Ser 150 | Ser | Pro | Ile | Ile | Pro 155 | Gly | Phe | Gly | Gly | Asp 160 |
| Phe | Asn | Leu | Thr | Leu 165 | Leu | Glu | Pro | Val | Ser 170 | Ile | Ser | Thr | Gly | Ser 175 | Arg |
| Ser | Ala | Arg | Ser 180 | Ala | Ile | Glu | Aab | Leu 185 | Leu | Phe | Asp | Гла | Val 190 | Thr | Ile |
| Ala | Asp | Pro 195 | Gly | Tyr | Met | Gln | Gly 200 | Tyr | Asp | Asp | САа | Met 205 | Gln | Gln | Gly |
| Pro | Ala 210 | Ser | Ala | Arg | Asp | Leu 215 | Ile | Сув | Ala | Gln | Tyr 220 | Val | Ala | Gly | Tyr |
| Lys 225 | Val | Leu | Pro | Pro | Leu 230 | Met | Aab | Val | Asn | Met 235 | Glu | Ala | Ala | Tyr | Thr 240 |
| Ser | Ser | Leu | Leu | Gly 245 | Ser | Ile | Ala | Gly | Val 250 | Gly | Trp | Thr | Ala | Gly 255 | Leu |
| Ser | Ser | Phe | Ala 260 | Ala | Ile | Pro | Phe | Ala 265 | Gln | Ser | Ile | Phe | Tyr 270 | Arg | Leu |
| Asn | Gly | Val 275 | Gly | Ile | Thr | Gln | Gln 280 | Val | Leu | Ser | Glu | Asn 285 | Gln | гуа | Leu |
| Ile | Ala 290 | Asn | Lys | Phe | Asn | Gln 295 | Ala | Leu | Gly | Ala | Met 300 | Gln | Thr | Gly | Phe |
| Thr 305 | Thr | Thr | Asn | Glu | Ala 310 | Phe | Gln | Гуа | Val | Gln 315 | Asp | Ala | Val | Asn | Asn 320 |
| Asn | Ala | Gln | Ala | Leu 325 | Ser | Гуз | Leu | Ala | Ser 330 | Glu | Leu | Ser | Asn | Thr 335 | Phe |
| Gly | Ala | Ile | Ser | | Ser | Ile | Gly | Asp | | Ile | Gln | Arg | Leu | | Val |
| | | | | | | | | | | | | | | | |

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464

| | | | | | | | | | | | _ | con | tin | ued | |
|------------|----------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | | 340 | | | | | 345 | | | | | 350 | | |
| Leu | Glu | Gln 355 | Aab | Ala | Gln | Ile | Asp 360 | Arg | Leu | Ile | Asn | Gly 365 | Arg | Leu | Thr |
| Thr | Leu 370 | Asn | Ala | Phe | Val | Ala 375 | Gln | Gln | Leu | Val | Arg 380 | Ser | Glu | Ser | Ala |
| Ala 385 | Leu | Ser | Ala | Gln | Leu 390 | Ala | Гуа | Asp | Lys | Val 395 | Asn | Glu | Суз | Val | Lys 400 |
| Ala | Gln | Ser | Lys | Arg 405 | Ser | Gly | Phe | Cys | Gly 410 | Gln | Gly | Thr | His | Ile 415 | Val |
| Ser | Phe | Val | Val 420 | Asn | Ala | Pro | Asn | Gly 425 | Leu | Tyr | Phe | Met | His 430 | Val | Gly |
| Tyr | Tyr | Pro 435 | Ser | Asn | His | Ile | Glu 440 | Val | Val | Ser | Ala | Tyr 445 | Gly | Leu | Cys |
| Asp | Ala 450 | Ala | Asn | Pro | Thr | Asn 455 | Суз | Ile | Ala | Pro | Val 460 | Asn | Gly | Tyr | Phe |
| Ile 465 | Lya | Thr | Asn | Asn | Thr 470 | Arg | Ile | Val | Asp | Glu 475 | Trp | Ser | Tyr | Thr | Gly 480 |
| Ser | Ser | Phe | Tyr | Ala 485 | Pro | Glu | Pro | Ile | Thr 490 | Ser | Leu | Asn | Thr | Lys 495 | Tyr |
| Val | Ala | Pro | Gln 500 | Val | Thr | Tyr | Gln | Asn 505 | Ile | Ser | Thr | Asn | Leu 510 | Pro | Pro |
| Pro | Leu | Leu 515 | | Asn | Ser | Thr | Gly 520 | | Asp | Phe | Gln | Asp 525 | | Leu | Asp |
| Glu | Phe 530 | | Lys | Asn | Val | Ser 535 | | Ser | Ile | Pro | Asn 540 | | Gly | Ser | Leu |
| Thr 545 | | Ile | Asn | Thr | Thr 550 | Leu | Leu | Asp | Leu | Thr 555 | | Glu | Met | Leu | Ser 560 |
| | Gln | Gln | Val | Val 565 | | Ala | Leu | Asn | Glu 570 | | Tyr | Ile | Asp | Leu 575 | |
| Glu | Leu | Gly | Asn 580 | | Thr | Tyr | Tyr | Asn 585 | | Trp | Pro | Asp | Lys 590 | | Glu |
| Glu | Ile | Leu 595 | | Lys | Ile | Tyr | His 600 | | Glu | Asn | Glu | Ile 605 | | Arg | Ile |
| ГЛа | Lys 610 | | Ile | Gly | Glu | Ala 615 | 000 | | | | | 003 | | | |
| | 910 | | | | | 012 | | | | | | | | | |
| |)> SH 1> LH | | | | | | | | | | | | | | |
| <212 | 2> TY | PE: | PRT | | dle | East | res | oira | torv | syna | drom | e co | ronav | /irue | 8 |
| |)> SH | | | | | | | | | -110 | | | | | - |
| Met 1 | Ile | His | Ser | Val 5 | Phe | Leu | Leu | Met | Phe 10 | Leu | Leu | Thr | Pro | Thr 15 | Glu |
| Ser | Tyr | Val | Asp 20 | Val | Gly | Pro | Asp | Ser 25 | Val | Lys | Ser | Ala | Суа 30 | Ile | Glu |
| Val | Asp | Ile 35 | Gln | Gln | Thr | Phe | Phe 40 | Asp | Lys | Thr | Trp | Pro 45 | Arg | Pro | Ile |
| Asp | Val 50 | | ГЛа | Ala | Asp | Gly 55 | | Ile | Tyr | Pro | Gln 60 | | Arg | Thr | Tyr |
| | | Ile | Thr | Ile | | Tyr | Gln | Gly | Leu | | | Tyr | Gln | Gly | _ |
| 65 His | Gly | Asp | Met | Tyr | 70 Val | Tyr | Ser | Ala | Gly | 75 His | Ala | Thr | Gly | Thr | 80 Thr |
| | | | | 85 | | | | | 90 | | | | | 95 | |

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466

| | | | | | | | | | | | _ | con | | uea | |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|
| Pro | Gln | Lys | Leu 100 | Phe | Val | Ala | Asn | Tyr 105 | Ser | Gln | Asp | Val | Lys 110 | Gln | Phe |
| Ala | Asn | Gly 115 | Phe | Val | Val | Arg | Ile 120 | Gly | Ala | Ala | Ala | Asn 125 | Ser | Thr | Gly |
| Thr | Val 130 | Ile | Ile | Ser | Pro | Ser 135 | Thr | Ser | Ala | Thr | Ile 140 | Arg | Lys | Ile | Tyr |
| Pro 145 | Ala | Phe | Met | Leu | Gly 150 | Ser | Ser | Val | Gly | Asn 155 | Phe | Ser | Asp | Gly | Lys 160 |
| Met | Gly | Arg | Phe | Phe 165 | Asn | His | Thr | Leu | Val 170 | Leu | Leu | Pro | Asp | Gly 175 | Суз |
| Gly | Thr | Leu | Leu 180 | Arg | Ala | Phe | Tyr | Cys 185 | Ile | Leu | Glu | Pro | Arg 190 | Ser | Gly |
| Asn | His | Cys 195 | Pro | Ala | Gly | Asn | Ser 200 | Tyr | Thr | Ser | Phe | Ala 205 | Thr | Tyr | His |
| Thr | Pro 210 | Ala | Thr | Asp | Сув | Ser 215 | Asp | Gly | Asn | Tyr | Asn 220 | Arg | Asn | Ala | Ser |
| Leu 225 | Asn | Ser | Phe | ГЛа | Glu 230 | Tyr | Phe | Asn | Leu | Arg 235 | Asn | Суз | Thr | Phe | Met 240 |
| Tyr | Thr | Tyr | Asn | Ile 245 | Thr | Glu | Asp | Glu | Ile 250 | Leu | Glu | Trp | Phe | G1y 255 | Ile |
| Thr | Gln | Thr | Ala 260 | Gln | Gly | Val | His | Leu 265 | Phe | Ser | Ser | Arg | Tyr 270 | Val | Asp |
| Leu | Tyr | Gly 275 | Gly | Asn | Met | Phe | Gln 280 | | Ala | Thr | Leu | Pro 285 | | Tyr | Asp |
| Thr | Ile 290 | | | Tyr | Ser | Ile 295 | | Pro | His | Ser | Ile 300 | | Ser | Ile | Gln |
| Ser 305 | | Arg | Lys | Ala | Trp 310 | Ala | Ala | Phe | Tyr | Val 315 | | Lys | Leu | Gln | Pro 320 |
| | Thr | Phe | Leu | Leu 325 | Asp | | Ser | Val | Asp 330 | | Tyr | Ile | Arg | Arg 335 | |
| Ile | Asp | Сув | Gly 340 | Phe | Asn | Asp | Leu | Ser 345 | | Leu | His | Сув | Ser 350 | | Glu |
| Ser | Phe | Asp 355 | Val | | Ser | Gly | Val 360 | | Ser | Val | Ser | Ser 365 | | Glu | Ala |
| ГÀа | Pro 370 | | | Ser | Val | Val 375 | | Gln | Ala | Glu | Gly 380 | | Glu | Суа | Asp |
| Phe 385 | | Pro | Leu | Leu | Ser 390 | | Thr | Pro | Pro | Gln 395 | | Tyr | Asn | Phe | Lys 400 |
| | Leu | Val | Phe | Thr 405 | Asn | Суз | Asn | Tyr | Asn 410 | | Thr | Lys | Leu | Leu 415 | |
| Leu | Phe | Ser | Val 420 | Asn | Aap | Phe | Thr | Cys 425 | Ser | Gln | Ile | Ser | Pro 430 | | Ala |
| Ile | Ala | Ser 435 | Asn | | Tyr | Ser | Ser 440 | Leu | | Leu | Asp | Tyr 445 | | Ser | Tyr |
| Pro | | | | Гуз | Ser | | | | Val | Ser | | | Gly | Pro | Ile |
| | 450 Gln | Phe | Asn | Tyr | Lys | 455 Gln | Ser | Phe | Ser | | 460 Pro | Thr | Сув | Leu | |
| 465 Leu | Ala | Thr | Val | Pro | 470 His | Asn | Leu | Thr | Thr | 475 Ile | Thr | Гла | Pro | Leu | 480 Lys |
| Tvr | Ser | Tvr | Ile | 485 Asn | Lys | Cvs | Ser | Ara | 490 Leu | Leu | Ser | Asp | Asp | 495 Arq | Thr |
| - | | - | 500 | | - | - | | 505 | | | | - | 510 | - | |
| GIU | va⊥ | F10 | eru | пец | Val | АЗП | AIđ | ASU | στΠ | туr | ser | F10 | сув | val | ber |

467

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| | | | | | | | | | | | | con | tin | ued | |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|
| | | 515 | | | | | 520 | | | | | 525 | | | |
| Ile | Val 530 | Pro | Ser | Thr | Val | Trp 535 | Glu | Asp | Gly | Aap | Tyr 540 | Tyr | Arg | Lys | Gln |
| Leu 545 | Ser | Pro | Leu | Glu | Gly 550 | Gly | Gly | Trp | Leu | Val 555 | Ala | Ser | Gly | Ser | Thr 560 |
| Val | Ala | Met | Thr | Glu 565 | Gln | Leu | Gln | Met | Gly 570 | Phe | Gly | Ile | Thr | Val 575 | Gln |
| Tyr | Gly | Thr | Asp 580 | Thr | Asn | Ser | Val | Cys 585 | Pro | Lys | Leu | Glu | Phe 590 | Ala | Asn |
| Asp | Thr | Lys 595 | Ile | Ala | Ser | Gln | Leu 600 | Gly | Asn | САв | Val | Glu 605 | Tyr | Ser | Leu |
| Tyr | Gly 610 | Val | Ser | Gly | Arg | Gly 615 | Val | Phe | Gln | Asn | Cys 620 | Thr | Ala | Val | Gly |
| 625 | • | | | - | Phe 630 | | - | - | | 635 | | | | | 640 |
| Tyr | Tyr | Ser | Aab | Asp 645 | Gly | Asn | Tyr | Tyr | Сув 650 | Leu | Arg | Ala | Сув | Val 655 | Ser |
| Val | Pro | Val | Ser 660 | Val | Ile | Tyr | Asp | Lys 665 | Glu | Thr | Lys | Thr | His 670 | Ala | Thr |
| Leu | Phe | Gly 675 | Ser | Val | Ala | Cys | Glu 680 | His | Ile | Ser | Ser | Thr 685 | Met | Ser | Gln |
| Tyr | Ser 690 | Arg | Ser | Thr | Arg | Ser 695 | Met | Leu | Гуа | Arg | Arg 700 | Asp | Ser | Thr | Tyr |
| Gly 705 | Pro | Leu | Gln | Thr | Pro 710 | Val | Gly | Суз | Val | Leu 715 | Gly | Leu | Val | Asn | Ser 720 |
| Ser | Leu | Phe | Val | Glu 725 | Asp | Cys | Lys | Leu | Pro 730 | Leu | Gly | Gln | Ser | Leu 735 | Cys |
| Ala | Leu | Pro | Asp 740 | Thr | Pro | Ser | Thr | Leu 745 | Thr | Pro | Arg | Ser | Val 750 | Arg | Ser |
| Val | Pro | Gly 755 | Glu | Met | Arg | Leu | Ala 760 | Ser | Ile | Ala | Phe | Asn 765 | His | Pro | Ile |
| Gln | Val 770 | Asp | Gln | Leu | Asn | Ser 775 | Ser | Tyr | Phe | Lys | Leu 780 | Ser | Ile | Pro | Thr |
| Asn 785 | Phe | Ser | Phe | Gly | Val 790 | Thr | Gln | Glu | Tyr | Ile 795 | Gln | Thr | Thr | Ile | Gln 800 |
| Lys | Val | Thr | Val | Asp 805 | Сув | Гла | Gln | Tyr | Val 810 | Суз | Asn | Gly | Phe | Gln 815 | Lys |
| Сүз | Glu | Gln | Leu 820 | Leu | Arg | Glu | Tyr | Gly 825 | Gln | Phe | Сүз | Ser | Lys 830 | Ile | Asn |
| Gln | Ala | Leu 835 | His | Gly | Ala | Asn | Leu 840 | Arg | Gln | Aap | Asp | Ser 845 | Val | Arg | Asn |
| Leu | Phe 850 | Ala | Ser | Val | Lys | Ser 855 | Ser | Gln | Ser | Ser | Pro 860 | Ile | Ile | Pro | Gly |
| Phe 865 | Gly | Gly | Asp | Phe | Asn 870 | Leu | Thr | Leu | Leu | Glu 875 | Pro | Val | Ser | Ile | Ser 880 |
| Thr | Gly | Ser | Arg | Ser 885 | Ala | Arg | Ser | Ala | Ile 890 | Glu | Asp | Leu | Leu | Phe 895 | Asp |
| ГЛа | Val | Thr | Ile 900 | Ala | Asp | Pro | Gly | Tyr 905 | Met | Gln | Gly | Tyr | Asp 910 | Aab | Суз |
| Met | Gln | Gln 915 | Gly | Pro | Ala | Ser | Ala 920 | Arg | Asp | Leu | Ile | Cys 925 | Ala | Gln | Tyr |
| Val | Ala 930 | Gly | Tyr | Гуз | Val | Leu 935 | Pro | Pro | Leu | Met | Asp 940 | Val | Asn | Met | Glu |
| | | | | | | | | | | | | | | | |

| Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp 945 950 955 960 |
|--|
| Thr Ala Gly Leu Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile 965 970 975 |
| Phe Tyr Arg Leu Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu 980 985 990 |
| Asn Gln Lys Leu Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met 995 1000 1005 |
| Gln Thr Gly Phe Thr Thr Asn Glu Ala Phe Arg Lys Val Gln 1010 1015 1020 |
| Asp Ala Val Asn Asn Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser 1025 1030 1035 |
| Glu Leu Ser Asn Thr Phe Gly Ala Ile Ser Ala Ser Ile Gly Asp 1040 1045 1050 |
| Ile Ile Gln Arg Leu Asp Val Leu Glu Gln Asp Ala Gln Ile Asp 1055 1060 1065 |
| Arg LeuIle Asn Gly Arg LeuThr Leu Asn AlaPhe Val Ala107010751080 |
| Gln Gln Leu Val Arg Ser Glu Ser Ala Ala Leu Ser Ala Gln Leu 1085 1090 1095 |
| Ala Lys Asp Lys Val Asn Glu Cys Val Lys Ala Gln Ser Lys Arg 1100 1105 1110 |
| Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val Ser Phe Val Val 1115 1120 1125 |
| Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly Tyr Tyr Pro 1130 1135 1140 |
| Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys Asp Ala 1145 1150 1155 |
| Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe Ile 1160 1165 1170 |
| Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly 1175 1180 1185 |
| Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys 1190 1195 1200 |
| Tyr Val Ala Pro His Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu 1205 1210 1215 |
| Pro Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp 1220 1225 1230 |
| Glu Leu Asp Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn 1235 1240 1245 |
| Phe Gly Ser Leu Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr 1250 1255 1260 |
| Tyr Glu Met Leu Ser Leu Gln Gln Val Val Lys Ala Leu Asn Glu 1265 1270 1275 |
| Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn 1280 1285 1290 |
| Lys Trp Pro Trp Tyr Ile Trp Leu Gly Phe Ile Ala Gly Leu Val 1295 1300 1305 |
| Ala Leu Ala Leu Cys Val Phe Phe Ile Leu Cys Cys Thr Gly Cys 1310 1315 1320 |
| Gly Thr Asn Cys Met Gly Lys Leu Lys Cys Asn Arg Cys Cys Asp 1325 1330 1335 |

| Arg | Tyr 134 | Glu | 1 Gl | u Ty: | r Asj | 2 Lei 134 | | lu P: | ro Hi | is Ly | | al 1 350 | His N | /al H | lis | | |
|------------|------------|----------------|------------|------------------------|------------|--------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|------|------|
| |)> SI | eq II Engti | | | | | | | | | | | | | | | |
| <212 | 2> T | YPE : | PRT | | | _ | | | | | | | | | | | |
| <21. | 3 > 01 | RGAN: | ISM: | Mide | dle 1 | East | res | pira | tory | syn¢ | drom | e co: | rona | viru | 3 | | |
| <400 |)> SI | EQUEN | ICE : | 28 | | | | | | | | | | | | | |
| Met 1 | Ile | His | Ser | Val 5 | Phe | Leu | Leu | Met | Phe 10 | Leu | Leu | Thr | Pro | Thr 15 | Glu | | |
| Ser | Tyr | Val | Asp 20 | Val | Gly | Pro | Aab | Ser 25 | Val | Lys | Ser | Ala | 30 Сув | Ile | Glu | | |
| Val | Asp | Ile 35 | Gln | Gln | Thr | Phe | Phe 40 | Asp | Lys | Thr | Trp | Pro 45 | Arg | Pro | Ile | | |
| Asp | Val 50 | Ser | Lys | Ala | Asp | Gly 55 | Ile | Ile | Tyr | Pro | Gln 60 | Gly | Arg | Thr | Tyr | | |
| Ser 65 | Asn | Ile | Thr | Ile | Thr 70 | Tyr | Gln | Gly | Leu | Phe 75 | Pro | Tyr | Gln | Gly | Asp 80 | | |
| His | Gly | Asp | Met | Tyr 85 | Val | Tyr | Ser | Ala | Gly 90 | His | Ala | Thr | Gly | Thr 95 | Thr | | |
| Pro | Gln | Lys | Leu 100 | Phe | Val | Ala | Asn | Tyr 105 | Ser | Gln | Asp | Val | Lys 110 | Gln | Phe | | |
| Ala | Asn | Gly 115 | Phe | Val | Val | Arg | Ile 120 | Gly | Ala | Ala | Ala | Asn 125 | Ser | Thr | Gly | | |
| Thr | Val 130 | Ile | Ile | Ser | Pro | Ser 135 | Thr | Ser | Ala | Thr | Ile 140 | Arg | Lys | Ile | Tyr | | |
| Pro 145 | Ala | Phe | Met | Leu | Gly 150 | Ser | Ser | Val | Gly | Asn 155 | Phe | Ser | Asp | Gly | Lys 160 | | |
| Met | Gly | Arg | Phe | Ph e 165 | Asn | His | Thr | Leu | Val 170 | Leu | Leu | Pro | Asp | Gly 175 | Сув | | |
| Gly | Thr | Leu | Leu 180 | Arg | Ala | Phe | Tyr | Cys 185 | Ile | Leu | Glu | Pro | Arg 190 | Ser | Gly | | |
| Asn | His | Cys 195 | Pro | Ala | Gly | Asn | Ser 200 | Tyr | Thr | Ser | Phe | Ala 205 | Thr | Tyr | His | | |
| Thr | Pro 210 | Ala | Thr | Asp | Суз | Ser 215 | Asp | Gly | Asn | Tyr | Asn 220 | Arg | Asn | Ala | Ser | | |
| Leu 225 | Asn | Ser | Phe | Гλа | Glu 230 | Tyr | Phe | Asn | Leu | Arg 235 | Asn | Сув | Thr | Phe | Met 240 | | |
| Tyr | Thr | Tyr | Asn | Ile 245 | Thr | Glu | Asp | Glu | Ile 250 | Leu | Glu | Trp | Phe | Gly 255 | Ile | | |
| Thr | Gln | Thr | Ala 260 | Gln | Gly | Val | His | Leu 265 | Phe | Ser | Ser | Arg | Tyr 270 | Val | Asp | | |
| Leu | Tyr | Gly 275 | Gly | Asn | Met | Phe | Gln 280 | Phe | Ala | Thr | Leu | Pro 285 | Val | Tyr | Asp | | |
| Thr | Ile 290 | Lys | Tyr | Tyr | Ser | Ile 295 | Ile | Pro | His | Ser | Ile 300 | Arg | Ser | Ile | Gln | | |
| Ser 305 | Asp | Arg | Lys | Ala | Trp 310 | Ala | Ala | Phe | Tyr | Val 315 | Tyr | Гла | Leu | Gln | Pro 320 | | |
| Leu | Thr | Phe | Leu | Leu 325 | Asp | Phe | Ser | Val | Asp 330 | Gly | Tyr | Ile | Arg | Arg 335 | Ala | | |
| Ile | Asp | Суя | Gly 340 | Phe | Asn | Asp | Leu | Ser 345 | Gln | Leu | His | Cys | Ser 350 | Tyr | Glu | | |
| Ser | Phe | Asp 355 | Val | Glu | Ser | Gly | Val 360 | Tyr | Ser | Val | Ser | Ser 365 | Phe | Glu | Ala | | |
| | | | | | | | | | | | | | | | | | |

| Lys | Pro 370 | Ser | Gly | Ser | Val | Val 375 | Glu | Gln | Ala | Glu | Gly 380 | Val | Glu | Суа | Asp |
|---|--|---|---|---|--|---|--|---|--|--|--|---|--|---|---|
| Phe 385 | Ser | Pro | Leu | Leu | Ser 390 | Gly | Thr | Pro | Pro | Gln 395 | Val | Tyr | Asn | Phe | Lys 400 |
| Arg | Leu | Val | Phe | Thr 405 | Asn | Cys | Asn | Tyr | Asn 410 | Leu | Thr | гуа | Leu | Leu 415 | Ser |
| Leu | Phe | Ser | Val 420 | Asn | Asp | Phe | Thr | Cys 425 | Ser | Gln | Ile | Ser | Pro 430 | Ala | Ala |
| Ile | Ala | Ser 435 | Asn | Суа | Tyr | Ser | Ser 440 | Leu | Ile | Leu | Asp | Tyr 445 | Phe | Ser | Tyr |
| Pro | Leu 450 | Ser | Met | Lys | Ser | Asp 455 | Leu | Ser | Val | Ser | Ser 460 | Ala | Gly | Pro | Ile |
| Ser 465 | Gln | Phe | Asn | Tyr | Lys 470 | Gln | Ser | Phe | Ser | Asn 475 | Pro | Thr | Сув | Leu | Ile 480 |
| Leu | Ala | Thr | Val | Pro 485 | His | Asn | Leu | Thr | Thr 490 | Ile | Thr | Гла | Pro | Leu 495 | Гла |
| Tyr | Ser | Tyr | Ile 500 | Asn | Lys | Сув | Ser | Arg 505 | Leu | Leu | Ser | Asp | Asp 510 | Arg | Thr |
| Glu | Val | Pro 515 | Gln | Leu | Val | Asn | Ala 520 | Asn | Gln | Tyr | Ser | Pro 525 | Cys | Val | Ser |
| Ile | Val 530 | Pro | Ser | Thr | Val | Trp 535 | Glu | Asp | Gly | Asp | Tyr 540 | Tyr | Arg | Lys | Gln |
| Leu 545 | Ser | Pro | Leu | Glu | Gly 550 | Gly | Gly | Trp | Leu | Val 555 | Ala | Ser | Gly | Ser | Thr 560 |
| Val | Ala | Met | Thr | Glu 565 | Gln | Leu | Gln | Met | Gly 570 | Phe | Gly | Ile | Thr | Val 575 | Gln |
| | | | | | | | | | | | | | | | |
| | | | 580 | Thr | | | | 585 | | | | | Phe 590 | | |
| | | | 580 | Thr | | | | 585 | | | | | | | |
| Asp | Thr | Lys 595 | 580 Ile | Thr Ala | Ser | Gln | Leu 600 | 585 Gly | Asn | Сүз | Val | Glu 605 | 590 | Ser | Leu |
| Asp Tyr | Thr Gly 610 | Lys 595 Val | 580 Ile Ser | Thr Ala Gly | Ser Arg | Gln Gly 615 | Leu 600 Val | 585 Gly Phe | Asn Gln | Cys Asn | Val Cys 620 | Glu 605 Thr | 590 Tyr | Ser Val | Leu Gly |
| Asp Tyr Val 625 | Thr Gly 610 Arg | Lys 595 Val Gln | 580 Ile Ser Gln | Thr Ala Gly Arg | Ser Arg Phe 630 | Gln Gly 615 Val | Leu 600 Val Tyr | 585 Gly Phe Asp | Asn Gln Ala | Cys Asn Tyr 635 | Val Cys 620 Gln | Glu 605 Thr Asn | 590 Tyr Ala | Ser Val Val | Leu Gly Gly 640 |
| Asp Tyr Val 625 Tyr | Thr Gly 610 Arg Tyr | Lys 595 Val Gln Ser | 580 Ile Ser Gln Asp | Thr Ala Gly Arg Asp 645 | Ser Arg Phe 630 Gly | Gly 615 Val Asn | Leu 600 Val Tyr Tyr | 585 Gly Phe Asp Tyr | Asn Gln Ala Cys 650 | Cys Asn Tyr 635 Leu | Val Cys 620 Gln Arg | Glu 605 Thr Asn Ala | 590 Tyr Ala Leu | Ser Val Val Val 655 | Leu Gly Gly 640 Ser |
| Asp Tyr Val 625 Tyr Val | Thr Gly 610 Arg Tyr Pro | Lys 595 Val Gln Ser Val | 580 Ile Ser Gln Asp Ser 660 | Thr Ala Gly Arg 645 Val | Ser Arg Phe 630 Gly Ile | Gln 615 Val Asn Tyr | Leu 600 Val Tyr Tyr Asp | 585 Gly Phe Asp Tyr Lys 665 | Asn Gln Ala 650 Glu | Cys Asn Tyr 635 Leu Thr | Val Cys 620 Gln Arg Lys | Glu 605 Thr Asn Ala Thr | 590 Tyr Ala Leu Cys His | Ser Val Val 655 Ala | Leu Gly Gly 640 Ser Thr |
| Asp Tyr Val 625 Tyr Val Leu | Thr Gly 610 Arg Tyr Pro Phe | Lys 595 Val Gln Ser Val Gly 675 | 580 Ile Ser Gln Asp Ser 660 Ser | Thr Ala Gly Arg 645 Val Val | Ser Arg Phe 630 Gly Ile Ala | Gln 615 Val Asn Tyr Cys | Leu 600 Val Tyr Tyr Asp Glu 680 | 585 Gly Phe Asp Tyr Lys 665 His | Asn Gln Ala Cys 650 Glu Ile | Cys Asn Tyr 635 Leu Thr Ser | Val Cys 620 Gln Arg Lys Ser | Glu 605 Thr Asn Ala Thr 685 | 590 Tyr Ala Leu Cys His 670 | Ser Val Val Val 655 Ala Ser | Leu Gly Gly 640 Ser Thr Gln |
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| Asp Tyr Val 625 Tyr Val Leu Tyr Gly 705 | Thr Gly 610 Arg Tyr Pro Phe Ser 690 Pro | Lys 595 Val Gln Ser Val Gly 675 Arg Leu | 580 Ile Ser Gln Asp Ser Ser Ser Gln | Thr Ala Gly Arg 645 Val Val Thr Thr | Ser Arg Phe 630 Gly Ile Ala Arg Pro 710 | Gln 615 Val Asn Tyr Cys Ser 695 Val | Leu 600 Val Tyr Tyr Asp Glu 680 Met Gly | 585 Gly Phe Asp Tyr Lys 665 His Leu Cys | Asn Gln Ala Cys 650 Glu Ile Lys Val | Cys Asn Tyr 635 Leu Thr Ser Arg Leu 715 | Val Cys 620 Gln Arg Lys Ser Arg 700 Gly | Glu 605 Thr Asn Ala Thr Thr 685 Asp Leu | 590 Tyr Ala Leu Cys His 670 Met Ser | Ser Val Val 655 Ala Ser Thr Asn | Leu Gly Gly 640 Ser Thr Gln Tyr Ser 720 |
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| Asn Phe Ser Phe Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln785790795800 | |
|--|--|
| Lys Val Thr Val Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys 805 810 815 | |
| Cys Glu Gln Leu Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn 820 825 830 | |
| Gln Ala Leu His Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn 835 840 845 | |
| Leu Phe Ala Ser Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly 850 855 860 | |
| Phe Gly Gly Asp Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser 865 870 875 880 | |
| Thr Gly Ser Arg Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp 885 890 895 | |
| Lys Val Thr Ile Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys 900 905 910 | |
| Met Gln Gln Gly Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr 915 920 925 | |
| Val Ala Gly Tyr Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu 930 935 940 | |
| Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp 945 950 955 960 | |
| Thr Ala Gly Leu Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile 965 970 975 | |
| Phe Tyr Arg Leu Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu 980 985 990 | |
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| Gln Thr Gly Phe Thr Thr Asn Glu Ala Phe Arg Lys Val Gln 1010 1015 1020 | |
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| Glu Leu Ser Asn Thr Phe Gly Ala Ile Ser Ala Ser Ile Gly Asp 1040 1045 1050 | |
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| Gln Gln Leu Val Arg Ser Glu Ser Ala Ala Leu Ser Ala Gln Leu 1085 1090 1095 | |
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| Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val Ser Phe Val Val 1115 1120 1125 | |
| Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly Tyr Tyr Pro 1130 1135 1140 | |
| Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys Asp Ala 1145 1150 1155 | |
| Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe Ile 1160 1165 1170 | |
| Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly 1175 1180 1185 | |
| Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys | |
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|------------|--------------|------------|------------|--------------|------------|--------------|------------|------------|------------|------------|--------------|--------------------|--------------|---------------------|--------------|
| | 1190 |) | | | | 11 | 95 | | | | 1 | L200 | | | |
| Tyr | Val 1205 | | ı Pr | ю Ні | s Va | 1 Th: 12: | | yr G | ln A | sn I | | Ser 1215 | Thr | Asn | Leu |
| Pro | Pro 1220 | | b Le | u Le | u Gl | y As: 12: | | er T | hr G | ly I | | Asp 1230 | Phe | Gln | Asp |
| Glu | Leu 1235 | - | Gl | u Ph | e Ph | e Ly: 12- | | sn V | al S | er T | | Ser 1245 | Ile | Pro | Asn |
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| Tyr | Glu 1265 | | Le | eu Se | r Le | u Gli 12' | | ln V | al V | al L | | Ala 1275 | Leu | Asn | Glu |
| Ser | Tyr 1280 | | e As | p Le | u Ly: | s Gl: 12: | | eu G | ly A | sn I | - | fhr 1290 | Tyr | Tyr | Asn |
| Lys | Trp 1295 | |) Tr | р Ту | r Il | e Trj 13 | | eu G | ly P | he I | | 41a 1305 | Gly | Leu | Val |
| Ala | Leu 1310 | | Le | eu Cy | s Va | l Ph 13: | | he I | le L | eu C | | Сув 1320 | Thr | Gly | Cys |
| Gly | Thr 1325 | | а Су | ns Me | t Gl | у Ly: 13: | | eu L | уз С | ys A | | Arg 1335 | Cys | Cya | Asp |
| Arg | Tyr 1340 | | ı Gl | u Ty | r Asj | p Lev 134 | | lu P | ro H | is L | - | /al L350 | His | Val | His |
| |)> SE Phe | | | | Leu | Phe | Leu | Thr | Leu 10 | . Thr | : Sei | r Gly | 7 Sei | r As <u>ı</u> 15 | o Leu |
| Asp | Arg | Сув | Thr 20 | Thr | Phe | Asp | Asp | Val 25 | Gln | . Ala | n Pro | > Asr | 1 Tyj 30 | r Thi | : Gln |
| His | Thr | Ser 35 | Ser | Met | Arg | Gly | Val 40 | Tyr | Tyr | Pro | Asp | 9 Glu 45 | ı Ile | e Phe | e Arg |
| Ser | Азр 50 | Thr | Leu | Tyr | Leu | Thr 55 | Gln | Asp | Leu | . Phe | e Lei 60 | ı Pro | > Phe | е Туз | ser |
| Asn 65 | Val | Thr | Gly | Phe | His 70 | Thr | Ile | Asn | His | Thr 75 | Phe | e Gl≯ | / Asr | ı Pro | > Val 80 |
| Ile | Pro | Phe | Lys | Asp 85 | Gly | Ile | Tyr | Phe | Ala 90 | Ala | 1 Thi | r Glu | ı Lyı | 95 Sei | : Asn |
| Val | Val | Arg | Gly 100 | | Val | Phe | Gly | Ser 105 | | Met | : Asr | n Asr | 110 Lys | | f Gln |
| Ser | Val | Ile 115 | Ile | lle | Asn | Asn | Ser 120 | Thr | Asn | . Val | . Val | L Ile 129 | - | g Ala | a Cys |
| Asn | Phe 130 | Glu | Leu | . Cys | Asp | Asn 135 | Pro | Phe | Phe | Ala | 1 Val 140 | | : Буз | s Pro | > Met |
| Gly 145 | Thr | Gln | Thr | His | Thr 150 | Met | Ile | Phe | Asp | Asn 155 | | a Phe | e Asr | ı Cys | F Thr 160 |
| Phe | Glu | Tyr | Ile | e Ser 165 | | Ala | Phe | Ser | Leu 170 | | va] | l Ser | Glu | 1 Lys 179 | s Ser |
| Gly | Asn | Phe | Lys 180 | | Leu | Arg | Glu | Phe 185 | | Phe | - Lys | a Asr | n Lys 19(| _ | Gly |
| Phe | Leu | Tyr 195 | | | Гуз | Gly | Tyr 200 | | | Ile | Asp | 9 Val 205 | . Val | | l yab |
| | | 190 | | | | | 200 | | | | | 205 | , | | |

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| Le | eu | Pro 210 | Ser | Gly | Phe | Asn | Thr 215 | Leu | Lys | Pro | Ile | Phe 220 | Гла | Leu | Pro | Leu |
|----------|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------------|------------|-------------------|
| G1 22 | | Ile | Asn | Ile | Thr | Asn 230 | Phe | Arg | Ala | Ile | Leu 235 | Thr | Ala | Phe | Ser | Pro 240 |
| Al | .a | Gln | Asp | Ile | Trp 245 | Gly | Thr | Ser | Ala | Ala 250 | Ala | Tyr | Phe | Val | Gly 255 | Tyr |
| Le | au | Гуз | Pro | Thr 260 | Thr | Phe | Met | Leu | Lys 265 | Tyr | Asp | Glu | Asn | Gly 270 | Thr | Ile |
| Τŀ | ır | Asp | Ala 275 | Val | Asp | Cys | Ser | Gln 280 | Asn | Pro | Leu | Ala | Glu 285 | Leu | ГЛа | Суз |
| Se | er | Val 290 | Lys | Ser | Phe | Glu | Ile 295 | Asp | Lys | Gly | Ile | Tyr 300 | Gln | Thr | Ser | Asn |
| Ph 30 | | Arg | Val | Val | Pro | Ser 310 | Gly | Asp | Val | Val | Arg 315 | Phe | Pro | Asn | Ile | Thr 320 |
| Aε | m | Leu | Сув | Pro | Phe 325 | Gly | Glu | Val | Phe | Asn 330 | Ala | Thr | Гла | Phe | Pro 335 | Ser |
| Va | 1 | Tyr | Ala | Trp 340 | Glu | Arg | Гла | ГЛа | Ile 345 | Ser | Asn | Сүз | Val | Ala 350 | Aab | Tyr |
| Se | er | Val | Leu 355 | Tyr | Asn | Ser | Thr | Phe 360 | Phe | Ser | Thr | Phe | Lys 365 | Cys | Tyr | Gly |
| Va | 1 | Ser 370 | Ala | Thr | Гла | Leu | Asn 375 | Asp | Leu | Сув | Phe | Ser 380 | Asn | Val | Tyr | Ala |
| Ас 38 | - | Ser | Phe | Val | Val | Lув 390 | Gly | Asp | Asp | Val | Arg 395 | Gln | Ile | Ala | Pro | Gly 400 |
| Gl | n | Thr | Gly | Val | Ile 405 | Ala | Yab | Tyr | Asn | Tyr 410 | Lys | Leu | Pro | Asp | Asp 415 | Phe |
| M€ | et | Gly | Сув | Val 420 | Leu | Ala | Trp | Asn | Thr 425 | Arg | Asn | Ile | Asp | Ala 430 | Thr | Ser |
| Th | ır | Gly | Asn 435 | Tyr | Asn | Tyr | Lys | Tyr 440 | Arg | Tyr | Leu | Arg | His 445 | Gly | Lys | Leu |
| Ar | g | Pro 450 | Phe | Glu | Arg | Asp | Ile 455 | Ser | Asn | Val | Pro | Phe 460 | Ser | Pro | Asp | Gly |
| Lу 46 | | Pro | Сув | Thr | Pro | Pro 470 | Ala | Leu | Asn | Сув | Tyr 475 | Trp | Pro | Leu | Asn | Asp 480 |
| Ту | r | Gly | Phe | Tyr | Thr 485 | Thr | Thr | Gly | Ile | Gly 490 | Tyr | Gln | Pro | Tyr | Arg 495 | Val |
| Va | 1 | Val | Leu | Ser 500 | Phe | Glu | Leu | Leu | Asn 505 | Ala | Pro | Ala | Thr | Val 510 | Сув | Gly |
| Pr | 0 | Lys | Leu 515 | Ser | Thr | Asp | Leu | Ile 520 | Lys | Asn | Gln | Сүз | Val 525 | Asn | Phe | Asn |
| Pł | he | Asn 530 | Gly | Leu | Thr | Gly | Thr 535 | Gly | Val | Leu | Thr | Pro 540 | Ser | Ser | ГАа | Arg |
| Ph 54 | | Gln | Pro | Phe | Gln | Gln 550 | Phe | Gly | Arg | Asp | Val 555 | Ser | Asp | Phe | Thr | Asp 560 |
| Se | er | Val | Arg | Asp | Pro 565 | Lys | Thr | Ser | Glu | 11e 570 | Leu | Asp | Ile | Ser | Pro 575 | Суз |
| Se | er | Phe | Gly | Gly 580 | Val | Ser | Val | Ile | Thr 585 | Pro | Gly | Thr | Asn | Ala 590 | Ser | Ser |
| Gl | .u | Val | Ala 595 | Val | Leu | Tyr | Gln | Asp 600 | Val | Asn | Сүя | Thr | Asp 605 | Val | Ser | Thr |
| Al | a | Ile 610 | His | Ala | Asp | Gln | Leu 615 | Thr | Pro | Ala | Trp | Arg 620 | Ile | Tyr | Ser | Thr |
| Gl | -y | Asn | Asn | Val | Phe | Gln | Thr | Gln | Ala | Gly | Суз | Leu | Ile | Gly | Ala | Glu |

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|------------|-------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 625 | | | | | 630 | | | | | 635 | | | | | 640 |
| His | Val | Asp | Thr | Ser 645 | - | Glu | САа | Asp | 11e 650 | Pro | Ile | Gly | Ala | Gly 655 | |
| Cys | Ala | Ser | Tyr 660 | | Thr | Val | Ser | Leu 665 | Leu | Arg | Ser | Thr | Ser 670 | Gln | Lys |
| Ser | Ile | Val 675 | Ala | Tyr | Thr | Met | Ser 680 | | Gly | Ala | Asp | Ser 685 | | Ile | Ala |
| Tyr | Ser 690 | Asn | Asn | Thr | Ile | Ala 695 | | Pro | Thr | Asn | Phe 700 | Ser | Ile | Ser | Ile |
| Thr 705 | Thr | Glu | Val | Met | Pro 710 | Val | Ser | Met | Ala | Lys 715 | Thr | Ser | Val | Asp | Суз 720 |
| Asn | Met | Tyr | Ile | Cys 725 | Gly | Asp | Ser | Thr | Glu 730 | Суз | Ala | Asn | Leu | Leu 735 | Leu |
| Gln | Tyr | Gly | Ser 740 | Phe | Сув | Thr | Gln | Leu 745 | Asn | Arg | Ala | Leu | Ser 750 | Gly | Ile |
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| Gln | Met 770 | Tyr | Lys | Thr | Pro | Thr 775 | Leu | Lys | Tyr | Phe | Gly 780 | Gly | Phe | Asn | Phe |
| Ser 785 | Gln | Ile | Leu | Pro | Asp 790 | Pro | Leu | Lys | Pro | Thr 795 | Lys | Arg | Ser | Phe | Ile 800 |
| Glu | Asp | Leu | Leu | Phe 805 | Asn | Lys | Val | Thr | Leu 810 | Ala | Asp | Ala | Gly | Phe 815 | Met |
| ГЛЗ | Gln | Tyr | Gly 820 | Glu | Суз | Leu | Gly | Asp 825 | Ile | Asn | Ala | Arg | Asp 830 | Leu | Ile |
| Суа | Ala | Gln 835 | Lys | Phe | Asn | Gly | Leu 840 | Thr | Val | Leu | Pro | Pro 845 | | Leu | Thr |
| Asp | Asp 850 | Met | Ile | Ala | Ala | Tyr 855 | Thr | Ala | Ala | Leu | Val 860 | Ser | Gly | Thr | Ala |
| Thr 865 | Ala | Gly | Trp | Thr | Phe 870 | Gly | Ala | Gly | Ala | Ala 875 | Leu | Gln | Ile | Pro | Phe 880 |
| Ala | Met | Gln | Met | Ala 885 | Tyr | Arg | Phe | Asn | Gly 890 | Ile | Gly | Val | Thr | Gln 895 | Asn |
| Val | Leu | Tyr | Glu 900 | Asn | Gln | Lys | Gln | Ile 905 | Ala | Asn | Gln | Phe | Asn 910 | Lya | Ala |
| Ile | Ser | Gln 915 | Ile | Gln | Glu | Ser | Leu 920 | Thr | Thr | Thr | Ser | Thr 925 | Ala | Leu | Gly |
| Lys | Leu 930 | Gln | Asp | Val | Val | Asn 935 | | Asn | Ala | Gln | Ala 940 | Leu | Asn | Thr | Leu |
| Val 945 | Гла | Gln | Leu | Ser | Ser 950 | Asn | Phe | Gly | Ala | Ile 955 | Ser | Ser | Val | Leu | Asn 960 |
| | Ile | Leu | Ser | Arg 965 | Leu | Asp | Lys | Val | Glu 970 | | Glu | Val | Gln | Ile 975 | Asp |
| Arg | Leu | Ile | Thr 980 | Gly | Arg | Leu | Gln | Ser 985 | Leu | Gln | Thr | Tyr | Val 990 | Thr | Gln |
| Gln | Leu | Ile 995 | Arg | Ala | Ala | Glu | Ile 100 | | g Ala | a Se: | r Al | a As 10 | | eu A | la Ala |
| Thr | Lys 1010 | Met | : Se | r Glı | u Cy: | s Va 10 | 1 ь | | ly G | ln S | | | | Val i | Asp |
| Phe | Cys | Gl | у Бу | a Gl | у Ту: | r Hi | s L | eu M | et Se | er Pl | he P: | ro | Gln ź | Ala i | Ala |
| Pro | 1025 His | Glγ | 7 Val | l Va | l Ph | | u H. | is V | al Tì | hr T | yr V | | Pro : | Ser (| Gln |
| | 1040 |) | | | | 104 | 45 | | | | 1 | 050 | | | |

| Glu Arg Asn Phe Thr Thr Ala Pro Ala Ile Cys His Glu Gly Lys 1055 1060 1065 | |
|--|---|
| Ala Tyr Phe Pro Arg Glu Gly Val Phe Val Phe Asn Gly Thr Ser 1070 1075 1080 | |
| Trp Phe Ile Thr Gln Arg Asn Phe Phe Ser Pro Gln Ile Ile Thr 1085 1090 1095 | |
| Thr Asp Asn Thr Phe Val Ser Gly Asn Cys Asp Val Val Ile Gly 1100 1105 1110 | |
| Ile Ile Asn Asn Thr Val Tyr Asp Pro Leu Gln Pro Glu Leu Asp 1115 1120 1125 | |
| Ser Phe Lys Glu Glu Leu Asp Lys Tyr Phe Lys Asn His Thr Ser 1130 1135 1140 | |
| Pro Asp Val Asp Leu Gly Asp Ile Ser Gly Ile Asn Ala Ser Val 1145 1150 1155 | |
| Val Asn Ile Gln Lys Glu Ile Asp Arg Leu Asn Glu Val Ala Lys 1160 1165 1170 | |
| Asn Leu Asn Glu Ser Leu Ile Asp Leu Gln Glu Leu Gly Lys Tyr 1175 1180 1185 | |
| Glu Gln Tyr Ile Lys Trp Pro Trp Tyr Val Trp Leu Gly Phe Ile 1190 1195 1200 | |
| Ala Gly Leu Ile Ala Ile Val Met Val Thr Ile Leu Leu Cys Cys 1205 1210 1215 | |
| Met Thr Ser Cys Cys Ser Cys Leu Lys Gly Ala Cys Ser Cys Gly 1220 1225 1230 | |
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| Pro Pro Pro Ile Ser Thr Asp Thr Val Asp Val Thr Asn Gly Leu Gly 35 40 45 | Y |
| Thr Tyr Tyr Val Leu Asp Arg Val Tyr Leu Asn Thr Thr Leu Phe Lev 50 55 60 | u |
| Asn Gly Tyr Tyr Pro Thr Ser Gly Ser Thr Tyr Arg Asn Met Ala Le 65 70 75 80 | u |
| Lys Gly Ser Val Leu Leu Ser Arg Leu Trp Phe Lys Pro Pro Phe Lev 85 90 95 | u |
| Ser Asp Phe Ile Asn Gly Ile Phe Ala Lys Val Lys Asn Thr Lys Va 100 105 110 | 1 |
| Ile Lys Asp Arg Val Met Tyr Ser Glu Phe Pro Ala Ile Thr Ile Gly 115 120 125 | Y |
| Ser Thr Phe Val Asn Thr Ser Tyr Ser Val Val Val Gln Pro Arg Th 130 135 140 | r |
| | |

485

486

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| | | | | | | | | | | | - | con | tin | ued | |
|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Val | Ser | Val | Суз | Gln 165 | Tyr | Asn | Met | Суз | Glu 170 | Tyr | Pro | Gln | Thr | Ile 175 | Суз |
| His | Pro | Asn | Leu 180 | Gly | Asn | His | Arg | Lys 185 | Glu | Leu | Trp | His | Leu 190 | Asp | Thr |
| Gly | Val | Val 195 | Ser | Сүз | Leu | Tyr | Lys 200 | Arg | Asn | Phe | Thr | Tyr 205 | Asp | Val | Asn |
| Ala | Asp 210 | Tyr | Leu | Tyr | Phe | His 215 | Phe | Tyr | Gln | Glu | Gly 220 | Gly | Thr | Phe | Tyr |
| Ala 225 | Tyr | Phe | Thr | Asp | Thr 230 | Gly | Val | Val | Thr | Lys 235 | Phe | Leu | Phe | Asn | Val 240 |
| Tyr | Leu | Gly | Met | Ala 245 | Leu | Ser | His | Tyr | Tyr 250 | Val | Met | Pro | Leu | Thr 255 | Cys |
| Asn | Ser | Lys | Leu 260 | Thr | Leu | Glu | Tyr | Trp 265 | Val | Thr | Pro | Leu | Thr 270 | Ser | Arg |
| Gln | Tyr | Leu 275 | Leu | Ala | Phe | Asn | Gln 280 | Asp | Gly | Ile | Ile | Phe 285 | Asn | Ala | Glu |
| Asp | Cys 290 | Met | Ser | Asp | Phe | Met 295 | Ser | Glu | Ile | Lys | Cys 300 | Lys | Thr | Gln | Ser |
| Ile 305 | Ala | Pro | Pro | Thr | Gly 310 | Val | Tyr | Glu | Leu | Asn 315 | Gly | Tyr | Thr | Val | Gln 320 |
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| Ile | Glu | Ala | Trp 340 | Leu | Asn | Aab | ГÀа | Ser 345 | Val | Pro | Ser | Pro | Leu 350 | Asn | Trp |
| Glu | Arg | Lys 355 | Thr | Phe | Ser | Asn | Сув 360 | Asn | Phe | Asn | Met | Ser 365 | Ser | Leu | Met |
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| Lуя 385 | Ile | Tyr | Gly | Met | Сув 390 | Phe | Ser | Ser | Ile | Thr 395 | Ile | Asp | Lys | Phe | Ala 400 |
| Ile | Pro | Asn | Gly | Arg 405 | Lys | Val | Aap | Leu | Gln 410 | Leu | Gly | Asn | Leu | Gly 415 | Tyr |
| Leu | Gln | Ser | Phe 420 | Asn | Tyr | Arg | Ile | Asp 425 | Thr | Thr | Ala | Thr | Ser 430 | Сүз | Gln |
| Leu | Tyr | Tyr 435 | Asn | Leu | Pro | Ala | Ala 440 | Asn | Val | Ser | Val | Ser 445 | Arg | Phe | Asn |
| Pro | Ser 450 | Thr | Trp | Asn | Гуз | Arg 455 | Phe | Gly | Phe | Ile | Glu 460 | Asp | Ser | Val | Phe |
| Lys 465 | Pro | Arg | Pro | Ala | Gly 470 | Val | Leu | Thr | Asn | His 475 | Asp | Val | Val | Tyr | Ala 480 |
| Gln | His | Cys | Phe | Lys 485 | Ala | Pro | Lys | Asn | Phe 490 | Cys | Pro | Cys | Lys | Leu 495 | Asn |
| Gly | Ser | Сув | Val 500 | Gly | Ser | Gly | Pro | Gly 505 | Lys | Asn | Asn | Gly | Ile 510 | Gly | Thr |
| Сүв | Pro | Ala 515 | Gly | Thr | Asn | Tyr | Leu 520 | Thr | Сув | Asp | Asn | Leu 525 | Сув | Thr | Pro |
| Asp | Pro 530 | Ile | Thr | Phe | Thr | Gly 535 | Thr | Tyr | Lys | Сув | Pro 540 | Gln | Thr | ГЛа | Ser |
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| | Сув | Gly | Gly | | | Суз | Thr | Сув | - | | Gln | Ala | Phe | | |
| | | | | 565 | | | | | 570 | | | | | 575 | |

| Т | rp | Ser | Ala | Asp 580 | Ser | Суз | Leu | Gln | Gly 585 | Asp | Lys | САа | Asn | Ile 590 | Phe | Ala |
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| A | sn | Phe | Ile 595 | Leu | His | Asp | Val | Asn 600 | Ser | Gly | Leu | Thr | Cys 605 | Ser | Thr | Asp |
| L | eu | Gln 610 | Lys | Ala | Asn | Thr | Asp 615 | Ile | Ile | Leu | Gly | Val 620 | Сүв | Val | Asn | Tyr |
| | sp 25 | Leu | Tyr | Gly | Ile | Leu 630 | Gly | Gln | Gly | Ile | Phe 635 | Val | Glu | Val | Asn | Ala 640 |
| Т | hr | Tyr | Tyr | Asn | Ser 645 | Trp | Gln | Asn | Leu | Leu 650 | Tyr | Asp | Ser | Asn | Gly 655 | Asn |
| L | eu | Tyr | Gly | Phe 660 | Arg | Asp | Tyr | Ile | Ile 665 | Asn | Arg | Thr | Phe | Met 670 | Ile | Arg |
| S | er | Cys | Tyr 675 | Ser | Gly | Arg | Val | Ser 680 | Ala | Ala | Phe | His | Ala 685 | Asn | Ser | Ser |
| G | lu | Pro 690 | Ala | Leu | Leu | Phe | Arg 695 | Asn | Ile | Lys | Суя | Asn 700 | Tyr | Val | Phe | Asn |
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| L | eu | Gly | Сув | Val | Val 725 | Asn | Ala | Tyr | Asn | Ser 730 | Thr | Ala | Ile | Ser | Val 735 | Gln |
| Т | hr | Сув | Asp | Leu 740 | Thr | Val | Gly | Ser | Gly 745 | Tyr | Суя | Val | Asp | Tyr 750 | Ser | Lys |
| A | sn | Arg | Arg 755 | Ser | Arg | Gly | Ala | Ile 760 | Thr | Thr | Gly | Tyr | Arg 765 | Phe | Thr | Asn |
| Р | he | Glu 770 | Pro | Phe | Thr | Val | Asn 775 | Ser | Val | Asn | Asp | Ser 780 | Leu | Glu | Pro | Val |
| | ly 85 | Gly | Leu | Tyr | Glu | Ile 790 | Gln | Ile | Pro | Ser | Glu 795 | Phe | Thr | Ile | Gly | Asn 800 |
| Μ | et | Val | Glu | Phe | Ile 805 | Gln | Thr | Ser | Ser | Pro 810 | Lys | Val | Thr | Ile | Asp 815 | Сүз |
| A | la | Ala | Phe | Val 820 | Сүз | Gly | Aab | Tyr | Ala 825 | Ala | Сув | Lys | Ser | Gln 830 | Leu | Val |
| G | lu | Tyr | Gly 835 | Ser | Phe | Суз | Yab | Asn 840 | Ile | Asn | Ala | Ile | Leu 845 | Thr | Glu | Val |
| A | sn | Glu 850 | Leu | Leu | Asp | Thr | Thr 855 | Gln | Leu | Gln | Val | Ala 860 | Asn | Ser | Leu | Met |
| | sn 65 | Gly | Val | Thr | Leu | Ser 870 | Thr | Lys | Leu | Lys | Asp 875 | Gly | Val | Asn | Phe | Asn 880 |
| v | al | Asp | Asp | Ile | Asn 885 | Phe | Ser | Pro | Val | Leu 890 | Gly | САа | Leu | Gly | Ser 895 | Glu |
| Ċ | уs | Ser | Lys | Ala 900 | Ser | Ser | Arg | Ser | Ala 905 | Ile | Glu | Asp | Leu | Leu 910 | Phe | Asp |
| L | уs | Val | Lys 915 | Leu | Ser | Asp | Val | Gly 920 | Phe | Val | Glu | Ala | Tyr 925 | Asn | Asn | Суз |
| Т | hr | Gly 930 | Gly | Ala | Glu | Ile | Arg 935 | Asp | Leu | Ile | Сув | Val 940 | Gln | Ser | Tyr | Гув |
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| er Thr Leu Val Lys Phe Ser Ala Ala Gln Ala Met Glu Lys Val 1100 1105 1110 |
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| sn Gly Asn His Ile Ile Ser Leu Val Gln Asn Ala Pro Tyr Gly 1130 1135 1140 |
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| la Pro Lys Ser Gly Tyr Phe Val Asn Val Asn Asn Thr Trp Met 1175 1180 1185 |
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| ro Tyr Val Met Leu Asn Thr Ser Ile Pro Asn Leu Pro Asp Phe 1220 1225 1230 |
| ys Glu Glu Leu Asp Gln Trp Phe Lys Asn Gln Thr Ser Val Ala 1235 1240 1245 |
| ro Asp Leu Ser Leu Asp Tyr Ile Asn Val Thr Phe Leu Asp Leu 1250 1255 1260 |
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| In Ser Tyr Ile Asn Leu Lys Asp Ile Gly Thr Tyr Glu Tyr Tyr 1280 1285 1290 |
| al Lys Trp Pro Trp Tyr Val Trp Leu Leu Ile Cys Leu Ala Gly 1295 1300 1305 |
| al Ala Met Leu Val Leu Leu Phe Phe Ile Cys Cys Thr Gly 1310 1315 1320 |
| ya Gly Thr Ser Cya Phe Lya Lya Cya Gly Gly Cya Cya Aap Aap 1325 1330 1335 |
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| | Tyr | Tyr 50 | Val | Leu | Asn | Arg | Val 55 | Tyr | Leu | Asn | Thr | Thr 60 | Leu | Leu | Phe | Thr |
| | Gly 65 | Tyr | Phe | Pro | Lys | Ser 70 | Gly | Ala | Asn | Phe | Arg 75 | Asp | Leu | Ala | Leu | Lys 80 |
| , | Gly | Ser | Ile | Tyr | Leu 85 | Ser | Thr | Leu | Trp | Tyr 90 | Lys | Pro | Pro | Phe | Leu 95 | Ser |
| | Asp | Phe | Asn | Asn 100 | Gly | Ile | Phe | Ser | Lys 105 | Val | Lys | Asn | Thr | Lys 110 | Leu | Tyr |
| | Val | Asn | Asn 115 | Thr | Leu | Tyr | Ser | Gl u 120 | Phe | Ser | Thr | Ile | Val 125 | Ile | Gly | Ser |
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| | Thr | Val | Сув | Lys | Ser 165 | Lys | Gly | Ser | Ile | Arg 170 | Asn | Glu | Ser | Trp | His 175 | Ile |
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| | | 210 | | - | - | | 215 | | - | | | 220 | | | Leu | |
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| | | - | 275 | | | | | 280 | - | - | | | 285 | | Leu | |
| | | 290 | | | | | 295 | | | | | 300 | | | Val | |
| | 305 | | | | | 310 | | | | | 315 | | | | Arg | 320 |
| | | | | | 325 | | | | | 330 | | | | | Asn 335 | |
| | | | | 340 | | | | | 345 | | | | | 350 | Asn | |
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| | Ser | Cys 370 | Asn | Asn | Leu | Asp | Lys 375 | Ser | Гла | Ile | Phe | Gly 380 | Ser | Сув | Phe | Asn |
| | Ser 385 | Ile | Thr | Val | Asp | Lys 390 | Phe | Ala | Ile | Pro | Asn 395 | Arg | Arg | Arg | Asp | Asp 400 |
| | Leu | Gln | Leu | Gly | Ser 405 | Ser | Gly | Phe | Leu | Gln 410 | Ser | Ser | Asn | Tyr | Lys 415 | Ile |
| | | | | | | | | | | | | | | | | |

| Asp | Ile | Ser | Ser 420 | Ser | Ser | Суз | Gln | Leu 425 | Tyr | Tyr | Ser | Leu | Pro 430 | Leu | Val |
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| His 465 | Сүз | Phe | Ser | Val | Asn 470 | Ser | Asp | Phe | Сув | Pro 475 | Сүз | Ala | Asp | Pro | Ser 480 |
| Val | Val | Asn | Ser | Суз 485 | Ala | Lys | Ser | Lys | Pro 490 | Pro | Ser | Ala | Ile | Суз 495 | Pro |
| Ala | Gly | Thr | Lys 500 | Tyr | Arg | His | Сув | Asp 505 | Leu | Asp | Thr | Thr | Leu 510 | Tyr | Val |
| Lys | Asn | Trp 515 | Суз | Arg | Суз | Ser | Сув 520 | Leu | Pro | Asp | Pro | Ile 525 | Ser | Thr | Tyr |
| Ser | Pro 530 | Asn | Thr | Сүя | Pro | Gln 535 | Lуя | Гуз | Val | Val | Val 540 | Gly | Ile | Gly | Glu |
| His 545 | Сүз | Pro | Gly | Leu | Gly 550 | Ile | Asn | Glu | Glu | Lys 555 | СЛа | Gly | Thr | Gln | Leu 560 |
| | | | | 565 | Phe | - | | | 570 | | | | - | 575 | |
| | - | | 580 | | Ser | | | 585 | - | | | | 590 | | |
| | | 595 | - | | Asn | | 600 | | | - | | 605 | _ | | |
| | 610 | | | | Ile | 615 | | | | | 620 | | | | |
| 625 | | | | | Gln 630 | | | | | 635 | | | | | 640 |
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| - | | - | 660 | | Ser | | | 665 | | - | | | 670 | | |
| | | 675 | | | Asn | | 680 | | | | | 685 | | | |
| | 690 | | - | - | Pro | 695 | - | - | | - | 700 | | | | |
| 705 | | | | | 710 Leu | | - | | _ | 715 | - | | - | - | 720 |
| Arg | Met | Gly | Ser | 725 Gly | Phe | Сув | Ile | Asp | 730 Tyr | Ala | Leu | Pro | Ser | 735 Ser | Arg |
| Arg | Lys | | 740 Arg | Gly | Ile | Ser | | 745 Pro | Tyr | Arg | Phe | | 750 Thr | Phe | Glu |
| Pro | | 755 Asn | Val | Ser | Phe | | 760 Asn | Asp | Ser | Val | Glu | 765 Thr | Val | Gly | Gly |
| Leu | 770 Phe | Glu | Ile | Gln | Ile | 775 Pro | Thr | Asn | Phe | Thr | 780 Ile | Ala | Gly | His | Glu |
| 785 Glu | Phe | Ile | Gln | Thr | 790 Ser | Ser | Pro | Гуа | Val | 795 Thr | Ile | Asp | Суя | Ser | 800 Ala |
| | | | | 805 | Tyr | | | - | 810 | | | - | - | 815 | |
| | | - | 820 | | Asn | | | 825 | | | | | 830 | | - |
| στλ | | - 11C | -Y8 | чар | AGII | - 1C | HOII | 0er | E | ueu | лан | JIU | vai | HOII | · ~ F |

| | | | | | | | | | | | | 00 | | 11 | ucu | • | |
|------------|-------------|------------|---------------|------------|------------|--------------|-------------|------------|------------|------------|----------|-------------|------------|------------|------------|------------|----|
| | | 835 | | | | | 840 | | | | | 84 | 15 | | | | |
| Leu | Leu 850 | Asp | Ile | Thr | Gln | Leu 855 | Gln | Val | Ala | Asn | 86 | | eu | Met | Gln | Gly | |
| Val 865 | Thr | Leu | Ser | Ser | Asn 870 | Leu | Asn | Thr | Asn | Leu 875 | | s S€ | er | Asp | Val | Asp 880 | |
| Asn | Ile | Asp | Phe | Lys 885 | Ser | Leu | Leu | Gly | Сув 890 | | Gl | y S€ | er | Gln | Cys 895 | Gly | • |
| Ser | Ser | Ser | Arg 900 | | Leu | Leu | Glu | Asp 905 | | Leu | . Ph | e Ae | | Lys 910 | | Lys | • |
| Leu | Ser | Asp 915 | | Gly | Phe | Val | Glu 920 | | Tyr | Asn | As: | n Cy 92 | | Thr | Gly | Gly | |
| Ser | Glu 930 | | | Asp | | Leu 935 | | Val | Gln | Ser | Ph 94 | | 'n | Gly | Ile | - Lys | • |
| Val 945 | Leu | Pro | Pro | Ile | Leu 950 | Ser | Glu | Thr | Gln | Ile 955 | | r Gl | y | Tyr | Thr | Thr 960 | |
| Ala | Ala | Thr | Val | Ala 965 | Ala | Met | Phe | Pro | Pro 970 | | Se | r Al | la | Ala | Ala 975 | Gly | |
| Val | Pro | Phe | Ser 980 | | Asn | Val | Gln | Tyr 985 | | Ile | As | n Gl | | Leu 990 | | Val | |
| Thr | Met | Asp 995 | | Leu | Asn | | Asn 1000 | | n Ly | s Le | u I | | Ala 100 | | sn A | la Pl | he |
| Asn | Lys 1010 | | ı Leı | ı Leı | ı Sei | r Il¢ 103 | | ln A | sn G | ly P | | Thr 1020 | | la | Thr | Asn | |
| Ser | Ala 1025 | | ı Ala | a Ly: | ∃ Il€ | e Glr 103 | | er V | al V | al A | | Ala 1035 | | sn. | Ala | Gln | |
| Ala | Leu 1040 | | n Sei | r Lei | ı Leı | 1 Gl1 104 | | ln L | eu P | he A | | Lys 1050 | | he | Gly | Ala | |
| Ile | Ser 1055 | | : Sei | r Lei | ı Glr | n Glu 106 | | le L | eu S | er A | _ | Leu 1065 | | ab . | Asn | Leu | |
| Glu | Ala 1070 | | n Val | l Glı | n Ile | e Asr 107 | | rg L | eu I | le A | | Gly 1080 | | rg | Leu | Thr | |
| Ala | Leu 1085 | | n Ala | а Туз | r Val | L Sei 109 | | ln G | ln L | eu S | | Asp 1095 | | le | Thr | Leu | |
| Ile | Lys 1100 | | a Gly | 7 Ala | a Sei | r Arg 11(| | la I | le G | lu L | | Val 1110 | | sn | Glu | Cys | |
| Val | | | | | r Pro | | | | | | | | | sn | Gly | Asn | |
| His | Ile 1130 | | ı Sei | r Lei | ı Val | l Glr 113 | | ən A | la P | ro T | | Gly 1140 | | eu | Leu | Phe | |
| Ile | His 1145 | | e Sei | r Tyj | r Lys | 9 Pro 119 | | ır S | er P | he L | - | Thr 1155 | | al | Leu | Val | |
| Ser | Pro 1160 | - | / Let | і Суя | s Lei | 1 Sei 110 | | ly A | sp A | rg G | - | Ile 1170 | | la | Pro | Lys | |
| Gln | Gly 1175 | - | : Phe | e Il∢ | e Lys | 3 Gl1 118 | | an A | sp S | er T | _ | Met 1185 | | he | Thr | Gly | |
| Ser | Ser 1190 | - | : Туз | r Tyi | r Pro | Glu 119 | | ro I | le S | er A | - | Lys 1200 | | sn j | Val | Val | |
| Phe | Met 1205 | | n Sei | r Cyi | s Sei | r Val 121 | | sn Pl | he T | hr L | - | Ala 1215 | | ro | Phe | Ile | |
| Tyr | Leu 1220 | | n Ası | n Sei | r Ile | e Pro 122 | | en L | eu S | er A | _ | Phe 1230 | | lu . | Ala | Glu | |
| Leu | Ser 1235 | | ı Tr <u>ı</u> | p Phe | е Буя | 3 ASI 124 | | is Ti | hr S | er I | | Ala 1249 | | ro. | Asn | Leu | |
| | | | | | | | | | | | | | | | | | |

| - | | | | | | | | | | | | | | | |
|--|---|--|-------------------------------------|--------------------|---------------|--------------|------------|------------|------------|-------------------|------------|-------------|------------|------------|------------|
| Thr | Phe 1250 | | n Se: | r Hi: | a Ile | e Ası 129 | | la Tì | nr Pł | ne Le | | ap 260 | Leu ' | [yr] | ſyr |
| Glu | Met 1269 | | n Va | l Il(| e Glr | n Glu 127 | | er I | le Ly | ∕s S€ | | eu . 275 | Asn : | Ser S | Ser |
| Phe | Ile 1280 | | n Lei | u Ly: | ; Glu | 1 Il. 129 | | ly Tì | ur Tj | yr G | | et 290 | Tyr ' | Val I | ууа |
| Trp | Pro 1299 | | p Ty: | r Ile | e Tr <u>p</u> | Lei 130 | | ∋u I: | le Va | al I: | | eu 305 | Phe : | Ile : | Ile |
| Phe | Leu 1310 | | t 11(| e Lei | ı Phe | e Phe 133 | | le Cy | ya Cj | ya Cj | | hr 320 | Gly (| Cya (| Зly |
| Ser | Ala 1329 | | s Ph | e Sei | t Lys | 5 Cyr 133 | | is A | an Cl | va Cl | | ap 335 | Glu ' | Tyr (| Зly |
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| <40 |)> SH | EQUEI | NCE: | 32 | | | | | | | | | | | |
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| Asp | Arg | Ala | Leu 20 | Ser | Gly | Ile | Ala | Ala 25 | Glu | Gln | Asp | Arg | Asn 30 | Thr | Arg |
| Glu | Val | Phe 35 | Ala | Gln | Val | Lys | Gln 40 | Met | Tyr | Lys | Thr | Pro 45 | Thr | Leu | Lys |
| Tyr | Phe 50 | Gly | Gly | Phe | Asn | Phe 55 | Ser | Gln | Ile | Leu | Pro 60 | Asp | Pro | Leu | Lys |
| Pro 65 | Thr | Lys | Arg | Ser | Phe 70 | Ile | Glu | Asp | Leu | Leu 75 | Phe | Asn | Гуз | Val | Thr 80 |
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| Val | Leu | Pro 115 | Pro | Leu | Leu | Thr | Asp 120 | Asp | Met | Ile | Ala | Ala 125 | Tyr | Thr | Ala |
| Ala | Leu 130 | Val | Ser | Gly | Thr | Ala 135 | Thr | Ala | Gly | Trp | Thr 140 | Phe | Gly | Ala | Gly |
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| Ala | Asn | Gln | Phe 180 | Asn | Lys | Ala | Ile | Ser 185 | Gln | Ile | Gln | Glu | Ser 190 | Leu | Thr |
| Thr | Thr | Ser 195 | Thr | Ala | Leu | Gly | Lув 200 | Leu | Gln | Asp | Val | Val 205 | Asn | Gln | Asn |
| Ala | Gln 210 | Ala | Leu | Asn | Thr | Leu 215 | Val | Гла | Gln | Leu | Ser 220 | Ser | Asn | Phe | Gly |
| Ala 225 | Ile | Ser | Ser | Val | Leu 230 | Asn | Asp | Ile | Leu | Ser 235 | Arg | Leu | Asp | Гуа | Val 240 |
| Glu | Ala | Glu | Val | Gln 245 | Ile | Asp | Arg | Leu | Ile 250 | Thr | Gly | Arg | Leu | Gln 255 | Ser |
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|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|---|
| Asp | Суз | Lys | Gln 100 | Tyr | Val | Суз | Asn | Gly 105 | Phe | Gln | Lya | Суз | Glu 110 | Gln | Leu | |
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| Gly | Ala 130 | Asn | Leu | Arg | Gln | Asp 135 | Asp | Ser | Val | Arg | Asn 140 | Leu | Phe | Ala | Ser | |
| Val 145 | Гуз | Ser | Ser | Gln | Ser 150 | Ser | Pro | Ile | Ile | Pro 155 | Gly | Phe | Gly | Gly | Asp 160 | |
| Phe | Asn | Leu | Thr | Leu 165 | Leu | Glu | Pro | Val | Ser 170 | Ile | Ser | Thr | Gly | Ser 175 | Arg | |
| Ser | Ala | Arg | Ser 180 | Ala | Ile | Glu | Asp | Leu 185 | Leu | Phe | Asp | Lys | Val 190 | Thr | Ile | |
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| Pro | Ala 210 | Ser | Ala | Arg | Asp | Leu 215 | Ile | Сув | Ala | Gln | Tyr 220 | Val | Ala | Gly | Tyr | |
| Lys 225 | Val | Leu | Pro | Pro | Leu 230 | Met | Asp | Val | Asn | Met 235 | Glu | Ala | Ala | Tyr | Thr 240 | |
| Ser | Ser | Leu | Leu | Gly 245 | Ser | Ile | Ala | Gly | Val 250 | Gly | Trp | Thr | Ala | Gly 255 | Leu | |
| Ser | Ser | Phe | Ala 260 | Ala | Ile | Pro | Phe | Ala 265 | Gln | Ser | Ile | Phe | Tyr 270 | Arg | Leu | |
| Asn | Gly | Val 275 | Gly | Ile | Thr | Gln | Gln 280 | Val | Leu | Ser | Glu | Asn 285 | Gln | ГАз | Leu | |
| Ile | Ala 290 | Asn | Lys | Phe | Asn | Gln 295 | Ala | Leu | Gly | Ala | Met 300 | Gln | Thr | Gly | Phe | |
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| Thr | Leu 370 | Asn | Ala | Phe | Val | Ala 375 | Gln | Gln | Leu | Val | Arg 380 | Ser | Glu | Ser | Ala | |
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| Ala | Gln | Ser | ГАа | Arg 405 | Ser | Gly | Phe | Cys | Gly 410 | Gln | Gly | Thr | His | Ile 415 | Val | |
| Ser | Phe | Val | Val 420 | Asn | Ala | Pro | Asn | Gly 425 | Leu | Tyr | Phe | Met | His 430 | Val | Gly | |
| Tyr | Tyr | Pro 435 | Ser | Asn | His | Ile | Glu 440 | Val | Val | Ser | Ala | Tyr 445 | Gly | Leu | Cys | |
| Asp | Ala 450 | Ala | Asn | Pro | Thr | Asn 455 | Сув | Ile | Ala | Pro | Val 460 | Asn | Gly | Tyr | Phe | |
| Ile 465 | ГЛа | Thr | Asn | Asn | Thr 470 | Arg | Ile | Val | Asp | Glu 475 | Trp | Ser | Tyr | Thr | Gly 480 | |
| Ser | Ser | Phe | Tyr | Ala 485 | Pro | Glu | Pro | Ile | Thr 490 | Ser | Leu | Asn | Thr | Lys 495 | Tyr | |
| Val | Ala | Pro | Gln 500 | Val | Thr | Tyr | Gln | Asn 505 | Ile | Ser | Thr | Asn | Leu 510 | Pro | Pro | |
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Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp Glu Leu Asp Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn Phe Gly Ser Leu Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr Tyr Glu Met Leu Ser Leu Gln Gln Val Val Lys Ala Leu Asn Glu Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn Lys Trp Pro <210> SEQ ID NO 34 <211> LENGTH: 526 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polypeptide <400> SEQUENCE: 34 Met Phe Ile Phe Leu Leu Phe Leu Thr Leu Thr Ser Gly Ser Asp Leu Asp Arg Ala Leu Ser Gly Ile Ala Ala Glu Gln Asp Arg Asn Thr Arg 20 25 30 Glu Val Phe Ala Gln Val Lys Gln Met Tyr Lys Thr Pro Thr Leu Lys Tyr Phe Gly Gly Phe Asn Phe Ser Gln Ile Leu Pro Asp Pro Leu Lys Pro Thr Lys Arg Ser Phe Ile Glu Asp Leu Leu Phe Asn Lys Val Thr Leu Ala Asp Ala Gly Phe Met Lys Gln Tyr Gly Glu Cys Leu Gly Asp Ile Asn Ala Arg Asp Leu Ile Cys Ala Gln Lys Phe Asn Gly Leu Thr Val Leu Pro Pro Leu Leu Thr Asp Asp Met Ile Ala Ala Tyr Thr Ala Ala Leu Val Ser Gly Thr Ala Thr Ala Gly Trp Thr Phe Gly Ala Gly Ala Ala Leu Gln Ile Pro Phe Ala Met Gln Met Ala Tyr Arg Phe Asn Gly Ile Gly Val Thr Gln Asn Val Leu Tyr Glu Asn Gln Lys Gln Ile Ala Asn Gln Phe Asn Lys Ala Ile Ser Gln Ile Gln Glu Ser Leu Thr Thr Thr Ser Thr Ala Leu Gly Lys Leu Gln Asp Val Val Asn Gln Asn 195 200 205 Ala Gln Ala Leu Asn Thr Leu Val Lys Gln Leu Ser Ser Asn Phe Gly Ala Ile Ser Ser Val Leu Asn Asp Ile Leu Ser Arg Leu Asp Lys Val Glu Ala Glu Val Gln Ile Asp Arg Leu Ile Thr Gly Arg Leu Gln Ser Leu Gln Thr Tyr Val Thr Gln Gln Leu Ile Arg Ala Ala Glu Ile Arg Ala Ser Ala Asn Leu Ala Ala Thr Lys Met Ser Glu Cys Val Leu Gly

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| Concinaca |
|---|
| Gln Ser Lys Arg Val Asp Phe Cys Gly Lys Gly Tyr His Leu Met Ser 290 295 300 |
| Phe Pro Gln Ala Ala Pro His Gly Val Val Phe Leu His Val Thr Tyr 305 310 315 320 |
| Val Pro Ser Gln Glu Arg Asn Phe Thr Thr Ala Pro Ala Ile Cys His 325 330 335 |
| Glu Gly Lys Ala Tyr Phe Pro Arg Glu Gly Val Phe Val Phe Asn Gly 340 345 350 |
| Thr Ser Trp Phe Ile Thr Gln Arg Asn Phe Phe Ser Pro Gln Ile Ile 355 360 365 |
| Thr Thr Asp Asn Thr Phe Val Ser Gly Asn Cys Asp Val Val Ile Gly 370 375 380 |
| Ile Ile Asn Asn Thr Val Tyr Asp Pro Leu Gln Pro Glu Leu Asp Ser |
| 385 390 395 400 Phe Lys Glu Glu Leu Asp Lys Tyr Phe Lys Asn His Thr Ser Pro Asp |
| 405 410 415 Val Asp Leu Gly Asp Ile Ser Gly Ile Asn Ala Ser Val Val Asn Ile |
| 420 425 430 Gln Lys Glu Ile Asp Arg Leu Asn Glu Val Ala Lys Asn Leu Asn Glu |
| 435 440 445 Ser Leu Ile Asp Leu Gln Glu Leu Gly Lys Tyr Glu Gln Tyr Ile Lys |
| 450 455 460 |
| Trp Pro Trp Tyr Val Trp Leu Gly Phe Ile Ala Gly Leu Ile Ala Ile 465 470 475 480 |
| Val Met Val Thr Ile Leu Leu Cys Cys Met Thr Ser Cys Cys Ser Cys 485 490 495 |
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| tatteatgge agtaetgtta aeteteeaaa eaceegeegg teaaatteat tggggeaate 180 |
| tetetaagat aggggtagta ggaataggaa gtgeaageta eaaagttatg aetegtteea 240 geeateaate attagteata aaattaatge eeaatataae teteeteaat aaetgeaega 300 |
| gggtagagat tgcagaatac aggagactac taagaacagt tttggaacca attagggatg 360 |
| cacttaatgc aatgacccag aacataaggc cggttcagag cgtagcttca agtaggagac 420 |
| acaagagatt tgegggagta gteetggeag gtgeggeeet aggtgttgee acagetgete 480 |
| agataacago oggoattgoa ottoacoggt ocatgotgaa ototoaggoo atogacaato 540 |
| tgagagegag cetggaaact actaateagg caattgagge aateagacaa geagggeagg 600 |
| agatgatatt ggetgtteag ggtgteeaag aetaeateaa taatgagetg ataeegteta 660 tgaaceaget atettgtgat etaateggte agaagetegg geteaaattg ettagataet 720 |
| eguarrayor accorgegar claarogger ayaayeteyy yereaaarey eerayatadt - 720 |

507

508

| atacagaaat cetgteatta tttggeeeea geetaeggga eeeeatatet geggagatat | 780 |
|---|--|
| ctatccaggc tttgagttat gcacttggag gagatatcaa taaggtgtta gaaaagctcg | 840 |
| gatacagtgg aggcgattta ctaggcatct tagagagcag aggaataaag gctcggataa | 900 |
| ctcacgtcga cacagagtee tactteatag teeteagtat ageetateeg aegetgteeg | 960 |
| agattaaggg ggtgattgtc caccggctag aggggggtctc gtacaacata ggctctcaag | 1020 |
| agtggtatac cactgtgccc aagtatgttg caacccaagg gtaccttatc tcgaattttg | 1080 |
| atgagtcatc atgtactttc atgccagagg ggactgtgtg cagccaaaat gccttgtacc | 1140 |
| cgatgagtee tetgeteeaa gaatgeetee gggggteeae caagteetgt getegtaeae | 1200 |
| togtatoogg gtottttggg aacoggttoa ttttatoaca agggaacota atagocaatt | 1260 |
| gtgcatcaat totttgtaag tgttacacaa caggtacgat tattaatcaa gacootgaca | 1320 |
| agateetaac atacattget geegateget geeeggtagt egaggtgaac ggegtgacea | 1380 |
| tccaagtcgg gagcaggagg tatccagacg ctgtgtactt gcacagaatt gacctcggtc | 1440 |
| ctcccatatc attggagagg ttggacgtag ggacaaatct ggggaatgca attgccaaat | 1500 |
| tggaggatgc caaggaattg ttggaatcat cggaccagat attgagaagt atgaaaggtt | 1560 |
| tatcgagcac tagcatagtc tacatcctga ttgcagtgtg tcttggaggg ttgataggga | 1620 |
| teeccaettt aatatgttge tgeaggggge gttgtaacaa aaagggagaa caagttggta | 1680 |
| tgtcaagacc aggectaaag eetgaeetta caggaacate aaaateetat gtaagatege | 1740 |
| tttgatgata ataggetgga geeteggtgg ceaagettet tgeeeettgg geeteeeee | 1800 |
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| <pre><211> LENGTH: 1653 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 36 atgggtetea aggtgaacgt etetgeegta tteatggeag taetgttaae tetecaaaca ceegeeggte aaatteattg gggeaatete tetaagatag gggtagtagg aataggaagt geaagetaca aagttatgae tegtteeage cateaateat tagteataaa attaatgeee aatataaete teeteaataa etgeaegagg gtaggagttg cagaatacag gagaetaeta agaacagttt tggaaceaat tagggatgea ettaatgeaa tgaeeeagaa eataaggeeg gtteagageg tagetteaag taggagaeac aagagattg egggagtagt eetggeaggt geggeeetag gtgttgeeae agetgeteag ataacageeg geattgeaet teaeeggtee atgetgaaet eteaggeeat egacaatetg agagegagee tggaaaetae taateaggea attgaggeaa teagacaage agggeaggag atgatattgg etgtteaggg tgteeaagae</pre> | 120 180 240 300 360 420 480 540 |
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| <pre><211> LENGTH: 1653 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 36 atgggtetca aggtgaacgt etetgeegta tteatggeag taetgttaae tetecaaaca ceegeeggte aaatteattg gggeaatete tetaagatag gggtagtagg aataggaagt geaagetaca aagttatgae tegtteeage cateaateat tagteataaa attaatgeee aatataaete teeteaataa etgeaegagg gtaggagttg cagaatacag gagaetaeta agaacagttt tggaaceaat tagggatgea ettaatgeaa tgaeeeagaa eataaggeeg gtteagageg tagetteaag taggagaeae aagagattg egggagtagt eetggeaggt geggeeetag gtgttgeeae agetgeteag ataacageeg geattgeaet teaeeggtee atgetgaaet eteaggeea eggegaggag atgatattg etgteaggat atgetgaaet eteaggeage agggeaggag atgatattg etgteagge tgeteeagae attgaggeaa teagaeaage agggeaggag atgatattg etgteagg tgteeaagae taeateaata atgagetgat acegtetatg aaceagetat ettgtgatet aateggteag aageteggge teaaattget tagatactat acagaaatee tgteattatt tggeeeeage aageteggge teaaattget tagatactat acagaaatee tgteattatt tggeeeeage aageteggge teaaattget tagatactat acagaaatee tgteattatt tggeeeeage</pre> | 120 180 240 300 360 420 480 540 600 |
| <pre><211> LENGTH: 1653 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 36 atgggtctca aggtgaacgt ctctgccgta ttcatggcag tactgttaac tctccaaaca cccgccggtc aaattcattg gggcaatctc tctaagatag gggtagtagg aataggaagt gcaagctaca aagttatgac tcgtccagc catcaatcat tagtcataaa attaatgccc aatataactc tcctcaataa ctgcacgagg gtagagattg cagaatacag gagactacta agaacagttt tggaaccaat tagggatgca cttaatgcaa tgacccagaa cataaggccg gttcagagcg tagcttcaag taggagacac aagagattg cgggagtagt cctggcaggt atgctgaact ctcaggccat cgacaatctg agagcgagce tggaaactac taatcaggca atgctgaact ctcaggccat cgacaatctg agagcgagce tggaaactac taatcaggca atgaggcaa tcagacaagc agggcaggag atgatattgg ctgttcaggg tgtccaagac tacatcaata atgagctgat accgtctatg aaccagctat cttgtgatct aatcggcag aagctegggc tcaaattgc tagatactat acagaaatcc tgtcattat tggccccaga atgctggacc ccatatctge ggagatatct atccaggctt tgagttatgc acttggagga gagctcgggc ccaaattgc tagatactat acagaaatcc tgtcattatt tggccccagc ctacgggacc ccatatctge ggagatatct atccaggctt tgagttatgc acttggagga gatatcaata aggtgttaga aaagctcgga tacagtggag gcgatttact aggcatctta</pre> | 120 180 240 300 360 420 480 540 600 660 720 780 |
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| ggggtetegt acaacatagg eteteaagag tggtatacea etgtgeecaa gtatgttgea | 960 |
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| acccaagggt accttatoto gaattttgat gagtoatoat gtaotttoat gooagaggg | 1020 |
| actgtgtgca gccaaaatgc cttgtacccg atgagteete tgetecaaga atgeeteegg | 1080 |
| gggtccacca agteetgtge tegtacaete gtateegggt ettttgggaa eeggtteatt | 1140 |
| ttatcacaag ggaacctaat agccaattgt gcatcaattc tttgtaagtg ttacacaaca | 1200 |
| ggtacgatta ttaatcaaga cootgacaag atootaacat acattgotgo ogatogotgo | 1260 |
| coggtagtog aggtgaacgg cgtgaccatc caagtoggga gcaggaggta tocagacgot | 1320 |
| gtgtacttgc acagaattga cctcggtcct cccatatcat tggagaggtt ggacgtaggg | 1380 |
| acaaatetgg ggaatgeaat tgecaaattg gaggatgeea aggaattgtt ggaateateg | 1440 |
| gaccagatat tgagaagtat gaaaggttta tcgagcacta gcatagtcta catectgatt | 1500 |
| gcagtgtgtc ttggagggtt gatagggatc cccactttaa tatgttgctg cagggggggt | 1560 |
| tgtaacaaaa agggagaaca agttggtatg tcaagaccag gcctaaagcc tgaccttaca | 1620 |
| ggaacatcaa aatcctatgt aagatcgctt tga | 1653 |
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| attcattggg gcaatctctc taagataggg gtagtaggaa taggaagtgc aagctacaaa | 180 |
| gttatgactc gttccagcca tcaatcatta gtcataaaat taatgcccaa tataactctc | 240 |
| ctcaataact gcacgagggt agagattgca gaatacagga gactactaag aacagttttg | |
| gaaccaatta gggatgcact taatgcaatg acccagaaca taaggccggt tcagagcgta | |
| getteaagta ggagacacaa gagatttgeg ggagtagtee tggeaggtge ggeeetaggt | 420 |
| gttgccacag ctgctcagat aacagccggc attgcacttc accggtccat gctgaactet | 480 |
| caggecateg acaatetgag agegageetg gaaactaeta ateaggeaat tgaggeaate | 540 |
| agacaagcag ggcaggagat gatattggct gttcagggtg tccaagacta catcaataat | 600 |
| gagetgatae egtetatgaa eeagetatet tgtgatetaa teggteagaa getegggete | 660 720 |
| aaattgetta gatactatac agaaateetg teattatttg geeeeageet aegggaeeee atatetgegg agatatetat ceaggetttg agttatgeae ttggaggaga tateaataag | |
| gtgttagaaa agotoggata cagtggaggo gatttactag goatottaga gagoagagga | 840 |
| ataaaggoto ggataactca cgtogacaca gagtoctact toatagtoot cagtatagoo | 900 |
| tatcogacge tgtcogagat taagggggtg attgtccace ggctagaggg ggtctcgtac | 960 |
| | 1020 |
| aacatagget etcaagagtg gtataccaet gtgeecaagt atgttgeaac ecaagggtae | 1020 |
| ettatetega attttgatga gteateatgt aettteatge eagaggggae tgtgtgeage | |
| caaaatgoot tgtaccogat gagtoototg otocaagaat gootoogggg gtocaccaag | |
| teetgtgete gtacaetegt atcegggtet tttgggaaee ggtteatttt atcaeaaggg | 1200 |
| aacctaatag ccaattgtgc atcaattett tgtaagtgtt acacaacagg tacgattatt | 1260 |
| | |

511

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| aatcaagacc ctgacaagat cctaacatac attgctgeeg atcgctgeec ggtagtegag | 1320 |
| gtgaacggcg tgaccatcca agtcgggagc aggaggtatc cagacgctgt gtacttgcac | 1380 |
| agaattgacc tcggtcctcc catatcattg gagaggttgg acgtagggac aaatctgggg | 1440 |
| aatgcaattg ccaaattgga ggatgccaag gaattgttgg aatcatcgga ccagatattg | 1500 |
| agaagtatga aaggtttatc gagcactagc atagtctaca teetgattge agtgtgtett | 1560 |
| ggagggttga tagggateee caetttaata tgttgetgea gggggegttg taacaaaaag | 1620 |
| ggagaacaag ttggtatgtc aagaccaggc ctaaagcetg acettacagg aacatcaaaa | 1680 |
| teetatgtaa gategetttg atgataatag getggageet eggtggeeaa gettettgee | 1740 |
| cettgggeet ceeeccagee ceteeteee tteetgeace egtaceeeeg tggtetttga | 1800 |
| ataaagtotg agtgggoggo aaaaaaaaa aaaaaaaaa aaaaaaaaaa | 1860 |
| AAAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAA | 1920 |
| tctag | 1925 |
| <210> SEQ ID NO 38 <211> LENGTH: 1864 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 38 | |
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| aaagaagagt aagaagaaat ataagagcca ccatgggtct caaggtgaac gtctctgtca | 120 |
| tattcatggc agtactgtta actetteaaa caeceaeegg teaaateeat tggggeaate | 180 |
| tetetaagat aggggtggta ggggtaggaa gtgeaageta eaaagttatg aetegtteea | 240 |
| gccatcaatc attagtcata aagttaatgc ccaatataac tctcctcaac aattgcacga | 300 |
| gggtagggat tgcagaatac aggagactac tgagaacagt tetggaacea attagagatg | 360 |
| cacttaatgc aatgacccag aatataagac cggttcagag tgtagcttca agtaggagac | 420 |
| acaagagatt tgegggagtt gteetggeag gtgeggeeet aggegttgee acagetgete | 480 |
| aaataacago oggtattgoa ottoaccagt coatgotgaa ototoaagoo atogacaato | 540 |
| tgagagegag eetagaaact actaateagg caattgagge aateagaeaa geagggeagg | 600 |
| agatgatatt ggctgttcag ggtgtccaag actacatcaa taatgagctg ataccgtcta | 660 |
| tgaatcaact atcttgtgat ttaatcggcc agaagctagg gctcaaattg ctcagatact | 720 |
| atacagaaat cotgtoatta tttggcooca gottacggga coccatatot goggagatat | 780 |
| ctatecagge tttgagetat gegettggag gagatateaa taaggtgttg gaaaageteg | 840 |
| gatacagtgg aggtgatcta ctgggcatct tagagagcag aggaataaag gcccggataa | 900 |
| ctcacgtcga cacagagtee tactteattg tactcagtat ageetateeg aegetateeg | 960 |
| agattaaggg ggtgattgtc caceggetag agggggtete gtacaacata ggeteteaag | 1020 |
| agtggtatac cactgtgccc aagtatgttg caacccaagg gtaccttatc tcgaattttg | 1080 |
| atgagtcatc atgcactttc atgccagagg ggactgtgtg cagccagaat gccttgtacc | 1140 |
| cgatgagtee tetgeteeaa gaatgeetee gggggteeae taagteetgt getegtaeae | 1200 |
| togtatoogg gtotttoggg aacoggttoa ttttatoaca ggggaacota atagooaatt | 1260 |
| gigcalcaat colligcaag igilacacaa caggaacaat callaalcaa gacooigaca | 1320 |
| agateetaac atacattget geegateact geeeggtggt egaggtgaat ggegtgaeea | 1380 |
| | |

| tecaagtegg gageaggagg tateeggaeg etgtgtaett geacaggatt gaeeteggte | 1440 | | | | | | |
|---|------|--|--|--|--|--|--|
| cteecatate tttggagagg ttggaegtag ggaeaaatet ggggaatgea attgetaagt | 1500 | | | | | | |
| tggaggatgc caaggaattg ttggagtcat cggaccagat attgaggagt atgaaaggtt | 1560 | | | | | | |
| tatogagoao tagtatagtt tacatootga ttgoagtgtg tottggagga ttgataggga | 1620 | | | | | | |
| teecegettt aatatgttge tgeaggggge gttgtaacaa gaagggagaa caagttggta | 1680 | | | | | | |
| tgtcaagacc aggectaaag cetgatetta caggaacate aaaateetat gtaaggteae | 1740 | | | | | | |
| totgatgata ataggotgga gootoggtgg coaagottot tgeocottgg gootococoo | 1800 | | | | | | |
| agececteet cecetteetg caccegtace ceegtggtet ttgaataaag tetgagtggg | 1860 | | | | | | |
| cggc | 1864 | | | | | | |
| <210> SEQ ID NO 39 <211> LENGTH: 1653 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 39 | | | | | | | |
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| cccaccggtc aaatccattg gggcaatctc tctaagatag gggtggtagg ggtaggaagt | 120 | | | | | | |
| gcaagctaca aagttatgac tegtteeage cateaateat tagteataaa gttaatgeee | 180 | | | | | | |
| aatataactc tcctcaacaa ttgcacgagg gtagggattg cagaatacag gagactactg | 240 | | | | | | |
| agaacagtto tggaaccaat tagagatgoa ottaatgoaa tgacocagaa tataagacog | 300 | | | | | | |
| gttcagagtg tagettcaag taggagacac aagagatttg egggagttgt eetggeaggt | 360 | | | | | | |
| geggeeetag gegttgeeae agetgeteaa ataacageeg gtattgeaet teaceagtee | 420 | | | | | | |
| atgetgaact etcaageeat egacaatetg agagegagee tagaaactae taateaggea | 480 | | | | | | |
| attgaggcaa tcagacaagc agggcaggag atgatattgg ctgttcaggg tgtccaagac | 540 | | | | | | |
| tacatcaata atgagetgat accgtetatg aatcaactat ettgtgattt aateggeeag | 600 | | | | | | |
| aagctagggc tcaaattgct cagatactat acagaaatcc tgtcattatt tggccccagc | 660 | | | | | | |
| ttacgggacc ccatatetge ggagatatet atccaggett tgagetatge gettggagga | 720 | | | | | | |
| gatatcaata aggtgttgga aaagctcgga tacagtggag gtgatctact gggcatctta | 780 | | | | | | |
| gagagcagag gaataaaggc ccggataact cacgtcgaca cagagtccta cttcattgta | 840 | | | | | | |
| ctcagtatag cotatoogac gotatoogag attaaggggg tgattgtooa coggotagag | 900 | | | | | | |
| ggggtetegt acaacatagg eteteaagag tggtatacea etgtgeeeaa gtatgttgea | 960 | | | | | | |
| acccaagggt accttatete gaattttgat gagteateat geaettteat geeagagggg | 1020 | | | | | | |
| actgtgtgca gecagaatge ettgtaeeeg atgagteete tgeteeaaga atgeeteegg | 1080 | | | | | | |
| gggtccacta agteetgtge tegtacaete gtateegggt etttegggaa eeggtteatt | 1140 | | | | | | |
| ttatcacagg ggaacctaat agccaattgt gcatcaatcc tttgcaagtg ttacacaaca | 1200 | | | | | | |
| ggaacaatca ttaatcaaga cootgacaag atootaacat acattgotgo ogatcactgo | 1260 | | | | | | |
| coggtggtog aggtgaatgg ogtgaccato caagtoggga goaggaggta tooggaogot | 1320 | | | | | | |
| gtgtacttgc acaggattga cctcggtcct cccatatctt tggagaggtt ggacgtaggg | 1380 | | | | | | |
| acaaatctgg ggaatgcaat tgctaagttg gaggatgcca aggaattgtt ggagtcatcg | 1440 | | | | | | |
| gaccagatat tgaggagtat gaaaggttta tcgagcacta gtatagttta catcctgatt | 1500 | | | | | | |
| | | | | | | | |

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| gcagtgtgtc ttggaggatt gatagggatc cccgctttaa tatgttgctg cagggggcgt | 1560 |
| tgtaacaaga agggagaaca agttggtatg tcaagaccag gcctaaagcc tgatcttaca | 1620 |
| ggaacatcaa aatcctatgt aaggtcactc tga | 1653 |
| <210> SEQ ID NO 40 <211> LENGTH: 1925 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide | |
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| gtgaacgtot otgtoatatt catggoagta otgttaacto ttoaaacaoo caooggtoaa | 120 |
| atccattggg gcaatctctc taagataggg gtggtagggg taggaagtgc aagctacaaa | 180 |
| gttatgactc gttccagcca tcaatcatta gtcataaagt taatgcccaa tataactctc | 240 |
| ctcaacaatt gcacgagggt agggattgca gaatacagga gactactgag aacagttetg | 300 |
| gaaccaatta gagatgcact taatgcaatg acccagaata taagaccggt tcagagtgta | 360 |
| getteaagta ggagacacaa gagatttgeg ggagttgtee tggeaggtge ggeeetagge | 420 |
| gttgccacag ctgctcaaat aacagccggt attgcacttc accagtccat gctgaactct | 480 |
| caagccatcg acaatctgag agcgagccta gaaactacta atcaggcaat tgaggcaatc | 540 |
| agacaagcag ggcaggagat gatattggct gttcagggtg tccaagacta catcaataat | 600 |
| gagetgatae egtetatgaa teaaetatet tgtgatttaa teggeeagaa getagggete | 660 |
| aaattgotoa gatactatac agaaatootg toattatttg goocoagott acgggacooo | 720 |
| atatotgogg agatatotat ocaggotttg agotatgogo ttggaggaga tatoaataag | 780 |
| gtgttggaaa ageteggata cagtggaggt gatetaetgg geatettaga gageagagga | 840 |
| ataaaggeee ggataactea egtegacaca gagteetaet teattgtaet eagtatagee | 900 |
| tateegaege tateegagat taagggggtg attgteeaee ggetagaggg ggtetegtae | 960 |
| aacatagget etcaagagtg gtataceaet gtgeeeaagt atgttgeaae eeaagggtae | 1020 |
| ettatetega attttgatga gteateatge aettteatge eagagggggae tgtgtgeage | 1080 |
| cagaatgoot tgtaccogat gagtoototg otocaagaat gootoogggg gtocactaag | 1140 |
| teetgtgete gtacaetegt ateegggtet ttegggaace ggtteatttt ateaeagggg | 1200 |
| aacctaatag ccaattgtgc atcaateett tgeaagtgtt acacaacagg aacaateatt | 1260 |
| aatcaagace etgacaagat eetaacatae attgetgeeg ateaetgeee ggtggtegag | 1320 |
| gtgaatggog tgaccatoca agtogggago aggaggtato oggaogotgt gtaottgoad | 1380 |
| aggattgace teggteetee catatetttg gagaggttgg acgtagggae aaatetgggg | 1440 |
| aatgcaattg ctaagttgga ggatgccaag gaattgttgg agtcatcgga ccagatattg | 1500 |
| aggagtatga aaggtttatc gagcactagt atagtttaca teetgattge agtgtgtett | 1560 |
| ggaggattga tagggateee egetttaata tgttgetgea gggggegttg taacaagaag | 1620 |
| ggagaacaag ttggtatgtc aagaccaggc ctaaageetg atettacagg aacatcaaaa | 1680 |
| teetatgtaa ggteaetetg atgataatag getggageet eggtggeeaa gettettgee | 1740 |
| cettgggeet ecceccagee estecteece tteetgeace egtaceeeg tggtetttga | 1800 |
| ataaagtotg agtgggoggo aaaaaaaaaa aaaaaaaaaa | 1860 |
| aaaaaaaaa aaaaaaaaaa aaaaaaaaa aaaaaaaa | 1920 |

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| Э | T | 1 |

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| <210> SEQ ID NO 41 <211> LENGTH: 2065 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide | | | | | | |
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| <400> SEQUENCE: 41 | | | | | | |
| teaagetttt ggaccetegt | acagaagcta | atacgactca | ctatagggaa | ataagagaga | 60 | |
| aaagaagagt aagaagaaat | ataagageea | ccatgtcacc | gcaacgagac | cggataaatg | 120 | |
| cettetacaa agataaceet | tateccaagg | gaagtaggat | agttattaac | agagaacatc | 180 | |
| ttatgattga cagaccctat | gttetgetgg | ctgttctgtt | cgtcatgttt | ctgagettga | 240 | |
| teggattget ggeaattgea | ggcattagac | tteateggge | agccatctac | accgcggaga | 300 | |
| tecataaaag eetcagtaee | aatctggatg | tgactaactc | categageat | caggtcaagg | 360 | |
| acgtgetgae accaetett | aaaatcatcg | gggatgaagt | gggcctgaga | acaceteaga | 420 | |
| gattcactga cctagtgaaa | ttcatctcgg | acaagattaa | atteettaat | ccggataggg | 480 | |
| agtacgaett cagagatete | acttggtgca | tcaaccegee | agagaggatc | aaactagatt | 540 | |
| atgatcaata ctgtgcagat | gtggetgetg | aagagctcat | gaatgcattg | gtgaactcaa | 600 | |
| ctctactgga gaccagaaca | accactcagt | tcctagctgt | ctcaaaggga | aactgeteag | 660 | |
| ggcccactac aatcagaggt | caatteteaa | acatgtcgct | gtccttgttg | gacttgtact | 720 | |
| taggtegagg ttacaatgtg | tcatctatag | tcactatgac | atcccaggga | atgtatgggg | 780 | |
| gaacctacct agttgaaaag | cctaatctga | acagcaaagg | gtcagagttg | tcacaactga | 840 | |
| gcatgtaccg agtgtttgaa | gtaggtgtga | tcagaaaccc | gggtttgggg | geteeggtgt | 900 | |
| tccatatgac aaactatttt | gagcaaccag | tcagtaatgg | tctcggcaac | tgtatggtgg | 960 | |
| ctttggggga geteaaaete | geagecettt | gtcacgggga | cgattctatc | ataatteeet | 1020 | |
| atcagggatc agggaaaggt | gtcagettee | agctcgtcaa | getgggtgte | tggaaatccc | 1080 | |
| caaccgacat gcaatectgg | gtccccttat | caacggatga | tccagtggta | gacaggettt | 1140 | |
| acctctcatc tcacagaggt | gtcatcgctg | acaatcaagc | aaaatgggct | gteeegacaa | 1200 | |
| cacgaacaga tgacaagttg | cgaatggaga | catgcttcca | gcaggcgtgt | aaaggtaaaa | 1260 | |
| tccaagcact ctgcgagaat | cccgagtggg | taccattgaa | ggataacagg | atteetteat | 1320 | |
| acggggteet gtetgttgat | ctgagtctga | cggttgagct | taaaatcaaa | attgettegg | 1380 | |
| gattegggee attgateaca | cacggeteag | ggatggacct | atacaaatcc | aactgcaaca | 1440 | |
| atgtgtattg getgaetatt | ccgccaatga | gaaatctagc | cttaggcgta | atcaacacat | 1500 | |
| tggagtggat accgagattc | aaggttagtc | ccaacctctt | cactgtccca | attaaggaag | 1560 | |
| caggogaaga ctgccatgcc | ccaacatacc | tacctgcgga | ggtggacggt | gatgtcaaac | 1620 | |
| tcagttecaa cetggtgatt | ctacctggtc | aagatctcca | atatgttttg | gcaacctacg | 1680 | |
| atacctccag ggttgagcat | getgtggttt | attacgttta | cageccaage | cgctcatttt | 1740 | |
| cttactttta tccttttagg | ttgcctataa | agggggtccc | aatcgaacta | caagtggaat | 1800 | |
| gcttcacatg ggatcaaaaa | ctctggtgcc | gtcacttctg | tgtgettgeg | gactcagaat | 1860 | |
| ccggtggact tatcactcac | tctgggatgg | tgggcatggg | agtcagetge | acagetacee | 1920 | |
| gggaagatgg aaccaatcgc | agataatgat | aataggetgg | ageeteggtg | gccaagcttc | 1980 | |

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|---------------------|--|-------------------------|------|
| ttgeeeettg ggeetee | cood cagecooted tecectteet | gcaccegtac ceeegtggte | 2040 |
| tttgaataaa gtotgag | jtgg gegge | | 2065 |
| <220> FEATURE: | | ectide | |
| <400> SEQUENCE: 42 | 2 | | |
| atgtcaccgc aacgaga | accg gataaatgcc ttctacaaag | g ataaccetta teecaaggga | 60 |
| agtaggatag ttattaa | acag agaacatett atgattgaca | a gaccotatgt totgotggot | 120 |
| gttetgtteg teatgtt | ttet gagettgate ggattgetge | y caattgeagg cattagaett | 180 |
| categggeag ceateta | acac cgcggagatc cataaaagcc | : tcagtaccaa tctggatgtg | 240 |
| actaactcca togagoa | atca ggtcaaggac gtgctgacac | : cactetttaa aateateggg | 300 |
| gatgaagtgg geetgaq | gaac acctcagaga ttcactgacc | tagtgaaatt catctoggac | 360 |
| aagattaaat toottaa | atee ggatagggag taegaettea | a gagateteae ttggtgeate | 420 |
| aaccogccag agaggat | tcaa actagattat gatcaatact | : gtgcagatgt ggctgctgaa | 480 |
| gageteatga atgeatt | tggt gaactcaact ctactggaga | a ccagaacaac cactcagttc | 540 |
| ctagctgtct caaaggg | gaaa ctgctcaggg cccactacaa | a tcagaggtca attetcaaac | 600 |
| atgtegetgt cettgti | tgga ettgtaetta ggtegaggtt | acaatgtgtc atctatagtc | 660 |
| actatgacat cccaggo | gaat gtatgggggga acctacctag | g ttgaaaagcc taatctgaac | 720 |
| agcaaagggt cagagtt | tgtc acaactgagc atgtaccgag | g tgtttgaagt aggtgtgatc | 780 |
| agaaaccegg gtttggg | gggc teeggtgtte catatgacaa | a actattttga gcaaccagtc | 840 |
| agtaatggtc toggcaa | actg tatggtgget ttggggggage | : tcaaactcgc agecetttgt | 900 |
| cacgggggacg attetat | teat aatteeetat cagggateag | g ggaaaggtgt cagetteeag | 960 |
| ctogteaage tgggtgt | tetg gaaateeeca acegacatge | aateetgggt eeesttatea | 1020 |
| acggatgatc cagtggt | taga caggetttac eteteatete | acagaggtgt categetgae | 1080 |
| aatcaagcaa aatgggo | ctgt coogacaaca ogaacagato | y acaagttgog aatggagaca | 1140 |
| | gtaa aggtaaaatc caagcactet | | 1200 |
| | ggat teetteatae ggggteetgt | | |
| | aaat tgetteggga ttegggeeat | | 1320 |
| | ccaa ctgcaacaat gtgtattggc | | 1380 |
| | taat caacacattg gagtggatac | | 1440 |
| - | caat taaggaagca ggcgaagact gtga tgtcaaactc agttccaacc | | 1500 |
| | | | |
| | tgge aacetaegat aceteeagge | | 1620 |
| | geeg cteattttet taettttate | | 1680 |
| | taca agtggaatgc ttcacatggg | | 1740 |
| cacttetgtg tgettge | egga etcagaatee ggtggaetta | a teacteacte tgggatggtg | 1800 |
| ggcatgggag teagetg | geac agetaceegg gaagatggaa | a ccaatcgcag ataa | 1854 |

<210> SEQ ID NO 43 <211> LENGTH: 2126

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<212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 43 ggggaaataa gagagaaaag aagagtaaga agaaatataa gagccaccat gtcaccgcaa 60 egagacegga taaatgeett etacaaagat aaceettate eeaagggaag taggatagtt 120 attaacagag aacatettat gattgacaga cectatgtte tgetggetgt tetgttegte 180 atgtttetga gettgategg attgetggea attgeaggea ttagaettea tegggeagee 240 atetacaceg eggagateea taaaageete agtaceaate tggatgtgae taaeteeate 300 gagcatcagg tcaaggacgt gctgacacca ctotttaaaa tcatcgggga tgaagtgggc 360 ctgagaacac ctcagagatt cactgaccta gtgaaattca tctcggacaa gattaaattc 420 480 ettaateegg atagggagta egaetteaga gateteaett ggtgeateaa eeegeeagag aggatcaaac tagattatga tcaatactgt gcagatgtgg ctgctgaaga gctcatgaat 540 gcattggtga actcaactet actggagace agaacaacea etcagtteet agetgtetea 600 aagggaaact geteagggee cactacaate agaggteaat teteaaacat gtegetgtee 660 ttgttggadt tgtadttagg tdgaggttad aatgtgtdat dtatagtdad tatgadated 720 cagggaatgt atgggggaac ctacctagtt gaaaageeta atetgaacag caaagggtea 780 840 gagttgtcac aactgagcat gtaccgagtg tttgaagtag gtgtgatcag aaacccgggt ttggggggtt cggtgtteca tatgacaaac tattttgagc aaccagtcag taatggtetc 900 ggcaactgta tggtggcttt gggggggctc aaactcgcag ccctttgtca cggggacgat 960 tetateataa tteeetatea gggateaggg aaaggtgtea getteeaget egteaagetg 1020 ggtgtctgga aatccccaac cgacatgcaa tcctgggtcc ccttatcaac ggatgatcca 1080 gtggtagaca ggetttacet eteateteae agaggtgtea tegetgacaa teaagcaaaa 1140 tgggctgtcc cgacaacacg aacagatgac aagttgcgaa tggagacatg cttccagcag 1200 gcgtgtaaag gtaaaatcca agcactctgc gagaatcccg agtgggtacc attgaaggat 1260 aacaggatte etteataegg ggteetgtet gttgatetga gtetgaeggt tgagettaaa 1320 atcaaaattg cttogggatt ogggooattg atcacacaog gotcagggat ggacotatac 1380 aaateeaact geaacaatgt gtattggetg actatteege caatgagaaa tetageetta 1440 ggegtaatea acacattgga gtggataeeg agatteaagg ttagteeeaa eetetteaet 1500 gtoccaatta aggaagcagg cgaagactgo catgocccaa catacotaco tgoggaggtg 1560 gacggtgatg teaaacteag ttecaacetg gtgattetae etggteaaga tetecaatat 1620 1680 gttttggcaa cotacgatac otocagggtt gagcatgotg tggtttatta ogtttacago ccaageeget cattitetta ettitateet titaggiige etataaaggg ggieeeaate 1740 gaactacaag tggaatgett cacatgggat caaaaactet ggtgeegtea ettetgtgtg 1800 ettgeggaet cagaateegg tggaettate acteactetg ggatggtggg catgggagte 1860 agetgeacag etaceeggga agatggaace aategeagat aatgataata ggetggagee 1920 teggtggeea agettettge ceettgggee teecceage cectecteee ettectgeae 1980 ccgtaccccc gtggtctttg aataaagtet gagtgggcgg caaaaaaaaaa aaaaaaaaaa 2040 2100 2126 aaaaaaaaaa aaaaaaaaaa atctag

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<210> SEQ ID NO 44 <211> LENGTH: 2065 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 44 tcaagetttt ggaceetegt acagaageta ataegaetea etatagggaa ataagagaga 60 aaagaagagt aagaagaaat ataagagcca ccatgtcacc acaacgagac cggataaatg 120 cettetacaa agacaaceee cateetaagg gaagtaggat agttattaac agagaacate 180 ttatgattga tagacettat gttttgetgg etgttetatt egteatgttt etgagettga 240 tegggttget agecattgea ggeattagae tteateggge agecatetae acegeagaga 300 tecataaaag eeteageace aatetggatg taactaacte aategageat caggttaagg 360 420 acgtgetgae accactette aagateateg gtgatgaagt gggettgagg acaceteaga gattcactga cetagtgaag ttcatetetg acaagattaa attcettaat ceggacaggg 480 aatacgactt cagagatete aettggtgta teaaceegee agagagaate aaattggatt 540 600 atgatcaata ctgtgcagat gtggctgctg aagaactcat gaatgcattg gtgaactcaa etetaetgga gaccagggea accaateagt teetagetgt eteaaaggga aactgeteag 660 ggeccactac aatcagagge caatteteaa acatgteget gteeetgttg gaettgtatt 720 taagtegagg ttacaatgtg teatetatag teactatgae ateceaggga atgtaegggg 780 qaacttacct aqtqqaaaaq cctaatctqa qcaqcaaaqq qtcaqaqttq tcacaactqa 840 gcatgcaccg agtgtttgaa gtaggtgtta tcagaaatcc gggtttgggg gctccggtat 900 tecatatgae aaactatett gageaaceag teagtaatga ttteageaae tgeatggtgg 960 etttgggggga geteaagtte geageeetet gteacaggga agattetate acaatteeet 1020 atcagggate agggaaaggt gteagettee agettgteaa getaggtgte tggaaateee 1080 caacegacat geaateetgg gteeceetat caacggatga teeagtgata gacaggettt 1140 acctctcatc tcacagagge gttatcgetg acaatcaage aaaatggget gteecgacaa 1200 cacggacaga tgacaagttg cgaatggaga catgottoca gcaggogtgt aagggtaaaa 1260 tecaageact ttgegagaat eeegagtgga caccattgaa ggataacagg atteetteat 1320 acggggtett gtetgttgat etgagtetga cagttgaget taaaateaaa attgttteag 1380 gattegggee attgateaca caeggtteag ggatggaeet atacaaatee aaceacaaca 1440 atatgtattg getgactate eegecaatga agaacetgge ettaggtgta ateaacacat 1500 tggagtggat accgagatte aaggttagte ceaacetett cactgtteea attaaggaag 1560 caggegagga etgecatgee ceaacatace tacetgegga ggtggatggt gatgteaaac 1620 1680 tcaqttccaa tctqqtqatt ctacctqqtc aaqatctcca atatqttctq qcaacctacq atactteeag agttgaacat getgtagttt attacgttta cageceaage egeteatttt 1740 ettaetttta teettttagg ttgeetgtaa gggggggteee eattgaatta caagtggaat 1800 getteacatg ggaccaaaaa etetggtgee gteacttetg tgtgettgeg gacteagaat 1860 etggtggaca tateacteac tetgggatgg tgggcatggg agteagetge acagecaete 1920 gggaagatgg aaccagcogc agatagtgat aataggotgg agootoggtg gocaagotto 1980 ttgeccettg ggeeteeeee cageceetee teeeetteet geaceegtae eeeegtggte 2040 tttgaataaa gtetgagtgg gegge 2065

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60

120

180

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300

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420

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540

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660 720

780

840

900

960

<210> SEQ ID NO 45 <211> LENGTH: 1854 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 45 atgtcaccac aacgagaccg gataaatgcc ttctacaaag acaaccecca tectaaggga agtaggatag ttattaacag agaacatett atgattgata gaeettatgt tttgetgget gttetatteg teatgtttet gagettgate gggttgetag ceattgeagg eattagaett categggeag ceatetaeae egeagagate cataaaagee teageaeeaa tetggatgta actaactcaa tegageatca ggttaaggae gtgetgaeae caetetteaa gateateggt gatgaagtgg gettgaggae aceteagaga tteactgaee tagtgaagtt catetetgae aagattaaat teettaatee ggacagggaa taegaettea gagateteae ttggtgtate aacccgccag agagaatcaa attggattat gatcaatact gtgcagatgt ggctgctgaa gaactcatga atgcattggt gaactcaact ctactggaga ccagggcaac caatcagttc ctagetgtet caaagggaaa etgeteaggg ceeactacaa teagaggeea atteteaaae atgtegetgt ceetgttgga ettgtattta agtegaggtt acaatgtgte atetatagte actatgacat cccagggaat gtacggggga acttacctag tggaaaagcc taatctgagc agcaaagggt cagagttgtc acaactgagc atgcaccgag tgtttgaagt aggtgttatc agaaateegg gtttgggggge teeggtatte catatgaeaa actatettga geaaceagte agtaatgatt teageaactg catggtgget ttgggggage teaagttege ageestetgt cacagggaag attetateac aatteestat cagggateag ggaaaggtgt cagetteeag ettgtcaage taggtgtetg gaaateeeca acegacatge aateetgggt eeeetatea 1020 acggatgate cagtgataga caggetttae eteteatete acagaggegt tategetgae 1080 aatcaagcaa aatgggetgt eeegacaaca eggacagatg acaagttgeg aatggagaca 1140 tgetteeage aggegtgtaa gggtaaaate caageaettt gegagaatee egagtggaca 1200 ccattgaagg ataacaggat teetteatae ggggtettgt etgttgatet gagtetgaca 1260 gttgagetta aaatcaaaat tgtttcagga ttegggeeat tgatcacaca eggttcaggg 1320 atggacetat acaaateeaa eeacaacaat atgtattgge tgactateee gecaatgaag 1380 aacctggcot taggtgtaat caacacattg gagtggatac cgagattcaa ggttagtcoc 1440 aacctettea etgtteeaat taaggaagea ggegaggaet geeatgeeee aacataeeta 1500 cctgcggagg tggatggtga tgtcaaactc agttccaatc tggtgattct acctggtcaa 1560 gatetecaat atgttetgge aacetaegat aettecagag ttgaacatge tgtagtttat 1620 tacgtttaca geocaageeg eteatttet taetttate ettttaggtt geetgtaagg 1680 ggggteecca ttgaattaca agtggaatge tteacatggg accaaaaaet etggtgeegt 1740 cacttetgtg tgettgegga etcagaatet ggtggacata teacteacte tgggatggtg 1800 ggcatgggag tcagctgcac agccactcgg gaagatggaa ccagccgcag atag 1854

<210> SEQ ID NO 46 <211> LENGTH: 2126 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE:

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| <223> OTHER | R INFORMATIO | DN: Synthet: | ic Polynucle | eotide | | | |
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| <400> SEQUE | ENCE: 46 | | | | | | |
| ggggaaataa | gagagaaaag | aagagtaaga | agaaatataa | gagecaccat | gtcaccacaa | 60 | |
| cgagaccgga | taaatgeett | ctacaaagac | aacccccatc | ctaagggaag | taggatagtt | 120 | |
| attaacagag | aacatettat | gattgataga | ccttatgttt | tgetggetgt | tctattcgtc | 180 | |
| atgtttctga | gettgategg | gttgctagcc | attgcaggca | ttagacttca | tcgggcagcc | 240 | |
| atctacaccg | cagagateca | taaaageete | agcaccaatc | tggatgtaac | taactcaatc | 300 | |
| gagcatcagg | ttaaggacgt | gctgacacca | ctcttcaaga | tcatcggtga | tgaagtgggc | 360 | |
| ttgaggacac | ctcagagatt | cactgaccta | gtgaagttca | tctctgacaa | gattaaattc | 420 | |
| cttaatcogg | acagggaata | cgacttcaga | gateteaett | ggtgtatcaa | cccgccagag | 480 | |
| agaatcaaat | tggattatga | tcaatactgt | gcagatgtgg | ctgctgaaga | actcatgaat | 540 | |
| gcattggtga | actcaactct | actggagacc | agggcaacca | atcagtteet | agetgtetea | 600 | |
| aagggaaact | gctcagggcc | cactacaatc | agaggccaat | tetcaaacat | gtegetgtee | 660 | |
| ctgttggact | tgtatttaag | tcgaggttac | aatgtgtcat | ctatagtcac | tatgacatcc | 720 | |
| cagggaatgt | acgggggaac | ttacctagtg | gaaaagceta | atetgageag | caaagggtca | 780 | |
| gagttgtcac | aactgagcat | gcaccgagtg | tttgaagtag | gtgttatcag | aaatccgggt | 840 | |
| ttggggggtc | cggtattcca | tatgacaaac | tatettgage | aaccagtcag | taatgatttc | 900 | |
| agcaactgca | tggtggettt | ggggggagete | aagttegeag | ccetetgtea | cagggaagat | 960 | |
| tctatcacaa | ttecctatea | gggatcaggg | aaaggtgtca | gettecaget | tgtcaagcta | 1020 | |
| ggtgtetgga | aatcoccaac | cgacatgcaa | teetgggtee | ccctatcaac | ggatgatcca | 1080 | |
| gtgatagaca | ggetttaeet | ctcatctcac | agaggegtta | tcgctgacaa | tcaagcaaaa | 1140 | |
| tgggetgtee | cgacaacacg | gacagatgac | aagttgegaa | tggagacatg | cttccagcag | 1200 | |
| gcgtgtaagg | gtaaaatcca | agcactttgc | gagaatcccg | agtggacacc | attgaaggat | 1260 | |
| aacaggattc | cttcatacgg | ggtettgtet | gttgatctga | gtetgaeagt | tgagettaaa | 1320 | |
| atcaaaattg | tttcaggatt | cgggccattg | atcacacacg | gttcagggat | ggacctatac | 1380 | |
| aaatccaacc | acaacaatat | gtattggetg | actatecege | caatgaagaa | cctggcctta | 1440 | |
| ggtgtaatca | acacattgga | gtggataccg | agattcaagg | ttagteccaa | cctcttcact | 1500 | |
| gttccaatta | aggaagcagg | cgaggactgc | catgeceeaa | catacctacc | tgcggaggtg | 1560 | |
| gatggtgatg | tcaaactcag | ttccaatctg | gtgattctac | ctggtcaaga | tctccaatat | 1620 | |
| gttetggeaa | cctacgatac | ttccagagtt | gaacatgetg | tagtttatta | cgtttacagc | 1680 | |
| ccaageeget | cattttetta | etttateet | tttaggttgc | ctgtaagggg | ggtecceatt | 1740 | |
| gaattacaag | tggaatgett | cacatgggac | caaaaactet | ggtgccgtca | cttetgtgtg | 1800 | |
| cttgcggact | cagaatctgg | tggacatatc | actcactctg | ggatggtggg | catgggagtc | 1860 | |
| agctgcacag | ccactcggga | agatggaacc | agccgcagat | agtgataata | ggetggagee | 1920 | |
| teggtggeea | agettettge | ccettgggcc | teccccage | ccetcctccc | cttcctgcac | 1980 | |
| cegtacecee | gtggtetttg | aataaagtct | gagtgggggg | caaaaaaaaaa | aaaaaaaaaa | 2040 | |
| aaaaaaaaaa | aaaaaaaaaa | aaaaaaaaaa | aaaaaaaaaa | aaaaaaaaaa | aaaaaaaaaa | 2100 | |
| | aaaaaaaaa | | | | | 2126 | |
| | | 5 | | | | | |

<210> SEQ ID NO 47 <211> LENGTH: 550

529

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| <213 <220 | 2> TY 3> OF 2> FE | RGAN EATUR | ESM: RE: | | | | - | | 0.01 | | lde | | | | | |
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| | > 01 > SE | | | | FION | : SYI | ntnet | 10 | Poly | pepti | lae | | | | | |
| Met 1 | Gly | Leu | Гла | Val 5 | Asn | Val | Ser | Ala | Val 10 | Phe | Met | Ala | Val | Leu 15 | Leu | |
| Thr | Leu | Gln | Thr 20 | Pro | Ala | Gly | Gln | Ile 25 | His | Trp | Gly | Asn | Leu 30 | Ser | Гуз | |
| Ile | Gly | Val 35 | Val | Gly | Ile | Gly | Ser 40 | Ala | Ser | Tyr | Lys | Val 45 | Met | Thr | Arg | |
| Ser | Ser 50 | His | Gln | Ser | Leu | Val 55 | Ile | ГÀЗ | Leu | Met | Pro 60 | Asn | Ile | Thr | Leu | |
| Leu 65 | Asn | Asn | Суз | Thr | Arg 70 | Val | Glu | Ile | Ala | Glu 75 | Tyr | Arg | Arg | Leu | Leu 80 | |
| Arg | Thr | Val | Leu | Glu 85 | Pro | Ile | Arg | Asp | Ala 90 | Leu | Asn | Ala | Met | Thr 95 | Gln | |
| Asn | Ile | Arg | Pro 100 | Val | Gln | Ser | Val | Ala 105 | Ser | Ser | Arg | Arg | His 110 | ГАз | Arg | |
| Phe | Ala | Gly 115 | Val | Val | Leu | Ala | Gly 120 | Ala | Ala | Leu | Gly | Val 125 | Ala | Thr | Ala | |
| Ala | Gln 130 | Ile | Thr | Ala | Gly | Ile 135 | Ala | Leu | His | Arg | Ser 140 | Met | Leu | Asn | Ser | |
| Gln 145 | Ala | Ile | Asp | Asn | Leu 150 | Arg | Ala | Ser | Leu | Glu 155 | Thr | Thr | Asn | Gln | Ala 160 | |
| Ile | Glu | Ala | Ile | Arg 165 | Gln | Ala | Gly | Gln | Glu 170 | Met | Ile | Leu | Ala | Val 175 | Gln | |
| Gly | Val | Gln | Asp 180 | Tyr | Ile | Asn | Asn | Glu 185 | Leu | Ile | Pro | Ser | Met 190 | Asn | Gln | |
| Leu | Ser | Суя 195 | Asp | Leu | Ile | Gly | Gln 200 | гуз | Leu | Gly | Leu | Lув 205 | Leu | Leu | Arg | |
| Tyr | Tyr 210 | Thr | Glu | Ile | Leu | Ser 215 | Leu | Phe | Gly | Pro | Ser 220 | Leu | Arg | Asp | Pro | |
| Ile 225 | Ser | Ala | Glu | Ile | Ser 230 | Ile | Gln | Ala | Leu | Ser 235 | Tyr | Ala | Leu | Gly | Gly 240 | |
| Asp | Ile | Asn | Lys | Val 245 | Leu | Glu | Lys | Leu | Gly 250 | Tyr | Ser | Gly | Gly | Asp 255 | Leu | |
| Leu | Gly | Ile | Leu 260 | Glu | Ser | Arg | Gly | Ile 265 | Гуз | Ala | Arg | Ile | Thr 270 | His | Val | |
| Asp | Thr | Glu 275 | Ser | Tyr | Phe | Ile | Val 280 | Leu | Ser | Ile | Ala | Tyr 285 | Pro | Thr | Leu | |
| Ser | Glu 290 | Ile | ГАз | Gly | Val | Ile 295 | Val | His | Arg | Leu | Glu 300 | Gly | Val | Ser | Tyr | |
| Asn 305 | Ile | Gly | Ser | Gln | Glu 310 | Trp | Tyr | Thr | Thr | Val 315 | Pro | Lys | Tyr | Val | Ala 320 | |
| Thr | Gln | Gly | Tyr | Leu 325 | Ile | Ser | Asn | Phe | Asp 330 | Glu | Ser | Ser | Сув | Thr 335 | Phe | |
| Met | Pro | Glu | Gly 340 | Thr | Val | Сув | Ser | Gln 345 | Asn | Ala | Leu | Tyr | Pro 350 | Met | Ser | |
| Pro | Leu | Leu 355 | Gln | Glu | Cys | Leu | Arg 360 | Gly | Ser | Thr | Lys | Ser 365 | Суя | Ala | Arg | |
| Thr | Leu 370 | Val | Ser | Gly | Ser | Phe 375 | Gly | Asn | Arg | Phe | Ile 380 | Leu | Ser | Gln | Gly | |

| | | | | | | | | | | | _ | con | C TII | ucu | |
|--------------------------------|---|---------------------------------|---------------------------------|--------------------------------|---------------------------------------|--|---------------------------------|--|--------------------------------|---------------------------------------|--|--|--|---------------------------------------|---------------------------------------|
| Asn 385 | Leu | Ile | Ala | Asn | Cys 390 | Ala | Ser | Ile | Leu | Cys 395 | ГЛЗ | Суз | Tyr | Thr | Thr 400 |
| Gly | Thr | Ile | Ile | Asn 405 | Gln | Asp | Pro | Asp | Lys 410 | Ile | Leu | Thr | Tyr | Ile 415 | Ala |
| Ala | Asp | Arg | Сув 420 | Pro | Val | Val | Glu | Val 425 | Asn | Gly | Val | Thr | Ile 430 | Gln | Val |
| Gly | Ser | Arg 435 | Arg | Tyr | Pro | Asp | Ala 440 | Val | Tyr | Leu | His | Arg 445 | Ile | Asp | Leu |
| Gly | Pro 450 | Pro | Ile | Ser | Leu | Glu 455 | Arg | Leu | Asp | Val | Gly 460 | Thr | Asn | Leu | Gly |
| Asn 465 | Ala | Ile | Ala | ГАа | Leu 470 | Glu | Asp | Ala | Lys | Glu 475 | Leu | Leu | Glu | Ser | Ser 480 |
| Asp | Gln | Ile | Leu | Arg 485 | Ser | Met | Lys | Gly | Leu 490 | Ser | Ser | Thr | Ser | Ile 495 | Val |
| Tyr | Ile | Leu | Ile 500 | Ala | Val | Сув | Leu | Gly 505 | Gly | Leu | Ile | Gly | Ile 510 | Pro | Thr |
| Leu | Ile | Сув 515 | САв | САа | Arg | Gly | Arg 520 | Суз | Asn | Lys | ГЛа | Gly 525 | Glu | Gln | Val |
| Gly | Met 530 | Ser | Arg | Pro | Gly | Leu 535 | Lys | Pro | Asp | Leu | Thr 540 | Gly | Thr | Ser | Lys |
| Ser 545 | Tyr | Val | Arg | Ser | Leu 550 | | | | | | | | | | |
| <21 <21 <22 <22 | 1 > L1 2 > T 3 > O1 0 > F1 3 > O' 0 > S1 | YPE: RGANI EATUR THER | PRT SM: E: INF | Art: DRMA | | | - | | olyj | pept: | ide | | | | |
| Met 1 | Gly | Leu | Lys | Val 5 | Asn | Val | Ser | Val | Ile 10 | Phe | Met | Ala | Val | Leu 15 | Leu |
| Thr | Leu | Gln | Thr 20 | Pro | Thr | Gly | Gln | Ile 25 | His | Trp | Gly | Asn | Leu 30 | Ser | Lys |
| Ile | Gly | Val 35 | Val | Gly | Val | Gly | Ser 40 | Ala | Ser | Tyr | ГЛа | Val 45 | Met | Thr | Arg |
| Ser | Ser 50 | His | Gln | Ser | Leu | Val | Ile | Lys | Leu | M≏+ | Dro | 3 | T1 = | Thr | Leu |
| | | | | | | 55 | | - | | nec | 60 | ASII | 110 | | Lea |
| Leu 65 | Asn | Asn | Сув | Thr | | | Gly | - | | | 60 | | | | |
| 65 | | | | | Arg 70 | Val | | Ile | Ala | Glu 75 | 60 Tyr | Arg | Arg | Leu | Leu 80 |
| 65 Arg | Asn | Val | Leu | Glu 85 | Arg 70 Pro | Val Ile | Arg | Ile Asp | Ala Ala 90 | Glu 75 Leu | 60 Tyr Asn | Arg Ala | Arg Met | Leu Thr 95 | Leu 80 Gln |
| 65 Arg Asn | Asn Thr | Val Arg | Leu Pro 100 | Glu 85 Val | Arg 70 Pro Gln | Val Ile Ser | Arg Val | Ile Asp Ala 105 | Ala Ala 90 Ser | Glu 75 Leu Ser | 60 Tyr Asn Arg | Arg Ala Arg | Arg Met His 110 | Leu Thr 95 Lys | Leu 80 Gln Arg |
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| 65 Arg Asn Phe Ala | Asn Thr Ile Ala Gln | Val Arg Gly 115 Ile | Leu Pro 100 Val Thr | Glu 85 Val Val Ala | Arg 70 Pro Gln Leu Gly | Val Ile Ser Ala Ile 135 | Arg Val Gly 120 Ala | Ile Asp Ala 105 Ala Leu | Ala 90 Ser Ala His | Glu 75 Leu Ser Leu Gln | 60 Tyr Asn Arg Gly Ser 140 | Arg Ala Arg Val 125 Met | Arg Met His 110 Ala Leu | Leu Thr 95 Lys Thr Asn | Leu 80 Gln Arg Ala Ser |

Ile Glu Ala Ile Arg Gln Ala Gly Gln Glu Met Ile Leu Ala Val Gln 165 170

Gly Val Gln Asp Tyr Ile Asn Asn Glu Leu Ile Pro Ser Met Asn Gln

| -continued |
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| Asp Ile Asn Lys Val Leu Glu Lys Leu Gly Tyr Ser Gly Gly Asp Leu Gly Ile Lat Gly Ile Leu Glu Ser Tyr Phe Ile Val Leu Ser Ile Ala Arg Ile Ala Arg Ile Val Zess Ile Ala Tyr Thr His Val Ser Glu Ile Lys Gly Val Try Thr Ala Tyr Thr Leu 225 To Thr Leu Ser Glu Gly Ser Tyr Glu Tyr Thr Thr Val Pro Lys Val Ala 300 Tyr Val Ala 300 | | | | | | | | | | | | | COIL | | ueu | | | | |
|---|--------------------------------------|---|--|-------------------------------------|--------------------|-----|-----|-----|-----|-------|-------|-----|------|-----|-----|-----|--|-----|-----|
| 21021522011e Ser Ala Guu Ile Ser Ile Gin Ala Leu Ger Tyr Ala Leu Gly Gly 230Asp Ile Asn Lys Val Leu Glu Lys Leu Cly Tyr Ser Gly Gly Asp Leu 240Asp Ile Asn Lys Val Leu Glu Ser Arg Gly Ile Lys Ala Arg Ile Thr His Val 260Leu Cly Ile Leu Glu Ser Arg Gly Ile Lys Ala Arg Ile Thr His Val 260Asp Thr 71Bar Thr 71Clu Ser Tyr Phe Ile Val Leu Ser Ile Ala Tyr Pro Thr Leu 200Ser Glu Ile Lys Gly Val Ile Val His Arg Leu Glu Gly Val Ser Tyr 290Asp Thr 71Clu Ser Gln Glu Trp Tyr Thr Thr Val Pro Lys Tyr Val Ala 305Ser Glu Gly Tyr Leu Ile Ser Asn Phe Asp Glu Ser Ser Cys Thr Phe 325Asn The Glu Gly Tyr Lu Ile Ser Asn Phe Asp Glu Ser Ser Cys Ala Arg 340Thr Gln Gly Tyr Leu Ile Ser Asn Phe Asp Glu Ser Ser Cys Ala Arg 340Ser Glu Glu Glu Cys Leu Arg Gly Ser Thr Lys Ser Cys Ala Arg 340Pro Leu Leu Gln Glu Cys Leu Arg Gly Ser Thr Lys Ser Cys Ala Arg 360Sas Thr Leu Val Ser Gly Ser Phe Gly Asn Arg Phe Ile Leu Ser Gln Gly 370Asn Phi Cys Pro Val Val Glu Asn Ala Cu Tyr Thr Thr 400An Arg His Cys Pro Val Val Glu Asn Ala Gly Val Thr Thr 400Ala Asp His Cys Pro Val Val Glu Val Asn Gly Val Thr Ile Glu Nal 420Ala Asp His Cys Pro Val Val Glu Val Asn Gly Val Thr Ser Ile Val 450Asn Ala Lue Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 450Asn Glu Tle Leu Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 450Asn Glu Tle Leu Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 450Asn Glu Tle Leu Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 450Asn Glu Hie Lau Arg Cys Asn Lys Lys Gly Glu Glu Val 550 <td>Leu</td> <td>Ser</td> <td></td> <td>Aab</td> <td>Leu</td> <td>Ile</td> <td>Gly</td> <td></td> <td>Lys</td> <td>Leu</td> <td>Gly</td> <td>Leu</td> <td></td> <td>Leu</td> <td>Leu</td> <td>Arg</td> | Leu | Ser | | Aab | Leu | Ile | Gly | | Lys | Leu | Gly | Leu | | Leu | Leu | Arg | | | |
| 225 230 235 240 Asp Ile Asn Lys Val Leu Glu Lys Leu Gly Tyr Ser Gly Gly Asp Leu 255 250 250 250 255 255 Leu Gly Ile Leu Glu Ser Arg Gly Ile Lys Ala Arg Ile Thr His Val 260 265 18 As Arg Ile Thr His Val 265 77 78 71 18 Val Leu Clu Ser Ile Ala Tyr Pro Thr Leu 280 Asp Thr Glu Ser Tyr Phe Ile Val Leu Ser Ile Ala Tyr Pro Thr Leu 275 290 295 300 295 77 74 144 Asp Thr Glu Ser Tyr Phe Ile Val Leu Ser Ile Ala Tyr Pro Thr Leu 275 300 295 300 295 77 74 141 200 Ser Glu Ile Lys Gly Val Ile Val For Thr Thr Val Pro Lys Tyr Val Ala 310 310 77 77 76 77 78 77 78 77 78 77 78 77 78 77 78 77 78 77 78 77 78 77 78 77 78 77 78 77 78 </td <td>Tyr</td> <td></td> <td>Thr</td> <td>Glu</td> <td>Ile</td> <td>Leu</td> <td></td> <td>Leu</td> <td>Phe</td> <td>Gly</td> <td>Pro</td> <td></td> <td>Leu</td> <td>Arg</td> <td>Asp</td> <td>Pro</td> | Tyr | | Thr | Glu | Ile | Leu | | Leu | Phe | Gly | Pro | | Leu | Arg | Asp | Pro | | | |
| 245 250 255 Leu Gly 1le Leu Glu Ser Arg Gly 1le Lys Ala Arg 1le Thr His Val 265 77 Phe 1e Val Cas 1e Ala Arg 1le Thr His Val 275 77 Asp Thr Glu Ser Tyr 200 Fyr Phe 1e Val Cas Fyr Val Arg 70 77 1e 295 1e Ala Arg 1le Thr His Val 275 77 1e 1e 216 77 78 1e 216 77 78 77 1e 295 1e Ala Arg 1le Thr His Val 290 77 78 79 78 78 79 79 | Ile 225 | Ser | Ala | Glu | Ile | | Ile | Gln | Ala | Leu | | Tyr | Ala | Leu | Gly | _ | | | |
| 260 265 270 Asp Thr Qlu Ser Tyr Phe Ile Val Leu Ser Ile Ala Tyr Pro Tor Leu 285 286 11e Ala Tyr Pro Tor Leu 285 Ser Glu Ile Lys Gly Val Ile Val His Arg Leu Glu Gly Val Ser Tyr 290 11e Val Fir Arg Leu Glu Gly Val Jam 310 11e Val Fir Arg Leu Glu Gly Val Jam 320 Asp Thr Glu Gly Ser Gln Glu Trp Tyr Thr Thr Val Pro Lys Tyr Val Jam 320 11e Ser Asn Phe Asp Glu Ser Ser Cys Thr Phe 325 Met Pro Glu Gly Thr Val Cys Ser Gln Asn Ala Leu Tyr Pro Met Ser 346 360 286 Pro Leu Leu Gln Glu Cyr Leu Arg Gly Ser Thr Lys Ser Cys Ala Arg 370 375 386 11e Leu Yr Thr Thr 390 Asm Leu 11e Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr 400 380 380 380 380 Gly Thr Ile Ile Asn Gln Asp Pro Asp Lys Ile Leu Thr Tyr 11e Ala 405 410 411 410 413 Ala Asp His Cys Tyr Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu Gly 455 440 11e Asp 445 450 Gly Ser Arg Arg Tyr Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu Gly 445 450 450 450 Gly Ser Arg Arg Tyr Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu Gly 445 450 450 450 Gly Pro Pro To Ile Ser Leu Glu Asp Ala Lys Gly Leu Heu Glu Ser Ser Met 440 450 450 450 450 Gly Met Ser Arg Pro Gly Cys Arg Gly Arg Cy | Asp | Ile | Asn | Гла | | Leu | Glu | Гуз | Leu | | Tyr | Ser | Gly | Gly | | Leu | | | |
| 275 280 285 Ser Glu Ile Lys Gly Val Ile Val His Arg Leu Glu Gly Val Ser Tyr 295 Aen Ile Gly Ser Gln Glu Trp Tyr Thr Thr Val Pro Lys Tyr Val Ala 300 305 11e Gly Ser Gln Glu Trp Tyr Thr Thr Val Pro Lys Tyr Val Ala 305 11e Gly Tyr Leu Ile Ser Asn Phe Asp Glu Ser Ser Cys Thr Phe 320 340 Thr Gln Gly Tyr Leu Ile Ser Asn Phe Asp Glu Ser Ser Cys Ala Met Pro Glu Gly Thr Val Cys Ser Gln Asn Ala Leu Tyr Pro Met Ser 340 340 Pro Leu Leu Gln Glu Cys Leu Arg Gly Ser Thr Lys Ser Cys Ala Arg 355 11e Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 370 375 386 11e Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 385 11e Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 385 390 Gly Thr Ile Ile Asn Gln Asp Pro Asp Lys Ile Leu Thr Tyr Ile Ala 400 410 411 405 Ala Asp His Cys Pro Val Val Glu Val Asn Gly Val Thr His Gln Val 420 Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu 440 420 440 440 441 445 61y Pro Pro Ile Ser Leu Glu Asp Ala Lys Glu Leu Leu Gly | Leu | Gly | Ile | | Glu | Ser | Arg | Gly | | Гла | Ala | Arg | Ile | | His | Val | | | |
| 290295300Amen Ile Gly Ser Gln Glu Trp Tyr Thr Thr Val Pro Lyg Tyr Val Ala 310310310Thr Gln Gly Tyr Leu Ile Ser Am Phe Amp Glu Ser Ser Cys Thr Phe 325320Thr Gln Gly Tyr Leu Ile Ser Am Phe Amp Glu Ser Ser Cys Thr Phe 325336Met Pro Glu Gly Thr Val Cys Ser Gln Am Ala Leu Tyr Pro Met Ser 346346Pro Leu Leu Gln Glu Cys Leu Arg Gly Ser Thr Lys Ser Cys Ala Arg 355366Pro Leu Leu Gln Glu Cys Leu Arg Gly Am Arg Phe Ile Leu Ser Gln Gly 370380Am Leu Ile Ala Am Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 390380Am Leu Ile Ala Am Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 390381Am Leu Ile Ala Am Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 390380Gly Thr Ile Ile Am Gln Amp Pro Amp Lys Ile Leu Thr Tyr Ile Ala 410415Ala Amp His Cys Pro Val Val Glu Val Am Gly Val Thr Ile Gln Val 420425Gly Pro Pro Ile Ser Leu Glu Arg Leu Amp Val Gly Thr Am Leu Gly 450440Am Ala Ile Ala Lys Leu Glu Amp Lys Glu Leu Leu Glu Ser Ser 470485Amp Gln Ile Leu Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 485480Amp Gln Ile Leu Arg Ser Met Lys Gly Leu Ser Set Or Gly Glu Gln Val 510520Ser Tyr Val Arg Ser Leu | Asp | Thr | | Ser | Tyr | Phe | Ile | | Leu | Ser | Ile | Ala | | Pro | Thr | Leu | | | |
| 305310315320Thr Gln Gly Tyr Leu Ile Ser Asn Phe Asp Glu Ser Ser Cys Thr Phe 325320Met Pro Glu Gly Thr Val Cys Ser Gln Asn Ala Leu Tyr Pro Met Ser 345345Pro Leu Leu Gln Glu Cys Leu Arg Gly Ser Thr Lys Ser Cys Ala Arg 355365Thr Leu Val Ser Gly Ser Phe Gly Asn Arg Phe Ile Leu Ser Gln Gly 370377Asn Leu Ile Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 395390Gly Thr Ile Ile Asn Gln Asp Pro Asp Lys Ile Leu Thr Tyr Ile Ala 400410Gly Ser Arg Arg Tyr Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu 425410Gly Ser Arg Arg Tyr Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu 435440Gly Pro Pro Ile Ser Leu Glu Asp Ala Lys Glu Leu Leu Glu Ser Ser 450455Asn Ala Ile Ala Lys Leu Glu Asp Ala Lys Glu Leu Leu Glu Ser Ser 455470Asp Gln Ile Leu Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 485490Asp Gln Ile Leu Ile Ala Val Cys Leu Gly Gly Leu Ile Gly Ile Pro Ala 500520Cys Cys Cys Arg Gly Arg Cys Asn Lys Lys Gly Glu Gln Val 515525Ser Tyr Val Arg Ser Leu 530520Calox SEQ ID NO 49 call> LENGTH: 617calox SEQ ID NO 49 call> LENGTH: 617calox Seq ID NO 49 call> LENGTH: 617calox Seq ID NO 49 call> Seq ID NO 49 call> Cys Cys Tyr Synthetic Polypeptide | Ser | | Ile | Lys | Gly | Val | | Val | His | Arg | Leu | | Gly | Val | Ser | Tyr | | | |
| 325330335Met Pro Glu Gly Thr Val Cys Ser Gln Asn Ala Leu Tyr Pro Met Ser 340Ser Thr Lys Ser Cys Ala Arg 360Pro Leu Leu Gln Glu Cys Leu Arg Gly Ser Thr Lys Ser Cys Ala Arg 355Thr Leu Val Ser Gly Ser Phe Gly Asn Arg Phe Ile Leu Ser Gln Gly 370Sam Leu Ile Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 390Gly Thr Ile Ile Asn Gln Asp Pro Asp Lys Ile Leu Thr Tyr Ile Ala 400Ala Asp His Cys Pro Val Val Glu Val Asn Gly Val Thr Ile Gln Val 420Gly Ser Arg Arg Tyr Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu 435Gly Pro Pro Ile Ser Leu Glu Arg Leu Asp Val Gly Thr Asn Leu Gly 455Asn Ala Ile Ala Lys Leu Glu Asp Ala Lys Glu Leu Leu Glu Ser Ser 470Asp Gln Ile Leu Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 485Asp Gln Ile Leu Arg Ser Met Lys Gly Gly Leu Ile Gly Ile Pro Ala 500Ser Tyr Val Arg Ser Leu 515Gly Met Ser Arg Pro Gly Leu Lys Pro Asp Leu Thr Gly Thr Ser Lys 530Ser Tyr Val Arg Ser Leu 530Ser Tyr Val Arg Ser Leu 520Cla SEQ ID NO 49 <211> LENGTH: 617 <212> TYPE: FRT | Asn 305 | Ile | Gly | Ser | Gln | | Trp | Tyr | Thr | Thr | | Pro | Гуз | Tyr | Val | | | | |
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| 355360365Thr Leu Val Ser Gly Ser Phe Gly Asn Arg Phe Ile Leu Ser Gln Gly 370375Asn Leu Ile Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 390395Gly Thr Ile Ile Asn Gln Asp Pro Asp Lys Ile Leu Thr Tyr Ile Ala 405400Gly Thr Ile Ile Asn Gln Asp Pro Asp Lys Ile Leu Thr Tyr Ile Ala | < | < | < | Met | Pro | Glu | | Thr | Val | Cys | Ser | | Asn | Ala | Leu | Tyr | | Met | Ser |
| 370375380Aam Leu Ile Ala Aan Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 395Thr The Ala Aan Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr 400Gly Thr Ile Ile Aan Gin Aap Pro Aap Lys Ile Leu Thr Tyr Ile Ala 405Aan Aap His Cys Pro Val Val Glu Val Aan Gly Val Thr Ile Gin Val 425Ala Aap His Cys Pro Val Val Glu Val Aan Gly Val Thr Ile Gin Val 420Gly Val Tyr Leu His Arg Ile Aap Leu 435Gly Ser Arg Arg Tyr Pro Aap Ala Val Tyr Leu His Arg Ile Aap Leu 435Gly Thr Aan Leu Gly 465Gly Pro Pro Ile Ser Leu Glu Aap Ala Lys Glu Leu Leu Glu Ser Ser 465Glu Ser Ser Thr Ser Ile Val 485Aasn Ala Ile Ala Lys Leu Glu Aap Ala Lys Gly Leu Ser Ser Thr Ser Ile Val 485Gly Cys Cys Arg Gly Arg Cys Aan Lys Lys Gly Glu Glu Gln Val 515Leu Ile Cys Cys Cys Arg Gly Arg Cys Aan Lys Lys Gly Glu Glu Gln Val 515Ser Arg Pro Gly Leu Lys Pro Aap Leu Thr Gly Thr Ser Lys 540Gly Met Ser Arg Pro Gly Leu Lys Pro Aap Leu Thr Gly Thr Ser Lys 530Sec Tyr Val Arg Ser Leu 550<<10> SEQ ID NO 49 <211> LENGTH: 617 <212> TYPE: PRT<113> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polypeptide | Pro | Leu | | Gln | Glu | Сув | Leu | - | Gly | Ser | Thr | Lys | | Сув | Ala | Arg | | | |
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| 435440445Gly ProProIleSerLeuGluArgLeuAspValGlyThrAsnLeuGlyAsnAlaIleAlaLysLeuGluAsnLeuGluSerSerSerSerSerSerSerSerSerSerSerSerGlyLeuGluLeuGluSerSerSerSerSerSerSerSerSerThrSerIleVal495SerThrSerIleVal495SerThrSerIleVal495SerThrSerIleVal495SerIleVal495SerIleVal495SerIleVal495SerIleVal495SerIleVal495SerIleVal495SerIleVal495SerIleVal495SerIleVal495SerIleVal495SerIleVal495SerIleVal495SerIleVal495SerSerIleVal495Ser< | Ala | Asp | His | | Pro | Val | Val | Glu | | Asn | Gly | Val | Thr | | Gln | Val | | | |
| 450 455 460 Asm Ala Ile Ala Lys Leu Glu Asp Ala Lys Glu Leu Leu Glu Ser Ser 465 470 475 475 480 Asp Gln Ile Leu Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 485 Tyr Ile Leu Ile Ala Val Cys Leu Gly Gly Leu Ile Gly Ile Pro Ala 500 505 505 Leu Ile Gly Glu Gln Val 515 500 520 Arg Gly Arg Cys Asn Lys Lys Gly Glu Gln Val 515 525 535 535 540 Ser Tyr Val Arg Ser Leu 540 550 <210> SEQ ID NO 49 <211> LENGTH: 617 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polypeptide | Gly | Ser | | Arg | Tyr | Pro | Asp | | Val | Tyr | Leu | His | | Ile | Asp | Leu | | | |
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535

Met Ser Pro Gln Arg Asp Arg Ile Asn Ala Phe Tyr Lys Asp Asn Pro 1 10 15 Tyr Pro Lys Gly Ser Arg Ile Val Ile Asn Arg Glu His Leu Met Ile 25 Asp Arg Pro Tyr Val Leu Leu Ala Val Leu Phe Val Met Phe Leu Ser 35 40 45 Leu Ile Gly Leu Leu Ala Ile Ala Gly Ile Arg Leu His Arg Ala Ala 50 55 60 Ile Tyr Thr Ala Glu Ile His Lys Ser Leu Ser Thr Asn Leu Asp Val65707580 Thr Asn Ser Ile Glu His Gln Val Lys Asp Val Leu Thr Pro Leu Phe 85 90 95 Lys Ile Ile Gly Asp Glu Val Gly Leu Arg Thr Pro Gln Arg Phe Thr 100 105 110 Asp Leu Val Lys Phe Ile Ser Asp Lys Ile Lys Phe Leu Asn Pro Asp 115 120 125 Arg Glu Tyr Asp Phe Arg Asp Leu Thr Trp Cys Ile Asn Pro Pro Glu130135140 Arg Ile Lys Leu Asp Tyr Asp Gln Tyr Cys Ala Asp Val Ala Ala Glu 145 150 155 160 Glu Leu Met Asn Ala Leu Val Asn Ser Thr Leu Leu Glu Thr Arg Thr 165 175 170 Thr Thr Gln Phe Leu Ala Val Ser Lys Gly Asn Cys Ser Gly Pro Thr 180 185 190 Thr Ile Arg Gly Gln Phe Ser Asn Met Ser Leu Ser Leu Leu Asp Leu 195 200 2.05 Tyr Leu Gly Arg Gly Tyr Asn Val Ser Ser Ile Val Thr Met Thr Ser 215 210 220 Gln Gly Met Tyr Gly Gly Thr Tyr Leu Val Glu Lys Pro Asn Leu Asn 230 235 225 240 Ser Lys Gly Ser Glu Leu Ser Gln Leu Ser Met Tyr Arg Val Phe Glu 245 250 Val Gly Val Ile Arg Asn Pro Gly Leu Gly Ala Pro Val Phe His Met 265 Thr Asn Tyr Phe Glu Gln Pro Val Ser Asn Gly Leu Gly Asn Cys Met 275 280 285 Val Ala Leu Gly Glu Leu Lys Leu Ala Ala Leu Cys His Gly Asp Asp 290 295 300 Ser Ile Ile Ile Pro Tyr Gln Gly Ser Gly Lys Gly Val Ser Phe Gln305310315320 Leu Val Lys Leu Gly Val Trp Lys Ser Pro Thr Asp Met Gln Ser Trp 325 330 335 Val Pro Leu Ser Thr Asp Asp Pro Val Val Asp Arg Leu Tyr Leu Ser 340 345 350 Ser His Arg Gly Val Ile Ala Asp Asn Gln Ala Lys Trp Ala Val Pro 355 360 365 Thr Thr Arg Thr Asp Asp Lys Leu Arg Met Glu Thr Cys Phe Gln Gln 370 375 380 Ala Cys Lys Gly Lys Ile Gln Ala Leu Cys Glu Asn Pro Glu Trp Val 390 400 385 395 Pro Leu Lys Asp Asn Arg Ile Pro Ser Tyr Gly Val Leu Ser Val Asp 405 410 415 Leu Ser Leu Thr Val Glu Leu Lys Ile Lys Ile Ala Ser Gly Phe Gly

| | | | | | | | | | | | _ | con | tin | ued | |
|--|-------------------------|---|---|--------------------------|------------|------------|---------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | | 420 | | | | | 425 | | | | | 430 | | |
| Pro | Leu | 11e 435 | Thr | His | Gly | Ser | Gly 440 | Met | Asp | Leu | Tyr | Lys 445 | Ser | Asn | Суз |
| Asn | Asn 450 | Val | Tyr | Trp | Leu | Thr 455 | Ile | Pro | Pro | Met | Arg 460 | Asn | Leu | Ala | Leu |
| Gly 465 | Val | Ile | Asn | Thr | Leu 470 | Glu | Trp | Ile | Pro | Arg 475 | Phe | Гуз | Val | Ser | Pro 480 |
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| Pro | Thr | Tyr | Leu 500 | Pro | Ala | Glu | Val | Asp 505 | Gly | Aab | Val | Lys | Leu 510 | Ser | Ser |
| Asn | Leu | Val 515 | Ile | Leu | Pro | Gly | Gln 520 | Asp | Leu | Gln | Tyr | Val 525 | Leu | Ala | Thr |
| Tyr | Asp 530 | Thr | Ser | Arg | Val | Glu 535 | His | Ala | Val | Val | Tyr 540 | Tyr | Val | Tyr | Ser |
| Pro 545 | Ser | Arg | Ser | Phe | Ser 550 | Tyr | Phe | Tyr | Pro | Phe 555 | Arg | Leu | Pro | Ile | Lys 560 |
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| Leu | Trp | Cys | Arg 580 | His | Phe | Cys | Val | Leu 585 | Ala | Asp | Ser | Glu | Ser 590 | Gly | Gly |
| Leu | Ile | Thr 595 | His | Ser | Gly | Met | Val 600 | Gly | Met | Gly | Val | Ser 605 | Сув | Thr | Ala |
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| His | Pro | Lys | Gly 20 | Ser | Arg | Ile | Val | Ile 25 | Asn | Arg | Glu | His | Leu 30 | Met | Ile |
| Asp | Arg | Pro 35 | Tyr | Val | Leu | Leu | Ala 40 | Val | Leu | Phe | Val | Met 45 | Phe | Leu | Ser |
| Leu | Ile 50 | Gly | Leu | Leu | Ala | 11e 55 | Ala | Gly | Ile | Arg | Leu 60 | His | Arg | Ala | Ala |
| Ile 65 | Tyr | Thr | Ala | Glu | Ile 70 | His | ГАа | Ser | Leu | Ser 75 | Thr | Asn | Leu | Yab | Val 80 |
| Thr | Asn | Ser | Ile | Glu 85 | His | Gln | Val | Lys | Asp 90 | Val | Leu | Thr | Pro | Leu 95 | Phe |
| Lys | Ile | Ile | Gly 100 | Asp | Glu | Val | Gly | Leu 105 | Arg | Thr | Pro | Gln | Arg 110 | Phe | Thr |
| Asp | Leu | Val 115 | Lys | Phe | Ile | Ser | Asp 120 | Lys | Ile | Lys | Phe | Leu 125 | Asn | Pro | Asp |
| Arg | Glu 130 | Tyr | Asp | Phe | Arg | Asp 135 | Leu | Thr | Trp | Сув | Ile 140 | Asn | Pro | Pro | Glu |
| | | | | | | | | | | | | | | | |
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| | | | | | | | | | | | | 0011 | CIII | | |
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| Thr | Ile | Arg 195 | | Gln | Phe | Ser | Asn 200 | Met | Ser | Leu | Ser | Leu 205 | Leu | Asp | Leu |
| Tyr | Leu 210 | Ser | Arg | Gly | Tyr | Asn 215 | | Ser | Ser | Ile | Val 220 | Thr | Met | Thr | Ser |
| Gln 225 | Gly | Met | Tyr | Gly | Gly 230 | Thr | Tyr | Leu | Val | Glu 235 | | Pro | Asn | Leu | Ser 240 |
| Ser | Lys | Gly | Ser | Glu 245 | | Ser | Gln | Leu | Ser 250 | Met | His | Arg | Val | Phe 255 | Glu |
| Val | Gly | Val | Ile 260 | | Asn | Pro | Gly | Leu 265 | | Ala | Pro | Val | Phe 270 | His | Met |
| Thr | Asn | Tyr 275 | | Glu | Gln | Pro | Val 280 | Ser | Asn | Asp | Phe | Ser 285 | Asn | Cys | Met |
| Val | Ala 290 | Leu | Gly | Glu | Leu | Lys 295 | | Ala | Ala | Leu | Суз 300 | His | Arg | Glu | Asp |
| Ser 305 | Ile | Thr | Ile | Pro | Tyr 310 | Gln | Gly | Ser | Gly | Lys 315 | | Val | Ser | Phe | Gln 320 |
| Leu | Val | Lys | Leu | Gly 325 | | Trp | Lys | Ser | Pro 330 | Thr | Asp | Met | Gln | Ser 335 | Trp |
| Val | Pro | Leu | Ser 340 | Thr | | Asp | | Val 345 | Ile | | Arg | | Tyr 350 | Leu | Ser |
| Ser | His | Arg 355 | | Val | Ile | Ala | Asp 360 | Asn | | Ala | | Trp 365 | Ala | Val | Pro |
| Thr | Thr 370 | Arg | Thr | Asp | Asp | Lys 375 | Leu | Arg | Met | Glu | Thr 380 | Cys | Phe | Gln | Gln |
| Ala 385 | Cys | Гуа | Gly | Lys | Ile 390 | Gln | Ala | Leu | Суз | Glu 395 | Asn | Pro | Glu | Trp | Thr 400 |
| Pro | Leu | Гуз | Asp | Asn 405 | | Ile | Pro | Ser | Tyr 410 | Gly | Val | Leu | Ser | Val 415 | Asp |
| Leu | Ser | Leu | Thr 420 | Val | Glu | Leu | Lya | Ile 425 | | Ile | Val | Ser | Gly 430 | Phe | Gly |
| Pro | Leu | Ile 435 | | His | Gly | Ser | Gly 440 | | Asp | Leu | Tyr | Lys 445 | Ser | Asn | His |
| Asn | Asn 450 | | | | | Thr 455 | | Pro | | | - | | Leu | Ala | Leu |
| Gly 465 | Val | | | | | Glu | | | | | | | Val | Ser | Pro 480 |
| | Leu | Phe | Thr | Val 485 | Pro | Ile | ГЛа | Glu | Ala 490 | Gly | Glu | Asp | Сув | His 495 | Ala |
| Pro | Thr | Tyr | Leu 500 | | Ala | Glu | Val | Asp 505 | | Asp | Val | Lys | Leu 510 | | Ser |
| Asn | Leu | Val 515 | Ile | Leu | Pro | Gly | Gln 520 | Asp | Leu | Gln | Tyr | Val 525 | Leu | Ala | Thr |
| Tyr | Asp 530 | | Ser | Arg | Val | Glu 535 | | Ala | Val | Val | Tyr 540 | | Val | Tyr | Ser |
| | | Arg | Ser | Phe | | Tyr | Phe | Tyr | Pro | | | Leu | Pro | Val | _ |
| 545 Gly | Val | Pro | Ile | | 550 Leu | Gln | Val | Glu | - | 555 Phe | Thr | Trp | Asp | | 560 Lys |
| Leu | Trp | Сув | Arg | 565 His | Phe | Cys | Val | Leu | 570 Ala | Asp | Ser | Glu | Ser | 575 Gly | Gly |
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| ucccagucug accucgacuc | cauccaggcu gaaau | caccc agcgccugaa | cgaaaucgac 420 |
|--|--------------------------|-------------------------|-----------------|
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| accauccagg uuggugccaa | cgacggugaa acuau | cgaua uugauuuaaa | agaaaucage 540 |
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| gcuguaaccg uugauaaaac | uaccuauaaa aaugg | uacag auccuauuac | ageccagage 660 |
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| aaauuuaaag auggucaaua | cuauuuagau guuaa | aggeg gugeuueuge | ugguguuuau 780 |
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| Ser Ser Gly Leu Arg I 35 | le Asn Ser Ala Ly 40 | s Asp Asp Ala Al 45 | a Gly Gln |
| Ala Ile Ala Asn Arg Pi 50 | he Thr Ala Asn Il 55 | e Lys Gly Leu Th: 60 | r Gln Ala |
| Ser Arg Asn Ala Asn A 65 7 | | e Ala Gln Thr Th 75 | r Glu Gly 80 |
| Ala Leu Asn Glu Ile A 85 | sn Asn Asn Leu Gl 90 | n Arg Val Arg Gl | u Leu Ala 95 |
| Val Gln Ser Ala Asn G 100 | ly Thr Asn Ser Gl 105 | n Ser Asp Leu Asj 11 | |

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| |)> SI Ala | | | | Asn | Thr | Asn | Ser | Leu | Ser | Leu | Leu | Thr | Gln | Asn |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
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| Gln | Ala | Glu 115 | Ile | Thr | Gln | Arg | Leu 120 | Asn | Glu | Ile | Asp | Arg 125 | Val | Ser | Gly |
| Gln | Thr 130 | Gln | Phe | Asn | Gly | Val 135 | Lys | Val | Leu | Ala | Gln 140 | Asp | Asn | Thr | Leu |
| Thr 145 | Ile | Gln | Val | Gly | Ala 150 | Asn | Asp | Gly | Glu | Thr 155 | Ile | Asp | Ile | Aab | Leu 160 |
| ГЛЗ | Gln | Ile | Asn | Ser 165 | Gln | Thr | Leu | Gly | Leu 170 | Asp | Thr | Leu | Asn | Val 175 | Gln |
| Gln | Lys | Tyr | Lys 180 | Val | Ser | Asp | Thr | Ala 185 | Ala | Thr | Val | Thr | Gly 190 | Tyr | Ala |
| Asp | Thr | Thr 195 | Ile | Ala | Leu | Asp | Asn 200 | Ser | Thr | Phe | Lys | Ala 205 | Ser | Ala | Thr |
| Gly | Leu 210 | Gly | Gly | Thr | Asp | Gln 215 | Lys | Ile | Asp | Gly | Asp 220 | Leu | Lys | Phe | Asp |
| Asp 225 | Thr | Thr | Gly | ГЛа | Tyr 230 | Tyr | Ala | Гла | Val | Thr 235 | Val | Thr | Gly | Gly | Thr 240 |
| Gly | Lys | Asp | Gly | Tyr 245 | Tyr | Glu | Val | Ser | Val 250 | Asp | Lys | Thr | Asn | Gly 255 | Glu |
| Val | Thr | Leu | Ala 260 | Gly | Gly | Ala | Thr | Ser 265 | Pro | Leu | Thr | Gly | Gly 270 | Leu | Pro |
| Ala | Thr | Ala 275 | Thr | Glu | Asp | Val | ГАа 780 | Asn | Val | Gln | Val | Ala 285 | Asn | Ala | Asp |
| Leu | Thr 290 | Glu | Ala | Lys | Ala | Ala 295 | Leu | Thr | Ala | Ala | Gly 300 | Val | Thr | Gly | Thr |
| Ala 305 | Ser | Val | Val | Lys | Met 310 | Ser | Tyr | Thr | Asp | Asn 315 | Asn | Gly | Lys | Thr | Ile 320 |
| Asp | Gly | Gly | Leu | Ala 325 | Val | Гла | Val | Gly | Asp 330 | Asp | Tyr | Tyr | Ser | Ala 335 | Thr |
| Gln | Asn | Lys | Asp 340 | Gly | Ser | Ile | Ser | Ile 345 | Asn | Thr | Thr | Lys | Tyr 350 | Thr | Ala |
| Asp | Asp | - | | Ser | Lys | Thr | | | Asn | Lys | Leu | - | | Ala | Asp |
| Gly | Гуз | 355 Thr | Glu | Val | Val | Ser | 360 Ile | Gly | Gly | Lys | Thr | 365 Tyr | Ala | Ala | Ser |
| - | 370 | | | | | 375 | | - | - | | 380 | | | | |

Lys Ala Glu Gly His Asn Phe Lys Ala Gln Pro Asp Leu Ala Glu Ala 385 390 395 400

| A | la | Ala | Thr | Thr | Thr 405 | Glu | Asn | Pro | Leu | Gln 410 | Lys | Ile | Asp | Ala | Ala 415 | Leu |
|---|---------------------------------|---|---------------|------------------------------------|--------------------|---------------|------------|-------------|------------|---------------|--------------|-------------|--------------|------------------|------------|------------|
| A | la | Gln | Val | Asp 420 | | Leu | Arg | Ser | Asp 425 | | Gly | Ala | Val | Gln 430 | | Arg |
| P | he | Asn | Ser 435 | | Ile | Thr | Asn | Leu 440 | | Asn | Thr | Val | Asn 445 | | Leu | Thr |
| S | er | Ala 450 | | Ser | Arg | Ile | Glu 455 | | Ser | Asp | Tyr | Ala 460 | Thr | Glu | Val | Ser |
| | sn 65 | | Ser | Arg | Ala | Gln 470 | | Leu | Gln | Gln | Ala 475 | | Thr | Ser | Val | Leu 480 |
| | | Gln | Ala | Asn | Gln 485 | | Pro | Gln | Asn | Val 490 | | Ser | Leu | Leu | Arg 495 | |
| G | ly | Gly | Gly | Ser 500 | Gly | Gly | Gly | Gly | Ser 505 | | Met | Ala | Pro | Asp 510 | | Asn |
| A | la | Asn | Pro 515 | | Ala | Asn | Pro | Asn 520 | | Asn | Pro | Asn | Ala 525 | | Pro | Asn |
| A | la | Asn 530 | | Asn | Ala | Asn | Pro 535 | | Ala | Asn | Pro | Asn 540 | Ala | Asn | Pro | Asn |
| | la 45 | | Pro | Asn | Ala | Asn 550 | | Asn | Ala | Asn | Pro 555 | | Ala | Asn | Pro | Asn 560 |
| | | Asn | Pro | Asn | Ala 565 | | Pro | Asn | Ala | Asn 570 | Pro | Asn | Ala | Asn | Pro 575 | |
| A | la | Asn | Pro | Asn 580 | | Asn | Pro | Asn | Ala 585 | | Pro | Asn | Lys | Asn 590 | | Gln |
| G | ly | Asn | Gly 595 | Gln | Gly | His | Asn | Met 600 | Pro | Asn | Asp | Pro | Asn 605 | Arg | Asn | Val |
| A | ab | Glu 610 | Asn | Ala | Asn | Ala | Asn 615 | Asn | Ala | Val | Lys | Asn 620 | Asn | Asn | Asn | Glu |
| | lu 25 | Pro | Ser | Asp | Lys | His 630 | Ile | Glu | Gln | Tyr | Leu 635 | Lys | Гуз | Ile | Lys | Asn 640 |
| S | er | Ile | Ser | Thr | Glu 645 | Trp | Ser | Pro | Суз | Ser 650 | Val | Thr | Cys | Gly | Asn 655 | Gly |
| I | le | Gln | Val | Arg 660 | Ile | Lys | Pro | Gly | Ser 665 | Ala | Asn | Lys | Pro | Lys 670 | Asp | Glu |
| L | eu | Asp | Tyr 675 | Glu | Asn | Asp | Ile | Glu 680 | Гуз | Ьуз | Ile | Суз | Lys 685 | Met | Glu | Гуз |
| C | Уa | Ser 690 | Ser | Val | Phe | Asn | Val 695 | Val | Asn | Ser | | | | | | |
| | 211 212 213 220 223 | L> LH 2> TY 3> OH 0> FH 3> OY | CATUR THER | I: 69 PRT SM: XE: INF(| 92 Art: DRMA | ific: FION | | - | | 9 0 1y | pepti | ide | | | | |
| | | | EQUER Ala | | | Dara | A ~~~ | 7 1- | 3.00 | Dma | D ~~~ | <u>م</u> ام | A ~~~ | Dme | 7.000 | مام |
| 1 | | | | | 5 | | | | | 10 | | | Asn | | 15 | |
| A | sn | Pro | Asn | Ala 20 | Asn | Pro | Asn | Ala | Asn 25 | Pro | Asn | Ala | Asn | Pro 30 | Asn | Ala |
| A | sn | Pro | Asn 35 | Ala | Asn | Pro | Asn | Ala 40 | Asn | Pro | Asn | Ala | Asn 45 | Pro | Asn | Ala |

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| Asn | Pro 50 | Asn | Ala | Asn | Pro | Asn 55 | Ala | Asn | Pro | Asn | Ala 60 | Asn | Pro | Asn | Ala |
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| Asn 65 | Pro | Asn | Ala | Asn | Pro 70 | Asn | Ala | Asn | Pro | Asn 75 | Ala | Asn | Pro | Asn | Ala 80 |
| Asn | Pro | Asn | Lүз | Asn 85 | Asn | Gln | Gly | Asn | Gly 90 | Gln | Gly | His | Asn | Met 95 | Pro |
| Asn | Asp | Pro | Asn 100 | Arg | Asn | Val | Asp | Glu 105 | Asn | Ala | Asn | Ala | Asn 110 | Asn | Ala |
| Val | Lys | Asn 115 | Asn | Asn | Asn | Glu | Glu 120 | Pro | Ser | Asp | Lya | His 125 | Ile | Glu | Gln |
| Tyr | Leu 130 | Гуа | ГАа | Ile | Lys | Asn 135 | Ser | Ile | Ser | Thr | Glu 140 | Trp | Ser | Pro | Суз |
| Ser 145 | Val | Thr | Cys | Gly | Asn 150 | Gly | Ile | Gln | Val | Arg 155 | Ile | Lys | Pro | Gly | Ser 160 |
| Ala | Asn | Гуз | Pro | Lys 165 | Asp | Glu | Leu | Asp | Tyr 170 | Glu | Asn | Asp | Ile | Glu 175 | Гуа |
| ГАз | Ile | Сув | Lys 180 | Met | Glu | ГАЗ | САа | Ser 185 | Ser | Val | Phe | Asn | Val 190 | Val | Asn |
| Ser | Arg | Pro 195 | Val | Thr | Met | Ala | Gln 200 | Val | Ile | Asn | Thr | Asn 205 | Ser | Leu | Ser |
| Leu | Leu 210 | Thr | Gln | Asn | Asn | Leu 215 | Asn | Гла | Ser | Gln | Ser 220 | Ala | Leu | Gly | Thr |
| Ala 225 | Ile | Glu | Arg | Leu | Ser 230 | Ser | Gly | Leu | Arg | Ile 235 | Asn | Ser | Ala | Lys | Asp 240 |
| Asp | Ala | Ala | Gly | Gln 245 | Ala | Ile | Ala | Asn | Arg 250 | Phe | Thr | Ala | Asn | Ile 255 | Гла |
| Gly | Leu | Thr | Gln 260 | Ala | Ser | Arg | Asn | Ala 265 | Asn | Asp | Gly | Ile | Ser 270 | Ile | Ala |
| Gln | Thr | Thr 275 | Glu | Gly | Ala | Leu | Asn 280 | Glu | Ile | Asn | Asn | Asn 285 | Leu | Gln | Arg |
| Val | Arg 290 | Glu | Leu | Ala | Val | Gln 295 | Ser | Ala | Asn | Ser | Thr 300 | Asn | Ser | Gln | Ser |
| Asp 305 | Leu | Asp | Ser | Ile | Gln 310 | Ala | Glu | Ile | Thr | Gln 315 | Arg | Leu | Asn | Glu | Ile 320 |
| Asp | Arg | Val | Ser | Gly 325 | Gln | Thr | Gln | Phe | Asn 330 | Gly | Val | Lys | Val | Leu 335 | Ala |
| Gln | Asp | Asn | Thr 340 | Leu | Thr | Ile | Gln | Val 345 | Gly | Ala | Asn | Asp | Gly 350 | Glu | Thr |
| Ile | Asp | Ile 355 | Asp | Leu | Lys | Gln | Ile 360 | Asn | Ser | Gln | Thr | Leu 365 | Gly | Leu | Азр |
| Thr | Leu 370 | Asn | Val | Gln | Gln | Lув 375 | Tyr | ГÀЗ | Val | Ser | Asp 380 | Thr | Ala | Ala | Thr |
| Val 385 | Thr | Gly | Tyr | Ala | Asp 390 | Thr | Thr | Ile | Ala | Leu 395 | Asp | Asn | Ser | Thr | Phe 400 |
| Lys | Ala | Ser | Ala | Thr 405 | Gly | Leu | Gly | Gly | Thr 410 | Asp | Gln | Lys | Ile | Asp 415 | Gly |
| Asp | Leu | Гуз | Phe 420 | Asp | Asp | Thr | Thr | Gly 425 | Lys | Tyr | Tyr | Ala | Lys 430 | Val | Thr |
| Val | Thr | Gly 435 | Gly | Thr | Gly | Гуз | Asp 440 | Gly | Tyr | Tyr | Glu | Val 445 | Ser | Val | Asp |
| Lys | Thr 450 | Asn | Gly | Glu | Val | Thr 455 | Leu | Ala | Gly | Gly | Ala 460 | Thr | Ser | Pro | Leu |
| Thr | Gly | Gly | Leu | Pro | Ala | Thr | Ala | Thr | Glu | Asp | Val | Lys | Asn | Val | Gln |

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|------|----------|----|-----|------------|-----|
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|--------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------|--------|--|--|
| | | | | | | | | | | - | con | tin | ued | | | | | |
| 465 | | | | 470 | | | | | 475 | | | | | 480 | | | | |
| Val Ala | Asn | Ala | Asp 485 | Leu | Thr | Glu | Ala | Lys 490 | Ala | Ala | Leu | Thr | Ala 495 | Ala | | | | |
| Gly Val | . Thr | Gly 500 | | Ala | Ser | Val | Val 505 | Lys | Met | Ser | Tyr | Thr 510 | Asp | Asn | | | | |
| Asn Gly | Lys 515 | Thr | Ile | Asp | Gly | Gly 520 | Leu | Ala | Val | Гуз | Val 525 | Gly | Asp | Asp | | | | |
| Tyr Tyr 530 | | Ala | Thr | Gln | Asn 535 | Lys | Asp | Gly | Ser | Ile 540 | Ser | Ile | Asn | Thr | | | | |
| Thr Lys | | Thr | Ala | | Aab | Gly | Thr | Ser | | | Ala | Leu | Asn | | | | | |
| 545 Leu Gly | , Gly | Ala | Asp | 550 Gly | | Thr | Glu | Val | 555 Val | Ser | Ile | Gly | Gly | 560 Lys | | | | |
| Thr Tyr | Ala | Ala | 565 Ser | | Ala | Glu | Glv | 570 His | Asn | Phe | Lvs | Ala | 575 Gln | Pro | | | | |
| _ | | 580 | | - | | | 585 | | | | - | 590 | | | | | | |
| Asp Leu | 595 b | GIu | Ala | Ala | Ala | Thr 600 | Thr | Thr | GIu | Asn | Pro 605 | Leu | GIn | ГЛЗ | | | | |
| Ile Asp 610 | | Ala | Leu | Ala | Gln 615 | Val | Asp | Thr | Leu | Arg 620 | Ser | Asp | Leu | Gly | | | | |
| Ala Val 625 | Gln | Asn | Arg | Phe 630 | | Ser | Ala | Ile | Thr 635 | Asn | Leu | Gly | Asn | Thr 640 | | | | |
| Val Asn | ı Asn | Leu | Thr 645 | Ser | Ala | Arg | Ser | Arg 650 | Ile | Glu | Asp | Ser | Asp 655 | Tyr | | | | |
| Ala Thr | Glu | Val 660 | Ser | Asn | Met | Ser | Arg 665 | Ala | Gln | Ile | Leu | Gln 670 | Gln | Ala | | | | |
| Gly Thr | Ser 675 | Val | Leu | Ala | Gln | Ala 680 | Asn | Gln | Val | Pro | Gln 685 | Asn | Val | Leu | | | | |
| Ser Leu 690 | | Arg | | | | | | | | | | | | | | | | |
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| <210> S <211> L | | | | | | | | | | | | | | | | | | |
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| gagagcu | lacc 1 | ugga | agag | ag ci | ugcu | ccace | c au | cacc | gagg | gcu | accu | gag (| egugo | cugegg | 120 | | | |
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| agegaeg | gcc | cuag | ccug | au c | aaga | ccgaç | g cuợ | ggac | cuga | cca | agago | cgc ı | ıcuga | agagag | 240 | | | |
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| ggagugg | jeca 1 | uuge | uaag | ac c | auca | gacuç | g gaa | aago | gagg | uga | cage | cau d | caaca | aaugee | 420 | | | |
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| geeguge | 999 | agcu | gaag | ga ci | uucg | ugago | c aaq | jaac | cuga | cca | gage | cau 🤇 | caaca | aagaac | 540 | | | |
| aagugeg | jaca 1 | ucga | ugac | cu g | aaga | uggco | c guợ | gagei | uucu | ccc | aguu | caa 🤇 | caga | egguue | 600 | | | |
| cugaacg | ugg | ugag | acagi | uu c | uccg | acaa | g gei | ıgga | auca | cac | cuge | cau 1 | lage | cuggad | 660 | | | |
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| aucaago | uga | ugcu | ggag | aa c | agag | ccauç | g gu | Jcgg: | agaa | agg | gcuu | cgg (| cauco | cugauu | . 780 | | | |
| ggggugu | laug | gaag | cucc | gu g | aucu | acauç | g guợ | gcag | cugc | cca | ucuu | egg (| guga | aucgac | 840 | | | |
| | | | | | | | | | | | | | | | | | | |

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| acacccugcu gga | ucgugaa | ggccgcuccu | ageugeuceg | agaagaaagg | aaacuaugcc | 900 | |
| ugucugcuga gag | aggacca | gggcugguac | ugccagaacg | ccggaagcac | aguguacuau | 960 | |
| cccaacgaga agg | acugega | gaccagaggc | gaccacgugu | ucugegacae | cgcugccgga | 1020 | |
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| cucaaaacag ucu | cugcuga | ucaguuggcg | agagaggagc | aaauugaaaa | ucccagacaa | 300 | |
| ucaagauuug ucu | | | | | | 360 | |
| ggcauugcaa uag | | | | | | 420 | |
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| gcagugagag agc | uaaaaga | auuugugage | aaaaaccuga | cuagugcaau | caacaggaac | 540 | |
| aaaugugaca uug | | | | | | 600 | |
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| cugaugacug aug | cugaguu | ggccagagcu | guaucauaca | ugccaacauc | ugcagggcag | 720 | |
| auaaaacuga ugu | uggagaa | ccgcgcaaug | guaaggagaa | aaggauuugg | aauccugaua | 780 | |
| ggggucuacg gaa | gcucugu | gauuuacaug | guucaauugc | cgaucuuugg | ugucauagau | 840 | |
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| ugecuccuaa gag | aggauca | agggugguau | uguaaaaaug | caggaucuac | uguuuacuac | 960 | |
| ccaaaugaaa aag | acugcga | aacaagaggu | gaucauguuu | uuugugacac | agcagcaggg | 1020 | |
| aucaauguug cug | agcaauc | aagagaaugc | aacaucaaca | uaucuacuac | caacuaccca | 1080 | |
| ugcaaaguca gca | caggaag | acacccuaua | agcaugguug | cacuaucacc | ucucggugcu | 1140 | |
| uugguggcuu gcu | auaaagg | gguaagcugc | ucgauuggca | gcaauugggu | uggaaucauc | 1200 | |
| aaacaauuac cca | aaggcug | cucauacaua | accaaccagg | augcagacac | uguaacaauu | 1260 | |
| gacaauaccg ugu | aucaacu | aagcaaaguu | gaaggugaac | agcauguaau | aaaagggaga | 1320 | |
| | | | | | | | |

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| | 222 | | | | | 500 |
|--|------------|------------|-------------|------------|------|-----|
| | | | -contin | nued | | |
| ccaguuucaa gcaguuuuga | uccaaucaag | uuuccugagg | aucaguucaa | uguugegeuu | 1380 | |
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| ugcaaaguca gcacaggaag | acacccuauc | agcaugguug | cacuaucacc | ucucggugcu | 1140 | |
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| <210> SEQ ID NO 60 | | | | | | |

LENGTH: 1725
<212> TYPE: RNA
<213> ORGANISM: Human respiratory syncytial virus

<400> SEQUENCE: 60

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| uuaaguaaua ucaaggaaaa | | | | - | 300 |
| caagaauuag auaaauauaa | | | | | |
| ccagcagcca acaaucgagc | | | | | 360 |
| aauaccaaaa auaccaaugu | | | | | 420 |
| uuguuaggug uuggaucugc | | | | | 480 |
| gaagggggaag ugaacaaaau | | | | | 540 |
| uuaucaaaug gaguuagugu | | | | | 600 |
| aaacaguugu uaccuauugu | | | | | 660 |
| auagaguucc aacaaaagaa | | | | | 720 |
| gcagguguaa cuacaccugu | aagcacuuau | auguuaacua | auagugaauu | auuaucauua | 780 |
| aucaaugaua ugecuauaac | aaaugaucag | aaaaaguuaa | uguccaacaa | uguucaaaua | 840 |
| guuagacago aaaguuacuc | uaucaugucc | auaauaaagg | aggaagucuu | agcauaugua | 900 |
| guacaauuac cacuauaugg | uguaauagau | acacccuguu | ggaaacugca | cacauceecu | 960 |
| cuauguacaa ccaacacaaa | ggaagggucc | aacaucugcu | uaacaagaac | cgacagagga | 1020 |
| ugguauugug acaaugcagg | aucaguaucu | uucuucccac | aagcugaaac | auguaaaguu | 1080 |
| caaucgaauc ggguauuuug | ugacacaaug | aacaguuuaa | cauuaccaag | ugaaguaaau | 1140 |
| cucugcaaca uugacauauu | caaccccaaa | uaugauugca | aaauuaugac | uucaaaaaca | 1200 |
| gauguaagca geueeguuau | cacaucucua | ggagccauug | ugucaugcua | uggcaaaacu | 1260 |
| aaauguacag cauccaauaa | aaaucguggg | aucauaaaga | cauuuucuaa | cgggugugau | 1320 |
| uauguaucaa auaagggggu | ggauacugug | ucuguaggua | auacauuaua | uuauguaaau | 1380 |
| aagcaagaag gcaaaagucu | cuauguaaaa | ggugaaccaa | uaauaaauuu | cuaugaccca | 1440 |
| uuaguguuce ccucugauga | auuugaugca | ucaauaucuc | aagucaauga | gaagauuaac | 1500 |
| cagageeuag cauuuauueg | uaaauccgau | gaauuauuac | auaauguaaa | ugcugguaaa | 1560 |
| uccaccacaa auaucaugau | aacuacuaua | auuauaguga | uuauaguaau | auuguuauca | 1620 |
| uuaauugcag uuggacugcu | ccuauacugc | aaggccagaa | gcacaccagu | cacacuaagu | 1680 |
| aaggaucaac ugagugguau | aaauaauauu | gcauuuagua | acuga | | 1725 |
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| <212> TYPE: RNA <213> ORGANISM: Human | parainflue | nza virus | | | |
| <400> SEQUENCE: 61 | | | | | |
| augecaauuu caauacuguu | aauuauuaca | accaugauca | uggcaucaca | cugccaaaua | 60 |
| gacaucacaa aacuacagca | | | | | 120 |
| ucacaaaacu ucgaaacaag | | | | | 180 |
| | | | | | |
| aacucuugug gugaccaaca | | | | | 240 |
| ccuuuauaug auggacuaag | auuacagaag | gaugugauag | ugacuaauca | agaauccaau | 300 |
| gaaaacacug aucccagaac | agaacgauuc | uuuggagggg | uaauuggaac | uauugcucua | 360 |
| | | | | | |

563

564

| | | | | -contir | luea | |
|---|------------|-------------|-------------|------------|------------|------|
| ggaguagcaa | ccucagcaca | aauuacagca | gcaguugcuc | ugguugaagc | caagcaggca | 420 |
| agaucagaca | uugaaaaacu | caaggaagca | aucagggaca | caaauaaagc | agugcaguca | 480 |
| guucagageu | cuguaggaaa | uuugauagua | gcaauuaaau | caguccagga | uuaugucaac | 540 |
| aaagaaaucg | ugccaucgau | ugegagaeua | gguugugaag | cagcaggacu | ucaguuaggg | 600 |
| auugcauuaa | cacagcauua | cucagaauua | acaaauauau | uuggugauaa | cauaggaucg | 660 |
| uuacaagaaa | aaggaauaaa | auuacaaggu | auagcaucau | uauaccguac | aaauaucaca | 720 |
| gaaauauuca | caacaucaac | aguugacaaa | uaugauauuu | augaucuauu | auuuacagaa | 780 |
| ucaauaaagg | ugagaguuau | agauguugau | uugaaugauu | acucaauaac | ccuccaaguc | 840 |
| agacucccuu | uauugaccag | acugcugaac | acucaaaucu | acaaaguaga | uuccauauca | 900 |
| uacaauaucc | aaaauagaga | augguauauc | ccucuuccca | gccauaucau | gacgaaaggg | 960 |
| gcauuucuag | guggagcaga | ugucaaagaa | ugcauagaag | cauucagcag | uuauauaugc | 1020 |
| ccuucugauc | caggauuugu | acuaaaccau | gaaauggaga | gcugucuauc | aggaaacaua | 1080 |
| ucccaauguc | caagaaccac | agucacauca | gacauaguuc | cuagguaugc | auuugucaau | 1140 |
| ggaggagugg | uugcgaauug | uauaacaacu | acauguacau | gcaaugguau | cgguaauaga | 1200 |
| aucaaccaac | caccugauca | aggagucaaa | auuauaacac | auaaagaaug | uaauacaaua | 1260 |
| gguaucaacg | gaaugcuauu | caacacaaac | aaagaaggaa | cucuugcauu | cuacacacca | 1320 |
| gacgacauaa | cauuaaacaa | uucuguugca | cuugaucega | uugacauauc | aaucgagcuc | 1380 |
| aacaaggcca | aaucagaucu | ugaggaauca | aaagaaugga | uaagaagguc | aaaucaaaag | 1440 |
| cuagauucua | uuggaaguug | gcaucaaucu | agcacuacaa | ucauaguuau | uuugauaaug | 1500 |
| augauuauau | uguuuauaau | uaauauaaca | auaauuacaa | uugcaauuaa | guauuacaga | 1560 |
| auucaaaaga | gaaaucgagu | ggaucaaaau | gauaageegu | auguauuaac | aaacaag | 1617 |
| <210> SEQ 1 <211> LENG <212> TYPE: <213> ORGAN | TH: 1716 | parainfluer | nza virus 3 | | | |
| <400> SEQUE | ENCE: 62 | | | | | |
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| acagecacue | auggcaacaa | gcucaccaac | aagauaacau | auauauugug | gacgauaacc | 120 |
| cugguguuau | uaucaauagu | cuucaucaua | gugcuaacua | auuccaucaa | aagugaaaag | 180 |
| gcccgcgaau | cauugcuaca | agacauaaau | aaugaguuua | uggaaguuac | agaaaagauc | 240 |
| caaguggcau | cggauaauac | uaaugaucua | auacagucag | gagugaauac | aaggcuucuu | 300 |
| acaauucaga | gucaugucca | gaauuauaua | ccaauaucau | ugacacaaca | aauaucggau | 360 |
| cuuaggaaau | ucauuaguga | aauuacaauu | agaaaugaua | aucaagaagu | gccaccacaa | 420 |
| agaauaacac | augauguggg | uauaaaaccu | uuaaauccag | augauuucug | gagaugcacg | 480 |
| ucuggucuuc | caucuuugau | gaaaacucca | aaaauaagau | uaaugeeggg | accaggauua | 540 |
| uuagcuaugc | caacgacugu | ugauggcugu | gucagaaccc | cguccuuagu | gauaaaugau | 600 |
| cugauuuaug | cuuacaccuc | aaaucuaauu | acucgagguu | gccaggauau | agggaaauca | 660 |
| uaucaaguau | uacagauagg | gauaauaacu | guaaacucag | acuugguacc | ugacuuaaau | 720 |
| ccuaggaucu | cucauaccuu | caacauaaau | gacaauagaa | agucauguuc | ucuagcacuc | 780 |
| cuaaauacag | auguauauca | acuguguuca | accccaaaag | uugaugaaag | aucagauuau | 840 |
| | | | | | | |
| gcaucaucag | gcauagaaga | uauuguacuu | gauauuguca | auuaugaugg | cucaaucucg | 900 |

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| acaacaagau uuaagaauaa uaauauaagu uuugauca | ac cauaugegge auuauaeeea 960 | | | | | | | | | | |
|--|---|--|--|--|--|--|--|--|--|--|--|
| ucuguuggac cagggauaua cuacaaaggc aaaauaau | au uucucgggua uggaggucuu 1020 | | | | | | | | | | |
| gaacauccaa uaaaugagaa ugcaaucugc aacacaac | ug gguguccugg gaaaacacag 1080 | | | | | | | | | | |
| agagacugua aucaagcauc ucauagucca ugguuuuc | ag auagaaggau ggucaacucu 1140 | | | | | | | | | | |
| auaauuguug uugacaaggg cuugaacuca guuccaaa | au ugaagguaug gacgauaucu 1200 | | | | | | | | | | |
| augagacaaa auuacugggg gucagaagga agauuacu | uc uacuagguaa caagaucuac 1260 | | | | | | | | | | |
| auauacacaa gaucuacaag uuggcacagc aaguuaca | au uaggaauaau ugacauuacu 1320 | | | | | | | | | | |
| gacuacagug auauaaggau aaaauggaca uggcauaa | ug ugcuaucaag accaggaaac 1380 | | | | | | | | | | |
| aaugaauguc cauggggaca uucauguccg gauggaug | ua uaacgggagu auauaccgau 1440 | | | | | | | | | | |
| gcauauccac ucaaucccac aggaagcauu guaucauc | ug ucauauugga cucacaaaaa 1500 | | | | | | | | | | |
| ucgagaguca acccagucau aacuuacuca acagcaac | cg aaaggguaaa cgagcuggcu 1560 | | | | | | | | | | |
| aucegaaaca aaacacucue ageuggguae acaacaac | aa gcugcauuac acacuauaac 1620 | | | | | | | | | | |
| aaaggguauu guuuucauau aguagaaaua aaucauaa | aa gcuuaaacac auuucaaccc 1680 | | | | | | | | | | |
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| | eg geaacgaget ggaaaceage oo | | | | | | | | | | |
| acagocacac acggcaacaa gougaccaac aagaucac | | | | | | | | | | | |
| | cu acauccugug gaccaucace 120 | | | | | | | | | | |
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| acagocacao acggoaacaa gougaccaao aagaucac cuggugougo ugagoauogu guucaucauo gugougac | cu acauccugug gaccaucacc 120 ca auagcaucaa gagcgagaag 180 ca uggaagugac cgagaagauc 240 | | | | | | | | | | |
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| acagecaeae aeggeaaeaa geugaeeaae aagaueae euggugeuge ugageauegu guueaueaue gugeugae geeagagaga geeugeugea ggaeaueaae aaegaguu eagguggeea gegaeaaeae eaaegaeeug auceagag | cu acauccugug gaccaucace 120 ca auagcaucaa gagcgagaag 180 ca uggaagugac cgagaagauc 240 cg gegugaacac ceggeugeug 300 ce ugaeccagea gaucagegae 360 | | | | | | | | | | |
| acagecacae aeggeaacaa geugaecaae aagaucae euggugeuge ugageauegu guucaucaue gugeugae geeagagaga geeugeugea ggaeaucaae aaegaguu eagguggeea gegaeaacae caaegaecug auceagag aceauceaga geeaegugea gaacuaeaue ceeaucag | cu acauccugug gaccaucacc 120 ca auagcaucaa gagcgagaag 180 ca uggaagugac cgagaagauc 240 cg gegugaacac ceggeugeug 300 ce ugaeccagea gaucagegae 360 ca accaggaagu geececceag 420 | | | | | | | | | | |
| acagccacac acggcaacaa gcugaccaac aagaucac cuggugcugc ugagcaucgu guucaucauc gugcugac gccagagaga gccugcugca ggacaucaac aacgaguu cagguggcca gcgacaacac caacgaccug auccagagu accauccaga gccacgugca gaacuacauc cccaucag cugcggaagu ucaucagcga gaucaccauc cggaacga | cu acauccugug gaccaucace 120 ca auagcaucaa gagcgagaag 180 ca uggaagugac cgagaagauc 240 cg gegugaacac ceggeugeug 300 ee ugacceagea gaucagegac 360 ca aceaggaagu geeececeag 420 cg acgauuucug gegguguaca 480 | | | | | | | | | | |
| acagecacae aeggeaacaa geugaecaae aagaucae euggugeuge ugageaucgu guucaucaue gugeugae geeagagaga geeugeugea ggaeaucaae aaegaguu eagguggeea gegaeaacae caaegaecug auceagag aceauceaga geeaegugea gaacuaeaue eegaaega eugeggaagu ucaucagega gaucaecaue eggaaega agaaucaece aegaeguggg caucaageee cugaaecee | cu acauccugug gaccaucacc 120 ca auagcaucaa gagcgagaag 180 ca uggaagugac cgagaagauc 240 cg gegugaacac ceggeugeug 300 ce ugaeccagea gaucagegac 360 ca accaggaagu geeeccecag 420 cg acgauuucug gegguguaca 480 ge ugaugecugg ceeuggacug 540 | | | | | | | | | | |
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| acagceacac acggeaacaa geugaceaac aagaucace euggugeuge ugageaucgu guucaucauc gugeugace geeagagaga geeugeugea ggacaucaac aacgaguu cagguggeea gegacaacac caacgaecug auceagag accauceaga geeaegugea gaacuacauc ceeaucaga eugeggaagu ucaucagega gaucaceauc eggaacga agaaucaece acgaeguggg caucaageee cugaaceee ageggeeuge ceageeugau gaagaeceee aagauceg euggeeauge cuaceacagu ggauggeugu gugeggae cugaucuaeg ceuacaecag caaceugauc aceegggg uaecagguge ugeagauegg caucaucaee gugaacude cuugeggauca geeaecug caaceugauc aceegggg | cu acauccugug gaccaucace 120 ca auagcaucaa gagcgagaag 180 ca uggaagugac cgagaagauc 240 cg gcgugaacac ccggcugcug 300 cc ugacccagca gaucagcgac 360 ca accaggaagu gccccccag 420 cg acgauuucug gcgguguaca 480 gc ugaugccugg cccuggacug 540 cc ccagccucgu gaucaacgau 600 cu gccaggauau cggcaagagc 660 cg accuggugcc cgaccugaac 720 aa agagcugcag ccuggcucug 780 gg uggacgagag aagcgacuac 640 | | | | | | | | | | |
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| gacuacagog acaucoggau caaguggaco uggcacaaog ugougagoag acooggoaac | 1380 |
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| agecagaacu ucgagacacg cuaccugauc cugagecuga uccecaagau cgaggacage | 180 |
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| ecccuguacg acggccugcg gcugcagaaa gacgugaucg ugaccaacca ggaaagcaac | 300 |
| gagaacaceg acceeeggae egagagauue uueggeggeg ugaueggeae aauegeeeug | 360 |
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| gagaucuuca ccaccagcac cguggauaag uacgacaucu acgaccugcu guucaccgag | 780 |
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| uacaacauce agaacegega gugguacaue ceucugeeca gecacauuau gaccaaggge | 960 |
| gccuuucugg gcggagccga cgugaaagag ugcaucgagg ccuucagcag cuacaucugc | 1020 |
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| gauaaaacuu ggeeuagg | cc aauugauguu | ucuaaggcug | acgguauuau | auacccucaa | 180 |
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| uuuguagcua acuauucu | ca ggacgucaaa | caguuugcua | auggguuugu | cguccguaua | 360 |
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| uauuauucug augaugge | | | | | 1980 |
| gucaucuaug auaaagaa | | | | | 2040 |
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571

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572

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573

574

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| uauuauucug | augauggcaa | cuacuacugu | uugegugeuu | guguuagugu | uccuguuucu | 1980 |
| gucaucuaug | auaaagaaac | uaaaacccac | gcuacucuau | uugguagugu | ugcaugugaa | 2040 |
| cacauuucuu | cuaccauguc | ucaauacucc | cguucuacgc | gaucaaugcu | uaaacggcga | 2100 |
| gauucuacau | auggeeeeeu | ucagacaccu | guugguugug | uccuaggacu | uguuaauucc | 2160 |
| ucuuuguucg | uagaggacug | caaguugccu | cuuggucaau | cucucugugc | ucuuccugac | 2220 |
| acaccuagua | cucucacacc | ucgcagugug | cgcucuguuc | caggugaaau | gcgcuuggca | 2280 |
| uccauugcuu | uuaaucaucc | uauucagguu | gaucaacuua | auaguaguua | uuuuaaauua | 2340 |
| aguauaccca | cuaauuuuuc | cuuuggugug | acucaggagu | acauucagac | aaccauucag | 2400 |
| | | | | | | |

575

576

_

| aaaguuacug uugauuguaa acaguacguu ugcaaugguu uccagaagug ugagcaauua | 2460 |
|---|------|
| cugegegagu auggeeaguu uuguuceaaa auaaaceagg cucuceaugg ugeeaauuua | 2520 |
| cgccaggaug auucuguacg uaauuuguuu gcgagcguga aaagcucuca aucaucuccu | 2580 |
| aucauaccag guuuuggagg ugacuuuaau uugacacuuc uggaaccugu uucuauaucu | 2640 |
| acuggcaguc guagugcacg uagugcuauu gaggauuugc uauuugacaa agucacuaua | 2700 |
| gcugauccug guuauaugca agguuacgau gauugcaugc agcaaggucc agcaucagcu | 2760 |
| cgugaucuua uuugugcuca auauguggcu gguuacaaag uauuaccucc ucuuauggau | 2820 |
| guuaauaugg aageegegua uacuucaucu uugeuuggea geauageagg uguuggeugg | 2880 |
| acugcuggcu uauccuccuu ugcugcuauu ccauuugcac agaguaucuu uuauagguua | 2940 |
| aacgguguug gcauuacuca acagguucuu ucagagaacc aaaagcuuau ugccaauaag | 3000 |
| uuuaaucagg cucugggagc uaugcaaaca ggcuucacua caacuaauga agcuuuucag | 3060 |
| aagguucagg augcugugaa caacaaugca caggcucuau ccaaauuagc uagcgagcua | 3120 |
| ucuaauacuu uuggugcuau uuccgccucu auuggagaca ucauacaacg ucuugauguu | 3180 |
| cucgaacagg acgeecaaau agacagacuu auuaauggee guuugacaae acuaaaugeu | 3240 |
| uuuguugcac agcagcuugu ucguuccgaa ucagcugcuc uuuccgcuca auuggcuaaa | 3300 |
| gauaaaguca augagugugu caaggcacaa uccaagcguu cuggauuuug cggucaaggc | 3360 |
| acacauauag uguccuuugu uguaaaugee eeuaauggee uuuacuucau geauguuggu | 3420 |
| uauuacccua gcaaccacau ugagguuguu ucugcuuaug gucuuugcga ugcagcuaac | 3480 |
| ccuacuaauu guauageeee uguuaaugge uacuuuauua aaacuaauaa cacuaggauu | 3540 |
| guugaugagu ggucauauac uggcucgucc uucuaugcac cugagcccau uaccucccuu | 3600 |
| aauacuaagu auguugcacc acaggugaca uaccaaaaca uuucuacuaa ccucccuccu | 3660 |
| ccucuucucg gcaauuccac cgggauugac uuccaagaug aguuggauga guuuuucaaa | 3720 |
| aauguuagca ccaguauacc uaauuuuggu ucccuaacac agauuaauac uacauuacuc | 3780 |
| gaucuuaccu acgagauguu gucucuucaa caaguuguua aagcccuuaa ugagucuuac | 3840 |
| auagaccuua aagagcuugg caauuauacu uauuacaaca aauggeegug guacauuugg | 3900 |
| canadanarca andendadea adandeeana denenanded acaneanean sendadeade | 3960 |
| acnàànnànà àcacaaacnà nanàààaaaa cunsaànàna ancànnànnà nàanaàanac | 4020 |
| gaggaauacg accucgagcc gcauaagguu cauguucacu aa | 4062 |
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| cuccegeugg gacagueecu gugugegeug ceugacaeue euageaeueu gaceceaege | 120 |
| uccgugcggu cggugccugg cgaaaugcgg cuggccucca ucgccuucaa ucacccaauc | 180 |
| caaguggauc agcugaauag cucguauuuc aagcugucca uccccacgaa cuucucguuc | 240 |
| ggggucaccc aggaguacau ccagaccaca auucagaagg ucaccgucga uugcaagcaa | 300 |
| uacgugugca acggcuucca gaagugcgag cagcugcuga gagaauacgg gcaguuuugc | 360 |
| agcaagauca accaggegeu geauggageu aacuugegee aggaegaeue egugegeaac | 420 |
| | |

578

| cucuuugeeu eugugaague aucceaguee ucceeaauea uccegggauu eggaggggae | 480 |
|---|------|
| uucaaccuga cccuccugga gcccgugucg aucagcaccg guagcagauc ggcgcgcuca | 540 |
| gccauugaag aucuucuguu cgacaagguc accaucgccg auccgggcua caugcaggga | 600 |
| uacgacgacu guaugcagca gggaccagcc uccgcgaggg accucaucug cgcgcaauac | 660 |
| guggeegggu acaaagugeu geeueeueug auggauguga acauggagge egeuuauaeu | 720 |
| nedneeende neddenenan edeeddedna ddanddaeed eeddeendne eneennedee | 780 |
| gcuauccccu uugcacaauc cauuuucuac cggcucaacg gcgugggcau uacucaacaa | 840 |
| guccugucgg agaaccagaa guugaucgca aacaaguuca aucaggcccu gggggccaug | 900 |
| cagacuggau ucacuacgac uaacgaagcg uuccagaagg uccaggacgc ugugaacaac | 960 |
| aacgeecagg egeucucaaa geuggeeuee gaacucagea acaecuuegg ageeaucage | 1020 |
| gcaucgaucg gugacauaau ucageggeug gaegugeugg ageaggaege ceagauegae | 1080 |
| cgccucauca acggacggcu gaccaccuug aaugccuucg uggcacaaca gcugguccgg | 1140 |
| agegaaucag eggeacuuue egeceaacue gecaaggaca aagucaaega augegugaag | 1200 |
| geecagueea agaggueegg uuueugeggu caaggaacee auauugugue euueguegug | 1260 |
| aacgcgccca acggucugua cuuuaugcac gucggcuacu acccgagcaa ucauaucgaa | 1320 |
| guggugueeg eeuaeggeeu gugegaugee geuaaceeea euaacuguau ugeeecugug | 1380 |
| aacggauauu uuauuaagac caacaacacc cgcauugugg acgaaugguc auacaccggu | 1440 |
| ucguccuucu acgegeeega geecaucaeu ucaeugaaca eeaaauaegu ggeueegeaa | 1500 |
| gugaccuace agaacaucue caccaauuug eegeegeege ugeueggaaa cageacegga | 1560 |
| auugauuuco aagaugaacu ggacgaauuo uucaagaacg uguccacuuc cauucccaac | 1620 |
| uucggaagee ugacacagau caacaceace cuucucgaee ugaceuacga gaugeugage | 1680 |
| cuucaacaag uggucaaggc ccugaacgag agcuacaucg accugaagga gcugggcaac | 1740 |
| uauaccuacu acaacaagug geeggacaag auugaggaga uucuguegaa aaucuaecae | 1800 |
| auugaaaacg agaucgccag aaucaagaag cuuaucggcg aagcc | 1845 |
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| agenandndd acdndddeec cdanadednd aadneedeen dnanedaadn ddacaneead | 120 |
| cagaccuuuu ucgacaagac cuggeecaga eecauegaeg ugueeaagge egaeggeaue | 180 |
| aucuauccac aaggeeggae cuacageaae aucaeeauua ecuaeeaggg ecuguuccea | 240 |
| uaucaaggeg accaeggega uauguaegug uaeueugeeg geeaegeeae | 300 |
| ccccagaaac uguucguggc caacuacagc caggacguga agcaguucgc caacggcuuc | 360 |
| gucgugcgga uuggcgccgc ugccaauagc accggcacag ugaucaucag ccccagcacc | 420 |
| agegeeacea uceggaagau cuaceeegee uucaugeugg geageueegu gggeaauuue | 480 |
| agegaeggea agaugggeeg guueuueaae eacaeeeugg ugeugeugee egauggeugu | 540 |
| ggcacacugc ugagagccuu cuacugcauc cuggaaccca gaagcggcaa ccacugcccu | 600 |
| | |

579

580

| | | | | -contir | nued | | |
|------------|------------|------------|------------|------------|------------|------|--|
| gccggcaaua | gcuacaccag | cuucgccacc | uaccacacac | ccgccaccga | uugcuccgac | 660 | |
| ggcaacuaca | accggaacgc | cagccugaac | agcuucaaag | aguacuucaa | ccugcggaac | 720 | |
| ugcaccuuca | uguacaccua | caauaucacc | gaggacgaga | uccuggaaug | guucggcauc | 780 | |
| acccagaccg | cccagggcgu | gcaccuguuc | agcagcagau | acguggaccu | guacggcggc | 840 | |
| aacauguucc | aguuugccac | ccugcccgug | uacgacacca | ucaaguacua | cagcaucauc | 900 | |
| ccccacagca | uccgguccau | ccagagegae | agaaaagccu | gggccgccuu | cuacguguac | 960 | |
| aagcugcagc | cccugaccuu | ccugcuggac | uucagcgugg | acggcuacau | cagacgggcc | 1020 | |
| aucgacugcg | gcuucaacga | ccugagecag | cugcacugcu | ccuacgagag | cuucgacgug | 1080 | |
| gaaageggeg | uguacagegu | guccageuuc | gaggccaagc | cuageggeag | cgugguggaa | 1140 | |
| caggcugagg | gcguggaaug | cgacuucagc | ccucugcuga | gcggcacccc | uccccaggug | 1200 | |
| uacaacuuca | agcggcuggu | guucaccaac | ugcaauuaca | accugaccaa | gcugcugagc | 1260 | |
| cuguucuccg | ugaacgacuu | caccuguagc | cagaucagee | cugccgccau | ugccagcaac | 1320 | |
| ugcuacagca | gccugauccu | ggacuacuuc | agcuacecce | ugagcaugaa | guccgaucug | 1380 | |
| agegugueeu | ccgccggacc | caucagecag | uucaacuaca | agcagagcuu | cagcaacccu | 1440 | |
| accugccuga | uucuggccac | cgugececae | aaucugacca | ccaucaccaa | gccccugaag | 1500 | |
| uacagcuaca | ucaacaagug | cagcagacug | cuguccgacg | accggaccga | agugeceeag | 1560 | |
| cucgugaacg | ccaaccagua | cagececuge | guguccaucg | ugeccageae | cgugugggag | 1620 | |
| gacggcgacu | acuacagaaa | gcagcugagc | ccccuggaag | gcggcggaug | gcugguggcu | 1680 | |
| ucuggaagca | caguggccau | gaccgagcag | cugcagaugg | gcuuuggcau | caccgugcag | 1740 | |
| uacggcaccg | acaccaacag | cgugugceec | aagcuggaau | ucgccaauga | caccaagauc | 1800 | |
| gccagccagc | ugggaaacug | cguggaauac | ucccuguaug | gcguguccgg | acggggggug | 1860 | |
| uuccagaauu | gcacagcagu | gggagugcgg | cagcagagau | ucguguacga | ugccuaccag | 1920 | |
| aaccucgugg | gcuacuacag | cgacgacggc | aauuacuacu | gccugcgggc | cugugugucc | 1980 | |
| gugecegugu | ccgugaucua | cgacaaagag | acaaagaccc | acgccacacu | guucggeucc | 2040 | |
| guggccugcg | agcacaucag | cuccaccaug | agccaguacu | cccgcuccac | ccgguccaug | 2100 | |
| cugaagcgga | gagauagcac | cuacggcccc | cugcagacac | cugugggaug | ugugeuggge | 2160 | |
| cucgugaaca | geucceuguu | uguggaagau | ugcaagcugc | cccugggcca | gagecugugu | 2220 | |
| gcccugccag | auaccccuag | cacccugacc | ccuagaagcg | ugegeueugu | gcccggcgaa | 2280 | |
| augeggeugg | ccucuaucgc | cuucaaucac | cccauccagg | uggaccagcu | gaacuccagc | 2340 | |
| uacuucaagc | ugagcauccc | caccaacuuc | agcuucggcg | ugacccagga | guacauccag | 2400 | |
| accacaaucc | agaaagugac | cguggacugc | aagcaguacg | ugugcaacgg | cuuucagaag | 2460 | |
| ugegaacage | ugeugegega | guacggccag | uucugcagca | agaucaacca | ggeccugcac | 2520 | |
| ggegecaace | ugagacagga | ugacagcgug | cggaaccugu | ucgecagegu | gaaaagcagc | 2580 | |
| caguccagcc | ccaucauccc | uggcuucggc | ggcgacuuua | accugacccu | gcuggaaccu | 2640 | |
| guguccauca | gcaccggcuc | cagaagegee | agaucegeea | ucgaggaccu | gcuguucgac | 2700 | |
| aaagugacca | uugccgaccc | cggcuacaug | cagggcuacg | acgauugcau | gcagcagggc | 2760 | |
| ccagccagcg | ccagggaucu | gaucugugee | caguaugugg | ccggcuacaa | ggugeugeee | 2820 | |
| | | | uacaccucca | | | 2880 | |
| | | | uuugeegeea | | | 2940 | |
| | | | | _ | | | |
| uucuaccggc | ugaacggcgu | gggcaucaca | caacaggugc | ugagegagaa | ecagaageug | 3000 | |

581

aucgecaaca aguuuaacea ggeaeuggge geeaugeaga eeggeuueae eaceaceaae

gaggeeuuca gaaaggugea ggaegeegug aacaacaaeg eecaggeueu gageaageug

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3060

3120

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583

584

| agauuaaggg ggugauuguc caccggcuag agggggucuc guacaacaua ggcucucaag | 1020 |
|--|---|
| agugguauac cacugugccc aaguauguug caacccaagg guaccuuauc ucgaauuuug | 1080 |
| augagucauc auguacuuuc augccagagg ggacugugug cagccaaaau gccuuguacc | 1140 |
| cgaugaguee ucugeueeaa gaaugeeuee gggggueeae caagueeugu geueguaeae | 1200 |
| ucguauccgg gucuuuuggg aaccgguuca uuuuaucaca agggaaccua auagccaauu | 1260 |
| gugcaucaau ucuuuguaag uguuacacaa cagguacgau uauuaaucaa gacccugaca | 1320 |
| agauccuaac auacauugcu gccgaucgcu gcccgguagu cgaggugaac ggcgugacca | 1380 |
| uccaagucgg gagcaggagg uauccagacg cuguguacuu gcacagaauu gaccucgguc | 1440 |
| cucccauauc auuggagagg uuggacguag ggacaaaucu ggggaaugca auugccaaau | 1500 |
| uggaggauge caaggaauug uuggaaucau eggaceagau auugagaagu augaaagguu | 1560 |
| uaucgagcac uagcauaguc uacauccuga uugcagugug ucuuggaggg uugauaggga | 1620 |
| uccccacuuu aauauguugc ugcagggggc guuguaacaa aaagggagaa caaguuggua | 1680 |
| ugucaagacc aggccuaaag ccugaccuua caggaacauc aaaauccuau guaagaucgc | 1740 |
| uuugaugaua auaggeugga geeueggugg eeaageuueu ugeeeeuugg geeueeeeee | 1800 |
| ageeccuccu ceecuuccug cacceguace ceeguggucu uugaauaaag ucugaguggg | 1860 |
| cggc | 1864 |
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| gcaagcuaca aaguuaugac ucguuccage caucaaucau uagucauaaa auuaaugcee | |
| | 120 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc | 120 180 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua | 120 180 240 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggccg | 120 180 240 300 |
| gcaagcuaca aaguuaugac ucguuccage caucaaucau uagucauaaa auuaaugeee aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugea cuuaaugeaa ugacceagaa cauaaggeeg guucagageg uagcuucaag uaggagacac aagagauuug egggaguagu ceuggeaggu | 120 180 240 300 360 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggccg guucagagcg uagcuucaag uaggagacac aagagauuug cgggaguagu ccuggcaggu geggeccuag guguugecac ageugcucag auaacageeg geauugcacu ucacegguce | 120 180 240 300 360 420 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggccg guucagagcg uagcuucaag uaggagacac aagagauuug cgggaguagu ccuggcaggu geggeccuag guguugccac agcugcucag auaacagceg gcauugcacu ucaceggucc augcugaacu cucaggecau cgacaaucug agagegagec uggaaacuac uaaucaggca | 120 180 240 300 360 420 480 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggccg guucagagcg uagcuucaag uaggagacac aagagauuug cgggaguagu ccuggcaggu gcggcccuag guguugccac agcugcucag auaacagccg gcauugcacu ucaccggucc augcugaacu cucaggccau cgacaaucug agagcgagcc uggaaacuac uaaucaggca auugaggcaa ucagacaagc agggcaggag augauauugg cuguucaggg uguccaagac | 120 180 240 300 360 420 480 540 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggccg guucagagcg uagcuucaag uaggagacac aagagauuug cgggaguagu ccuggcaggu geggeecuag guguugceac ageugcucag auaacageeg gcauugcacu ucaecgguce augcugaacu cucaggecau cgacaaucug agagegagec uggaaacuac uaaucaggca auugaggcaa ucagacaage agggcaggag augauauugg cuguucaggg uguccaagac uacaucaaua augageugau acegucuaug aaccageuau cuugugaucu aaucggucag | 120 180 240 300 360 420 480 540 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugcoc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggcog guucagagog uagcuucaag uaggagacac aagagauuug cgggaguagu ccuggcaggu goggcccuag guguugccac agcugcucag auaacagcog gcauugcacu ucaccgguco augcugaacu cucaggccau cgacaaucug agagcgagcc uggaaacuac uaaucaggca auugaggcaa ucagacaagc agggcaggag augauauugg cuguucaggg uguccaagac uacaucaaua augagcugau accgucuaug aaccagcuau cuugugaucu aaucggucag aagcucgggc ucaaauugcu uagauacuau acagaaaucc ugucauuauu uggccccagc | 120 180 240 300 360 420 480 540 600 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggeeg guucagageg uagcuucaag uaggagacac aagagauuug egggaguagu ecuggeaggu geggeecuag guguugeeac ageugeucag auaacageeg geauugeacu ucaeegguee augeugaacu cucaggeeau egacaaucug agagegagee uggaaacuac uaaucaggea auugaggeaa ucagacaage agggeaggag augauauugg euguucaggg ugueeaagae uacaucaaua augageugau acegueuaug aaceageuau euugugaucu aaueggueag aageueggge ucaaauugeu uagauacuau acagaaauee ugucauuauu uggeeecage cuaegggaee ecauaucuge ggagauaueu auceaggeuu ugaguuauge acuuggagga | 120 180 240 300 360 420 480 540 600 660 720 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggccg guucagagcg uagcuucaag uaggagacac aagagauuug cgggaguagu ccuggcaggu gcggcccuag guguugccac agcugcucag auaacagccg gcauugcacu ucaccggucc augcugaacu cucaggccau cgacaaucug agagcgagcc uggaaacuac uaaucaggca auugaggcaa ucagacaagc agggcaggag augauauugg cuguucaggg uguccaagac uacaucaaua augagcugau accgucuaug aaccagcuau cuugugaucu aaucggucag aagcucgggc ccauaucug ggagauaucu auccaggcuu ugaguuaug acuuggagga gauaucaaua agguguuaga aaagcucgga uacaguggag gcgauuuacu aggcaucuua | 120 180 240 300 360 420 480 540 600 660 720 780 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugcoo aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggcog guucagagog uagcuucaag uaggagacac aagagauuug cgggaguagu ccuggcaggu geggeccuag guguugecac ageugeucag auaacageeg geauugeacu ucaecegguee augeugaacu cucaggecau egacaaucug agagegagee uggaaacuac uaaucaggea auugaggeaa ucagacaage agggeaggag augauauugg euguucaggg ugueeaagae uacaucaaua augageugau acegueuaug aaceageuau cuugugaucu aaucaggeag aageueggge ucaaauugeu uagauacuau acagaaauee ugueauuauu uggeeeceage cuaeggggaee ecauaucuge ggagauaucu auceaggeuu ugaguuauge acuuggagga gauaucaaua agguguuaga aaageuegga uacaguggag gegauuuacu aggeaucuua gagageagag gaauaaagge ueggauaacu caeguegaea cagagueeua cuucauague | 120 180 240 300 360 420 480 540 600 660 720 780 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggeeg guucagageg uagcuucaag uaggagacac aagagauuug egggaguagu ecuggeaggu geggeecuag guguugeeac ageugeucag auaacageeg geauugeacu ucaeegguee augeugaacu cucaggeeau egacaaucug agagegagee uggaaacuac uaaucaggea auugaggeaa ucagacaage agggeaggag augauauugg euguucaggg ugueeaagae uacaucaaua augageugau acegueuaug aaceageuau euugugaucu aaueggueag aageueggge ucaaauugeu uagauacuau acegaaauee ugueauuauu uggeeecage cuaegggaee ecauaucuge ggagauaueu auceaggeuu ugaguuauge acuuggagga gauaucaaua agguguuaga aaageuegga uacaguggag gegauuuacu aggeaucuua gagageagag gaauaaagge ueggauaacu caeguegaea cagagueeua euucauague cucaguauag ecuaucegae geugueegag auuaaggggg ugauugueea eeggeuagag | 120 180 240 300 360 420 480 540 600 660 720 780 840 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggccg guucagagcg uagcuucaag uaggagacac aagagauuug cgggaguagu ccuggcaggu gcggcccuag guguugccac agcugcucag auaacagccg gcauugcacu ucaccggucc augcugaacu cucaggccau cgacaaucug agagcgagcc uggaaacuac uaaucaggca auugaggcaa ucagacaagc agggcaggag augauauugg cuguucaggg uguccaagac uacaucaaua augagcugau accgucuaug aaccagcuau cuugugaucu aaucggucag gauaucaaua agguguuaga aaagcucgga uacaguggag gcgauuuacu aggccaucuua gagagcagag gaauaaaggc ucggauaacu cacgucgaca cagaguccua cuucauguc cucaguauag ccuauccgac gcuguccgag auuaaggggg ugauugucca ccggcuagag gagagcagag gaauaaaggc ucggauaacu cacgucgaca cagaguccua cuucauaguc cucaguauag ccuauccgac gcuguccgag auuaaggggg ugauugucca ccggcuagag gagggucucgu acaacauagg cucucaagag ugguauacca cugugcccaa guauguaga | 120 180 240 300 360 420 480 540 600 660 720 780 840 900 |
| gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggccg guucagagcg uagcuucaag uaggagacac aagagauuug cgggaguagu ccuggcaggu gcggcccuag guguugccac agcugcucag auaacagceg gcauugcacu ucaccggucc augcugaacu cucaggccau cgacaaucug agagcgagcc uggaaacuac uaaucaggca auugaggcaa ucagacaage agggcaggag augauauugg cuguucaggg uguccaagac uacaucaaua augagcugau accgucuaug aaccagcuau cuugugaucu aaucggucag aagcucggge ucaaauugeu uagauacuau acagaaauee ugucauuauu uggecccage cuacggggace ccauaucuge ggagauaucu auccaggcuu ugaguuauge acuuggagga gauaucaaua agguguuaga aaagcucgga uacaguggag gcgauuuacu aggcaucuua gagagcagag gaauaaagge ucggauaacu cacgucgaca cagaguccua cuucauaguc cucaguauag ccuaucegae gcugucegag auuaaggggg ugauugucea ceggcuagag gagggucucgu acaacauagg cucucaagag ugguauacea cugugcceaa guauguugea acccaagggu accuuaucue gaauuuugau gagucaucau guacuucau gccagagggg | 120 180 240 300 360 420 480 540 600 660 720 780 840 900 960 1020 |

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| uuaucacaag | ggaaccuaau | agccaauugu | gcaucaauuc | uuuguaagug | uuacacaaca | 1200 |
|-------------|------------|------------|------------|------------|-------------|------|
| gguacgauua | uuaaucaaga | cccugacaag | auccuaacau | acauugcugc | cgaucgeuge | 1260 |
| ccgguagucg | aggugaacgg | cgugaccauc | caagucggga | gcaggaggua | uccagacgcu | 1320 |
| guguacuugc | acagaauuga | ccucgguccu | cccauaucau | uggagagguu | ggacguaggg | 1380 |
| acaaaucugg | ggaaugcaau | ugccaaauug | gaggaugcca | aggaauuguu | ggaaucaucg | 1440 |
| gaccagauau | ugagaaguau | gaaagguuua | ucgagcacua | gcauagucua | cauccugauu | 1500 |
| gcaguguguc | uuggaggguu | gauagggauc | cccacuuuaa | uauguugcug | caggggggcgu | 1560 |
| uguaacaaaa | agggagaaca | aguugguaug | ucaagaccag | gccuaaagcc | ugaccuuaca | 1620 |
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LENGTH: 1925
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 71

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| auucauuggg gcaaucucuc | uaagauaggg | guaguaggaa | uaggaagugc | aagcuacaaa | 180 |
| guuaugacuc guuccagcca | ucaaucauua | gucauaaaau | uaaugeecaa | uauaacucuc | 240 |
| cucaauaacu gcacgagggu | agagauugca | gaauacagga | gacuacuaag | aacaguuuug | 300 |
| gaaccaauua gggaugcacu | uaaugcaaug | acccagaaca | uaaggeeggu | ucagagegua | 360 |
| gcuucaagua ggagacacaa | gagauuugeg | ggaguagucc | uggcaggugc | ggeecuaggu | 420 |
| guugecacag cugeucagau | aacagcegge | auugcacuuc | accgguccau | gcugaacucu | 480 |
| caggecaucg acaaucugag | agegageeug | gaaacuacua | aucaggcaau | ugaggcaauc | 540 |
| agacaagcag ggcaggagau | gauauuggcu | guucagggug | uccaagacua | caucaauaau | 600 |
| gagcugauac cgucuaugaa | ccagcuaucu | ugugaucuaa | ucggucagaa | gcucgggcuc | 660 |
| aaauugcuua gauacuauac | agaaauccug | ucauuauuug | gccccagccu | acgggacccc | 720 |
| auaucugcgg agauaucuau | ccaggcuuug | aguuaugcac | uuggaggaga | uaucaauaag | 780 |
| guguuagaaa agcucggaua | caguggaggc | gauuuacuag | gcaucuuaga | gagcagagga | 840 |
| auaaaggcuc ggauaacuca | cgucgacaca | gaguccuacu | ucauaguccu | caguauagee | 900 |
| uauccgacgc uguccgagau | uaaggggggug | auuguccacc | ggcuagaggg | ggucucguac | 960 |
| aacauaggcu cucaagagug | guauaccacu | gugeccaagu | auguugcaac | ccaaggguac | 1020 |
| cuuaucucga auuuugauga | gucaucaugu | acuuucaugc | cagaggggac | ugugugcagc | 1080 |
| caaaaugeeu uguaceegau | gaguccucug | cuccaagaau | gccuccgggg | guccaccaag | 1140 |
| uccugugcuc guacacucgu | auccgggucu | uuugggaacc | gguucauuuu | aucacaaggg | 1200 |
| aaccuaauag ccaauugugc | aucaauucuu | uguaaguguu | acacaacagg | uacgauuauu | 1260 |
| aaucaagacc cugacaagau | ccuaacauac | auugeugeeg | aucgcugccc | gguagucgag | 1320 |
| gugaacggcg ugaccaucca | aguegggage | aggagguauc | cagacgcugu | guacuugcac | 1380 |
| agaauugaee ueggueeuee | cauaucauug | gagagguugg | acguagggac | aaaucugggg | 1440 |
| aaugcaauug ccaaauugga | ggaugccaag | gaauuguugg | aaucaucgga | ccagauauug | 1500 |

| -continu | |
|----------|--|

| | 30/ | | | | | 200 | |
|--|--------------------------|--------------------------|------------|-------------|--------------|-----|--|
| | | | -contir | nued | | | |
| agaaguauga aagguuuauc | gagcacuagc | auagucuaca | uccugauugc | agugugucuu | 1560 | | |
| gaggguuga uagggauccc | cacuuuaaua | uguugcugca | ggggggguug | uaacaaaaag | 1620 | | |
| gagaacaag uugguauguc | aagaccaggc | cuaaagccug | accuuacagg | aacaucaaaa | 1680 | | |
| iccuauguaa gaucgcuuug | augauaauag | gcuggagccu | cgguggccaa | geuueuugee | 1740 | | |
| ccuugggccu cccccagce | | | | | 1800 | | |
| auaaagucug agugggcggc | aaaaaaaaaa | aaaaaaaaaa | aaaaaaaaaa | aaaaaaaaaa | 1860 | | |
| aaaaaaaaaa aaaaaaaaaaa | aaaaaaaaaa | aaaaaaaaaa | aaaaaaaaaa | aaaaaaaaaaa | 1920 | | |
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| uauucaugge aguacuguua | | | | | 180 | | |
| ucucuaagau agggggggggaa | | | | | 240 | | |
| gccaucaauc auuagucaua | | | | | 300 | | |
| ggguagggau ugcagaauac | | | | | 360 | | |
| cacuuaaugc aaugacccag | | | | | 420 | | |
| acaagagauu ugegggaguu | | | | | 480 | | |
| aaauaacagc cgguauugca | _ | | - | - | 540 | | |
| ugagagegag ceuagaaacu | | | | | 600 | | |
| agaugauauu ggcuguucag | | | | _ | 660 | | |
| ugaaucaacu aucuugugau | | | | | 720 | | |
| auacagaaau ccugucauua | | | | | 780 | | |
| cuauccaggc uuugagcuau | | | | | 840 | | |
| gauacagugg aggugaucua | | | | | 900 | | |
| cucacgucga cacagagucc | | | | | 960 | | |
| agauuaaggg ggugauuguc | | | | | 1020 | | |
| agugguauac cacugugeee | | | | | 1080 | | |
| augagucauc augcacuuuc | | | | | 1140 | | |
| cgaugagucc ucugcuccaa | | | | | 1200 | | |
| ucguauccgg gucuuucggg | aaccgguuca | uuuuaucaca | ggggaaccua | auagccaauu | 1260 | | |
| gugcaucaau ccuuugcaag | uguuacacaa | caggaacaau | cauuaaucaa | gacccugaca | 1320 | | |
| | | acceaauaau | cgaggugaau | ggcgugacca | 1380 | | |
| agauccuaac auacauugcu | gccgaucacu | 333-35 | | | | | |
| agauccuaac auacauugcu uccaagucgg gagcaggagg | | | gcacaggauu | gaccucgguc | 1440 | | |
| | uauccggacg | cuguguacuu | | | 1440 1500 | | |
| nccaadncdd dadcaddadd | uauccggacg uuggacguag | cuguguacuu ggacaaaucu | ggggaaugca | auugcuaagu | | | |

| - | COL | ιt | 1 | n | u | ed. |
|---|-----|----|---|---|---|-----|

| uccccgcuuu aauauguugc ugcagggggc guuguaacaa gaagggagaa caaguuggua | 1680 |
|---|------|
| ugucaagacc aggccuaaag ccugaucuua caggaacauc aaaauccuau guaaggucac | 1740 |
| nendandana anaddendda deeneddndd eesadennen ndeecenndd deeneesees | 1800 |
| agecceucen cecenneend caccednace ceednadnen nndaanaaad nendaandda | 1860 |
| cggc | 1864 |
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| gcaagcuaca aaguuaugac ucguuccage caucaaucau uagucauaaa guuaaugcee | 180 |
| aauauaacuc uccucaacaa uugcacgagg guagggauug cagaauacag gagacuacug | 240 |
| agaacaguuc uggaaccaau uagagaugca cuuaaugcaa ugacccagaa uauaagaccg | 300 |
| guncagagna nadenneaad naddagaeae aadadannna caddaadnnan cenddeaddn | 360 |
| geggeeeuag geguugeeae ageugeueaa auaacageeg guauugeaeu ueaceaguee | 420 |
| augeugaaeu eucaageeau egacaaueug agagegagee uagaaaeuae uaaueaggea | 480 |
| auugaggcaa ucagacaagc agggcaggag augauauugg cuguucaggg uguccaagac | 540 |
| uacaucaaua augagcugau accgucuaug aaucaacuau cuugugauuu aaucggccag | 600 |
| aagcuaggge ucaaauugeu cagauacuau acagaaauee ugucauuauu uggeeecage | 660 |
| uuaegggaee ceauaueuge ggagauaueu auceaggeuu ugageuauge geuuggagga | 720 |
| gauaucaaua agguguugga aaagcucgga uacaguggag gugaucuacu gggcaucuua | 780 |
| gagagcagag gaauaaagge ceggauaacu caeguegaca cagaguecua cuucauugua | 840 |
| cucaguauag ccuaucegac gcuaucegag auuaaggggg ugauugueca eeggeuagag | 900 |
| ggggucucgu acaacauagg cucucaagag ugguauacca cugugcccaa guauguugca | 960 |
| acccaagggu accuuaucuc gaauuuugau gagucaucau gcacuuucau gccagagggg | 1020 |
| acugugugea gecagaauge cuuguaceeg augagueeue ugeueeaaga augeeueegg | 1080 |
| ggguccacua aguccuguge ucguacacue guaucegggu cuuucgggaa cegguucauu | 1140 |
| uuaucacagg ggaaccuaau agccaauugu gcaucaaucc uuugcaagug uuacacaaca | 1200 |
| ggaacaauca uuaaucaaga cccugacaag auccuaacau acauugcuge cgaucacuge | 1260 |
| ccddnddarcd addndaandd cdndaccanc caadnoddda dcaddadda nccddacdon | 1320 |
| guguacuugo acaggauuga ccucgguccu cccauaucuu uggagagguu ggacguaggg | 1380 |
| acaaaucugg ggaaugcaau ugcuaaguug gaggaugcca aggaauuguu ggagucaucg | 1440 |
| gaccagauau ugaggaguau gaaagguuua ucgagcacua guauaguuua cauccugauu | 1500 |
| geagugugue uuggaggauu gauagggaue eeegeuuuaa uauguugeug cagggggegu | 1560 |
| uguaacaaga agggagaaca aguugguaug ucaagaccag gccuaaagcc ugaucuuaca | 1620 |
| ggaacaucaa aauccuaugu aaggucacuc uga | 1653 |
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<210> SEQ ID NO 74

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<210> SEQ ID NO 76 <211> LENGTH: 1854 <212> TYPE: RNA

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595

<213> ORGANISM: Artificial Sequence

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US 10,702,600 B1

596

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597

598

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| auguuucuga | gcuugaucgg | auugeuggea | auugcaggca | uuagacuuca | ucgggcagec | 240 |
| aucuacaccg | cggagaucca | uaaaagccuc | aguaccaauc | uggaugugac | uaacuccauc | 300 |
| gagcaucagg | ucaaggacgu | gcugacacca | cucuuuaaaa | ucaucgggga | ugaagugggc | 360 |
| cugagaacac | cucagagauu | cacugaccua | gugaaauuca | ucucggacaa | gauuaaauuc | 420 |
| cuuaauccgg | auagggagua | cgacuucaga | gaucucacuu | ggugcaucaa | cccgccagag | 480 |
| aggaucaaac | uagauuauga | ucaauacugu | gcagaugugg | cugcugaaga | gcucaugaau | 540 |
| gcauugguga | acucaacucu | acuggagacc | agaacaacca | cucaguuccu | ageugueuca | 600 |
| aagggaaacu | gcucagggcc | cacuacaauc | agaggucaau | ucucaaacau | guegeuguee | 660 |
| uuguuggacu | uguacuuagg | ucgagguuac | aaugugucau | cuauagucac | uaugacaucc | 720 |
| cagggaaugu | augggggaac | cuaccuaguu | gaaaagccua | aucugaacag | caaaggguca | 780 |
| gaguugucac | aacugagcau | guaccgagug | uuugaaguag | gugugaucag | aaacccgggu | 840 |
| uuggggggcuc | cgguguucca | uaugacaaac | uauuuugagc | aaccagucag | uaauggucuc | 900 |
| ggcaacugua | ugguggcuuu | gggggageuc | aaacucgcag | cccuuuguca | cggggacgau | 960 |
| ucuaucauaa | uucccuauca | gggaucaggg | aaagguguca | gcuuccagcu | cgucaagcug | 1020 |
| ggugucugga | aauccccaac | cgacaugcaa | uccugggucc | ccuuaucaac | ggaugaucca | 1080 |
| gugguagaca | ggcuuuaccu | cucaucucac | agagguguca | ucgcugacaa | ucaagcaaaa | 1140 |
| ugggcugucc | cgacaacacg | aacagaugac | aaguugegaa | uggagacaug | cuuccagcag | 1200 |
| gcguguaaag | guaaaaucca | ageacucuge | gagaaucccg | aguggguacc | auugaaggau | 1260 |
| aacaggauuc | cuucauacgg | gguccugucu | guugaucuga | gucugacggu | ugagcuuaaa | 1320 |
| aucaaaauug | cuucgggauu | cgggccauug | aucacacacg | gcucagggau | ggaccuauac | 1380 |
| aaauccaacu | gcaacaaugu | guauuggcug | acuauuccgc | caaugagaaa | ucuagccuua | 1440 |
| ggcguaauca | acacauugga | guggauaccg | agauucaagg | uuagucccaa | ccucuucacu | 1500 |
| gucccaauua | aggaagcagg | cgaagacugc | caugececaa | cauaccuacc | ugcggaggug | 1560 |
| gacggugaug | ucaaacucag | uuccaaccug | gugauucuac | cuggucaaga | ucuccaauau | 1620 |
| guuuuggcaa | ccuacgauac | cuccaggguu | gagcaugcug | ugguuuauua | cguuuacagc | 1680 |
| ccaageegeu | cauuuucuua | cuuuuauccu | uuuagguugc | cuauaaaggg | ggueecaaue | 1740 |
| gaacuacaag | uggaaugcuu | cacaugggau | caaaaacucu | ggugeeguea | cuucugugug | 1800 |
| cuugeggaeu | cagaauccgg | uggacuuauc | acucacucug | ggaugguggg | caugggaguc | 1860 |
| agcugcacag | cuacccggga | agauggaacc | aaucgcagau | aaugauaaua | ggeuggagee | 1920 |
| ucgguggeca | agcuucuugc | cccuugggcc | uccccccage | cccuccuccc | cuuccugcac | 1980 |
| ccguaccccc | guggucuuug | aauaaagucu | gagugggcgg | caaaaaaaaa | aaaaaaaaaa | 2040 |
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence

<223> OTHER INFORMATION: Synthetic Polynucleotide

<220> FEATURE:

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| aaagaagagu aagaagaaau | auaagagcca | ccaugucacc | acaacgagac | cggauaaaug | 120 |
| ccuucuacaa agacaacccc | cauccuaagg | gaaguaggau | aguuauuaac | agagaacauc | 180 |
| uuaugauuga uagaccuuau | guuuugcugg | cuguucuauu | cgucauguuu | cugagcuuga | 240 |
| ucggguugcu agccauugca | ggcauuagac | uucaucgggc | agccaucuac | accgcagaga | 300 |
| uccauaaaag ccucagcacc | aaucuggaug | uaacuaacuc | aaucgagcau | cagguuaagg | 360 |
| acgugeugae accaeucuue | aagaucaucg | gugaugaagu | gggcuugagg | acaccucaga | 420 |
| gauucacuga ccuagugaag | uucaucucug | acaagauuaa | auuccuuaau | ccggacaggg | 480 |
| aauacgacuu cagagaucuc | acuuggugua | ucaacccgcc | agagagaauc | aaauuggauu | 540 |
| augaucaaua cugugcagau | guggeugeug | aagaacucau | gaaugcauug | gugaacucaa | 600 |
| cucuacugga gaccagggca | accaaucagu | uccuagcugu | cucaaaggga | aacugcucag | 660 |
| ggcccacuac aaucagaggc | caauucucaa | acaugucgcu | gucccuguug | gacuuguauu | 720 |
| uaagucgagg uuacaaugug | ucaucuauag | ucacuaugac | aucccaggga | auguacgggg | 780 |
| gaacuuaccu aguggaaaag | ccuaaucuga | gcagcaaagg | gucagaguug | ucacaacuga | 840 |
| gcaugcaccg aguguuugaa | guagguguua | ucagaaaucc | ggguuugggg | gcuccgguau | 900 |
| uccauaugac aaacuaucuu | gagcaaccag | ucaguaauga | uuucagcaac | ugcauggugg | 960 |
| cuuuggggga gcucaaguuc | gcageccucu | gucacaggga | agauucuauc | acaauucccu | 1020 |
| aucagggauc agggaaaggu | gucagcuucc | agcuugucaa | gcuagguguc | uggaaauccc | 1080 |
| caaccgacau gcaauccugg | gucccccuau | caacggauga | uccagugaua | gacaggcuuu | 1140 |
| accucucauc ucacagaggo | guuaucgeug | acaaucaagc | aaaaugggcu | gucccgacaa | 1200 |
| cacggacaga ugacaaguug | cgaauggaga | caugcuucca | gcaggcgugu | aaggguaaaa | 1260 |
| uccaagcacu uugcgagaau | cccgagugga | caccauugaa | ggauaacagg | auuccuucau | 1320 |
| acggggucuu gucuguugau | cugagucuga | caguugagcu | uaaaaucaaa | auuguuucag | 1380 |
| gauucgggcc auugaucaca | cacgguucag | ggauggaccu | auacaaaucc | aaccacaaca | 1440 |
| auauguauug geugaeuaue | ccgccaauga | agaaccuggc | cuuaggugua | aucaacacau | 1500 |
| uggaguggau accgagauuc | aagguuaguc | ccaaccucuu | cacuguucca | auuaaggaag | 1560 |
| caggcgagga cugccaugec | ccaacauacc | uaccugcgga | gguggauggu | gaugucaaac | 1620 |
| ucaguuccaa ucuggugauu | cuaccugguc | aagaucucca | auauguucug | gcaaccuacg | 1680 |
| auacuuccag aguugaacau | gcuguaguuu | auuacguuua | cageccaage | cgcucauuuu | 1740 |
| cuuacuuuua uccuuuuagg | uugccuguaa | ggggggueee | cauugaauua | caaguggaau | 1800 |
| gcuucacaug ggaccaaaaa | cucuggugee | gucacuucug | ugugeuugeg | gacucagaau | 1860 |
| cugguggaca uaucacucac | ucugggaugg | ugggcauggg | agucagcugc | acagecacue | 1920 |
| gggaagaugg aaccagccgc | agauagugau | aauaggcugg | agccucggug | gecaageuuc | 1980 |
| uugeeeeuug ggeeueeeee | cagececuce | uccccuuccu | gcacccguac | ccccgugguc | 2040 |
| uuugaauaaa gucugagugg | gegge | | | | 2065 |
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| <210> SEQ ID NO 79 | | | | | |

<210> SEQ ID NO 79 <211> LENGTH: 1854 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide

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| aguaggauag uuauuaacag agaacaucuu augauugaua gaccuuaugu uuugcuggcu | 120 |
| guucuauucg ucauguuucu gagcuugauc ggguugcuag ccauugcagg cauuagacuu | 180 |
| caucgggcag ccaucuacac cgcagagauc cauaaaagcc ucagcaccaa ucuggaugua | 240 |
| acuaacucaa ucgagcauca gguuaaggac gugcugacac cacucuucaa gaucaucggu | 300 |
| gaugaagugg gcuugaggac accucagaga uucacugacc uagugaaguu caucucugac | 360 |
| aagauuaaau uccuuaaucc ggacagggaa uacgacuuca gagaucucac uugguguauc | 420 |
| aacccgccag agagaaucaa auuggauuau gaucaauacu gugcagaugu ggcugcugaa | 480 |
| gaacucauga augcauuggu gaacucaacu cuacuggaga ccagggcaac caaucaguuc | 540 |
| cuageugueu caaagggaaa cugeucaggg eecacuacaa ucagaggeea auucucaaac | 600 |
| auguegeugu eecuguugga cuuguauuua aguegagguu acaaugugue aucuauague | 660 |
| acuaugacau eecagggaau guacgggggga acuuaccuag uggaaaagee uaaucugage | 720 |
| agcaaagggu cagaguuguc acaacugagc augcaccgag uguuugaagu agguguuauc | 780 |
| agaaauccgg guuugggggc uccgguauuc cauaugacaa acuaucuuga gcaaccaguc | 840 |
| aguaaugauu ucagcaacug caugguggcu uugggggagc ucaaguucgc agcccucugu | 900 |
| cacagggaag auucuaucac aauucccuau cagggaucag ggaaaggugu cagcuuccag | 960 |
| cuugucaage uaggugucug gaaauceeca acegacauge aauceugggu eeceeuauca | 1020 |
| acggaugauc cagugauaga caggcuuuac cucucaucuc acagaggegu uaucgcugac | 1080 |
| aaucaagcaa aaugggcugu ceegacaaca eggacagaug acaaguugeg aauggagaca | 1140 |
| ugcuuccago aggoguguaa ggguaaaauo caagoacuuu gogagaauoo ogaguggaca | 1200 |
| ccauugaagg auaacaggau uccuucauac ggggucuugu cuguugaucu gagucugaca | 1260 |
| guugagcuua aaaucaaaau uguuucagga uucgggccau ugaucacaca cgguucaggg | 1320 |
| auggaccuau acaaauccaa ccacaacaau auguauugge ugacuaucce gccaaugaag | 1380 |
| aaccuggccu uagguguaau caacacauug gaguggauac cgagauucaa gguuaguccc | 1440 |
| aaccucuuca cuguuccaau uaaggaagca ggcgaggacu gccaugcccc aacauaccua | 1500 |
| ccugcggagg uggaugguga ugucaaacuc aguuccaauc uggugauucu accuggucaa | 1560 |
| gaucuccaau auguucuggc aaccuacgau acuuccagag uugaacaugc uguaguuuau | 1620 |
| uacguuuaca geecaageeg cucauuuucu uacuuuuaue cuuuuagguu geeuguaagg | 1680 |
| ggggucccca uugaauuaca aguggaaugc uucacauggg accaaaaacu cuggugccgu | 1740 |
| cacuucugug ugcuugegga cucagaaucu gguggacaua ucacucacuc ugggauggug | 1800 |
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603

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604

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| auguuucuga gcuugaucgg guugcuagee auugcaggea uuagacuuca ucgggeagee | 240 |
| aucuacaceg cagagaucea uaaaageeue ageaceaaue uggauguaae uaaeueaaue | 300 |
| gagcaucagg uuaaggacgu gcugacacca cucuucaaga ucaucgguga ugaagugggc | 360 |
| uugaggacac cucagagauu cacugaccua gugaaguuca ucucugacaa gauuaaauuc | 420 |
| cuuaaucegg acagggaaua cgacuucaga gaucucacuu gguguaucaa ceegecagag | 480 |
| agaaucaaau uggaunauga ucaanacugu gcagaugugg cugcugaaga acucaugaau | 540 |
| gcauugguga acucaacucu acuggagacc agggcaacca aucaguuccu agcugucuca | 600 |
| aagggaaacu geucagggee cacuacaauc agaggeeaau ucucaaacau guegeuguee | 660 |
| cuguuggacu uguauuuaag ucgagguuac aaugugucau cuauagucac uaugacaucc | 720 |
| cagggaaugu acgggggaac uuaccuagug gaaaagccua aucugagcag caaaggguca | 780 |
| gaguugucac aacugagcau gcaccgagug uuugaaguag guguuaucag aaauccgggu | 840 |
| uugggggcuc cgguauucca uaugacaaac uaucuugagc aaccagucag uaaugauuuc | 900 |
| adcaacudca udduddcuuu dddddadcuc aaduucdcad cccucuduca cadddaadau | 960 |
| ucuaucacaa uucccuauca gggaucaggg aaagguguca gcuuccagcu ugucaagcua | 1020 |
| ggugucugga aauccecaac egacaugeaa ueeuggguee eecuaucaac ggaugaucea | 1080 |
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| cuugeggaeu cagaaucugg uggacauauc acucacucug ggaugguggg caugggague | 1860 |
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| ccguaccocc guggucuuug aauaaagucu gagugggcgg caaaaaaaaa aaaaaaaaa | 2040 |
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606

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| aaacuaccua | uaaaaauggu | acagauccua | uuacageeca | gagcaauacu | gauauccaaa | 720 |
| cugcaauugg | cgguggugca | acgggggguua | cugggggcuga | uaucaaauuu | aaagaugguc | 780 |
| aauacuauuu | agauguuaaa | ggcggugcuu | cugcuggugu | uuauaaagcc | acuuaugaug | 840 |
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| aggguguuga | uacgaccaca | guugeggeue | aacuugcugc | agcagggguu | acuggegeeg | 1020 |
| auaaggacaa | uacuagecuu | guaaaacuau | cguuugagga | uaaaaacggu | aagguuauug | 1080 |
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| ucccaguccg | cacugggcac | ugcuaucgag | cguuugucuu | ccggucugcg | uaucaacage | 120 |
| gcgaaagacg | augeggeagg | acaggegauu | gcuaaceguu | uuaccgcgaa | caucaaaggu | 180 |
| cugacucagg | cuucceguaa | cgcuaacgac | gguaucucca | uugegeagae | cacugaaggc | 240 |
| acaciidaaca | | | | | | |
| gogougunog | aaaucaacaa | caaccugcag | egugugegug | aacuggcggu | ucagucugcq | 300 |
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| -00110 | . mueu |

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609

610

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| caggceggua | ccuccguucu | ggcgcaggc | g aaccagguu | c egcaaaacgu | ccucucuuua | 1560 |
| cugeguugau | aauaggcugg | agccucggu | g gecaugeuu | c uugeeeeuug | ggeeucceec | 1620 |
| cageceeuce | uccccuuccu | gcacccgua | e ecceguggu | c uuugaauaaa | gucugagugg | 1680 |
| gcggcaaaaa | aaaaaaaaaa | aaaaaaaaa | a aaaaaaaaa | a aaaaaaaaaa | aaaaaaaaaa | 1740 |
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| Glu Gly Tyr 35 | Leu Ser V | al Leu Arg 40 | Thr Gly Tr | p Tyr Thr As 45 | n Val Phe | |
| Thr Leu Glu 50 | Val Gly A | sp Val Glu 55 | Asn Leu Th | r Cys Ser As 60 | p Gly Pro | |
| Ser Leu Ile 65 | - | lu Leu Asp 0 | Leu Thr Ly 75 | s Ser Ala Le | u Arg Glu 80 | |
| Leu Lys Thr | Val Ser A 85 | la Asp Gln | Leu Ala Ar 90 | g Glu Glu Gl | n Ile Glu 95 | |
| Asn Pro Gly | Ser Gly S 100 | er Phe Val | Leu Gly Al 105 | a Ile Ala Le 11 | - | |
| Ala Ala Ala 115 | | al Thr Ala 120 | Gly Val Al | a Ile Cys Ly 125 | s Thr Ile | |
| Arg Leu Glu 130 | Ser Glu V | al Thr Ala 135 | Ile Asn As | n Ala Leu Ly 140 | s Lys Thr | |
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| Ala | Val | Arg | Glu | Leu 165 | Lys | Asp | Phe | Val | Ser 170 | Lys | Asn | Leu | Thr | Arg 175 | Ala |
| Leu | Asn | Lys | Asn 180 | Lys | Cys | Asp | Ile | Asp 185 | Asp | Leu | Lys | Met | Ala 190 | Val | Ser |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser |
| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Азр |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 |
| Ile | Lys | Leu | Met | Leu 245 | Glu | Asn | Arg | Ala | Met 250 | Val | Arg | Arg | Lys | Gly 255 | Phe |
| Gly | Ile | Leu | Сув 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu | Pro | 11e 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Сув | Trp | Ile 285 | Val | ГАа | Ala |
| Ala | Pro 290 | Ser | Cys | Ser | Glu | Lys 295 | Lys | Gly | Asn | Tyr | Ala 300 | Cys | Leu | Leu | Arg |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Cys | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro | Asn | Glu | ГЛа | Asp 325 | Сув | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Сув 335 | Asp |
| Thr | Ala | Ala | Gly 340 | Ile | Asn | Val | Ala | Glu 345 | Gln | Ser | Lys | Glu | Cys 350 | Asn | Ile |
| Asn | Ile | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Cys | Lys | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Сув |
| Tyr 385 | Гуз | Gly | Val | Ser | Сув 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| Lys | Gln | Leu | Asn | Lys 405 | Gly | Сув | Ser | Tyr | 11e 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr | Val | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly |
| Glu | Gln | His 435 | Val | Ile | Гуз | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| Ile | Lys 450 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Asn | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Asn | Ile | Glu | | Ser 470 | Gln | Ala | Leu | | Asp 4 75 | Gln | Ser | Asn | Arg | Ile 480 |

Glu Asn II Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser

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Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile

| | | | | | | | | | | | - | con | tin | ued | |
|--------------------------------------|----------------------------------|--------------------------------|--------------------------|--------------|------------|------------|------------|------------|------------|------------|------------|--------------|------------|------------|--------------|
| 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| Lys | Gln | Leu | Asn | Lys 405 | Gly | Сув | Ser | Tyr | 11e 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr | Val | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly |
| Glu | Gln | His 435 | Val | Ile | Гла | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| | Lys 450 | Phe | Pro | Glu | His | Gln 455 | Trp | His | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Asn | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| | Ser | Ser | Åla | Glu 485 | | Gly | Asn | Thr | Gly 490 | | Ile | Ile | Val | Ile 495 | |
| Leu | Ile | Ala | Val 500 | | Gly | Ser | Ser | Met 505 | | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | | | Thr | Lys | гуз | | | Gly | Ala | Pro | | | Leu | Ser |
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| | | EQUEN | | | 17-7 | 710 | 71.0 | Dhe | Cor | T | T en | T 1 o | The se | Dmo | 6 1 m |
| nec 1 | Ser | тр | гув | 5 5 | vai | те | тте | Pne | ser 10 | Leu | Leu | IIe | III | Pro 15 | GIN |
| His | Glγ | Leu | Lуя 20 | Glu | Ser | Tyr | Leu | Glu 25 | Glu | Ser | Сүз | Ser | Thr 30 | Ile | Thr |
| 31u | Gly | T yr 35 | Leu | Ser | Val | Leu | Arg 40 | Thr | Gly | Trp | Tyr | Thr 45 | Asn | Val | Phe |
| | Leu 50 | Glu | Val | Gly | Asp | Val 55 | Glu | Asn | Leu | Thr | Суз 60 | Ser | Asp | Gly | Pro |
| Ser 65 | Leu | Ile | ГЛа | Thr | Glu 70 | Leu | Asp | Leu | Leu | Lys 75 | Ser | Ala | Leu | Arg | Glu 80 |
| Leu | Гуз | Thr | Val | Ser 85 | Ala | Asp | Gln | Leu | Ala 90 | Arg | Glu | Glu | Gln | Ile 95 | Glu |
| Asn | Pro | Gly | Ser 100 | Gly | Ser | Phe | Val | Leu 105 | Gly | Ala | Ile | Ala | Leu 110 | Gly | Val |
| Ala | Ala | Ala 115 | | Ala | Val | Thr | Ala 120 | | Val | Ala | Ile | Ala 125 | | Thr | Ile |
| | Leu 130 | | Ser | Glu | Val | Thr 135 | | Ile | Asn | Asn | Ala 140 | | Lys | Lys | Thr |
| Asn | | Ala | Val | Ser | | | Gly | Asn | Gly | | | Val | Leu | Ala | |
| 145 Ala | Val | Arg | Glu | | 150 Lys | Asp | Phe | Val | | 155 Lys | Asn | Leu | Thr | Arg | 160 Ala |
| Ile | Asn | Lys | Asn | 165 Lys | Cys | Asp | Ile | Pro | 170 Asp | Leu | Lys | Met | Ala | 175 Val | Ser |
| | | - | 180 | - | - | - | | 185 | _ | | - | | 190 | | |
| Phe | aer | GIN 195 | riie | ASU | чтд | чтд | 200 | ьeu | ASU | val | var | Arg 205 | GIN | FIIG | ser |
| Asp | Asn | Ala | Gly | Ile | Thr | Pro | Ala | Ile | Ser | Leu | Asp | Leu | Met | Thr | Asp |

| | | | | | | | | | | | - | con | tin | ued | |
|------------------------------|------------|---------------------------------|-----------------------------|------------|------------|------------|------------|---------------|------------|------------|------------|-------------------|------------|------------|-------------------|
| | 210 | | | | | 215 | | | | | 220 | | | | |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 |
| Ile | Lys | Leu | Met | Leu 245 | Glu | Asn | Arg | Ala | Met 250 | Val | Arg | Arg | Lys | Gly 255 | Phe |
| Gly | Ile | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu | Pro | Ile 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Сув | Trp | Ile 285 | Val | ГЛа | Ala |
| Ala | Pro 290 | Ser | САа | Ser | Glu | Lys 295 | ГАа | Gly | Asn | Tyr | Ala 300 | Суз | Leu | Leu | Arg |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Cys | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro | Asn | Glu | Lys | Asp 325 | Cys | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Cys 335 | Asp |
| Thr | Ala | Ala | Gly 340 | Ile | Asn | Val | Ala | Glu 345 | Gln | Ser | ГЛа | Glu | Сув 350 | Asn | Ile |
| Asn | Ile | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Сүз | Lys | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Суз |
| Tyr 385 | Гла | Gly | Val | Ser | Сув 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| ГЛЗ | Gln | Leu | Asn | Lys 405 | Gly | Cys | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr | Val | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly |
| Glu | Gln | His 435 | Val | Ile | Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| Ile | Lys 450 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Asn | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lys 515 | Lys | Thr | Lys | Lys | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| His | Gly | Leu | Lys 20 | Glu | Ser | Tyr | Leu | Glu 25 | Glu | Ser | Сүз | Ser | Thr 30 | Ile | Thr |
| Glu | Gly | Tyr | Leu | Ser | Val | Leu | Arg | Thr | Gly | Trp | Tyr | Thr | Asn | Val | Phe |

| Thr | Leu 50 | Glu | Val | Gly | Asp | Val 55 | Glu | Asn | Leu | Thr | Суз 60 | Ser | Asp | Gly | Pro | |
|------------|------------|------------|------------|------------|------------|--------------------|-------------------|------------|------------|------------|------------|------------|------------|------------|-------------------|--|
| Ser 65 | Leu | Ile | Lys | Thr | Glu 70 | Leu | Asp | Leu | Leu | Lys 75 | Ser | Ala | Leu | Arg | Glu 80 | |
| Leu | Lys | Thr | Val | Ser 85 | Ala | Asp | Gln | Leu | Ala 90 | Arg | Glu | Glu | Gln | Ile 95 | Glu | |
| Asn | Pro | Gly | Ser 100 | | Ser | Phe | Val | Leu 105 | Gly | Ala | Ile | Ala | Leu 110 | Gly | Val | |
| Ala | Ala | Ala 115 | Ala | Ala | Val | Thr | Ala 120 | | Val | Ala | Ile | Ala 125 | Lys | Thr | Ile | |
| Arg | Leu 130 | Glu | Ser | Glu | Val | Thr 135 | Ala | Ile | Asn | Asn | Ala 140 | Leu | Lys | Lys | Thr | |
| Asn 145 | Glu | Ala | Val | Ser | Thr 150 | Leu | Gly | Asn | Gly | Val 155 | Arg | Val | Leu | Ala | Thr 160 | |
| Ala | Val | Arg | Glu | Leu 165 | Lys | Аар | Phe | Val | Ser 170 | ГАЗ | Asn | Leu | Thr | Arg 175 | Ala | |
| Ile | Asn | Lys | Asn 180 | ГАЗ | Суз | Asp | Ile | Pro 185 | Asp | Leu | Lys | Met | Ala 190 | Val | Ser | |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser | |
| Asp | Asn 210 | Ala | Gly | Ile | Thr | P ro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp | |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 | |
| | - | | | 245 | | | - | | 250 | | - | - | - | Gly 255 | | |
| Gly | Ile | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln | |
| Leu | Pro | Ile 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Суз | Trp | Ile 285 | Val | Гүз | Ala | |
| Ala | Pro 290 | Ser | САа | Ser | Glu | Lys 295 | гуа | Gly | Asn | Tyr | Ala 300 | Суз | Leu | Leu | Arg | |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 | |
| Pro | Asn | Glu | Lys | Asp 325 | Суз | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Cys 335 | Asp | |
| Thr | Ala | | - | Ile | | | Ala | | | | - | Glu | - | Asn | Ile | |
| Asn | Ile | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Суз | Гуз | Val | Ser | Thr 365 | Gly | Arg | His | |
| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Сүз | |
| Tyr 385 | Lys | Gly | Val | Ser | Cys 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 | |
| Lys | Gln | Leu | Asn | Lys 405 | Gly | Сув | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp | |
| Thr | Val | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly | |
| Glu | Gln | His 435 | Val | Ile | Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro | |
| Ile | Lys 450 | Phe | Pro | Glu | Asn | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe | |
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Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn <210> SEQ ID NO 89 <211> LENGTH: 539 <212> TYPE: PRT <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polypeptide <400> SEQUENCE: 89 Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln 1 5 10 15 His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45 Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu 65 70 75 80 Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr 145 150 155 160 Ala Val Arg Glu Leu Lys Asp Phe Val Leu Lys Asn Leu Thr Arg Ala Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala

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| Glu Asp Gln 305 | Gly Tr | p Tyr 310 | Cys | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro Asn Glu | Lys As 32 | | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Сүя 335 | Asp |
| Thr Ala Ala | Gly I1 340 | e Asn | Val | Ala | Glu 345 | Gln | Ser | Lys | Glu | Суя 350 | Asn | Ile |
| Asn Ile Ser 355 | Thr Th | r Asn | Tyr | Pro 360 | Суз | Гуз | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro Ile Ser 370 | Met Va | l Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Суз |
| Tyr Lys Gly 385 | Val Se | r Cys 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| Lys Gln Leu | Asn Ly 40 | - | Суя | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr Val Thr | Ile As 420 | p Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly |
| Glu Gln His 435 | Val Il | e Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| Ile Lys Phe 450 | Pro Gl | u Asp | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu Asn Ile 465 | Glu As | n Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| Leu Ser Ser | Ala Gl 48 | - | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu Ile Ala | Val Le 500 | u Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile Ile Lys 515 | Lys Th | r Lys | Гла | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
| Gly Val Thr 530 | Asn As | n Gly | Phe 535 | Ile | Pro | His | Asn | | | | | |
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| His Gly Leu | Lys Gl 20 | u Ser | Tyr | Leu | Glu 25 | Glu | Ser | Сув | Ser | Thr 30 | Ile | Thr |
| Glu Gly Tyr 35 | Leu Se | r Val | Leu | Arg 40 | Thr | Gly | Trp | Tyr | Thr 45 | Asn | Val | Phe |
| Thr Leu Glu 50 | Val Gl | y Asp | Val 55 | Glu | Asn | Leu | Thr | Сүв 60 | Ser | Asp | Gly | Pro |
| Ser Leu Ile 65 | Lys Th | r Glu 70 | Leu | Азр | Leu | Leu | Lys 75 | Ser | Ala | Leu | Arg | Glu 80 |
| Leu Lys Thr | Val Se | r Ala | Asp | Gln | Leu | Ala | Arg | Glu | Glu | Gln | Ile | Glu |

Leu Lys Thr Val Ser Ala Asp Gl
n Leu Ala Arg Glu Glu Glu Gln Ile Glu 85 90 95

Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110

| Ala | Ala | Ala 115 | Ala | Ala | Val | Thr | Ala 120 | Gly | Val | Ala | Ile | Ala 125 | Lys | Thr | Ile |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Arg | Leu 130 | Glu | Ser | Glu | Val | Thr 135 | Ala | Ile | Asn | Asn | Ala 140 | Leu | Lys | Lys | Thr |
| Asn 145 | Glu | Ala | Val | Ser | Thr 150 | Leu | Gly | Asn | Gly | Val 155 | Arg | Val | Leu | Ala | Thr 160 |
| Ala | Val | Arg | Glu | Leu 165 | Lys | Asp | Phe | Val | Leu 170 | Lys | Asn | Leu | Thr | Arg 175 | Ala |
| Ile | Asn | Lys | Asn 180 | Lys | Суз | Aab | Ile | Pro 185 | Asp | Leu | Lys | Met | Ala 190 | Val | Ser |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser |
| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 |
| Ile | Lys | Leu | Met | Leu 245 | Glu | Asn | Arg | Ala | Met 250 | Val | Arg | Arg | Lys | Gly 255 | Phe |
| Gly | Ile | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu | Pro | Ile 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Суз | Trp | Ile 285 | Val | Lys | Ala |
| Ala | Pro 290 | Ser | Суз | Ser | Glu | Lys 295 | ГАа | Gly | Asn | Tyr | Ala 300 | Суз | Leu | Leu | Arg |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Сув | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro | Asn | Glu | Lys | Asp 325 | Cys | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Сув 335 | Asp |
| Thr | Ala | Ala | Gly 340 | Ile | Asn | Val | Ala | Glu 345 | Gln | Ser | Lys | Glu | Сув 350 | Asn | Ile |
| Asn | Ile | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Cys | Lys | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Суз |
| Tyr 385 | Lys | Gly | Val | Ser | Cys 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| Lys | Gln | Leu | Asn | Lys 405 | Gly | Cys | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr | Val | Thr | 11e 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | ГЛЗ | Val 430 | Glu | Gly |
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| Ile | Lys 450 | Phe | Pro | Glu | Asn | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Asn | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lys 515 | Lys | Thr | Гуз | Гуз | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| Asn | | | | | | | | | | | | | | | |
|--|---|--|--|--|---|--|---|--|---|---|---|---|--|---|---|
| | Ile | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Суз | Lys | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Суз |
| Tyr 385 | Lys | Gly | Val | Ser | Суз 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| Lys | Gln | Leu | Asn | Lys 405 | Gly | Cys | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr | Val | Thr | 11e 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly |
| Glu | Gln | His 435 | Val | Ile | Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| Ile | Lys 450 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Asn | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lys 515 | Lys | Thr | Гуз | Lys | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| <213 | 3 > OI | | | Arti | ific | ial S | Seque | ence | | | | | | | |
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| <21: <220 <222 <400 Met 1 | 3> 01)> F1 3> 07 3> 57 Ser | RGANI BATUH THER SQUEN Trp | ISM: RE: INFO NCE: Lys | ORMAN 92 Val 5 | TION Val | : Syı Ile | Ile | ic I Phe | Ser 10 | Leu | Leu | | | 15 | |
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| Ile | Asn | Lys | Asn 180 | Lys | Суз | Yab | Ile | Asp 185 | Asp | Leu | Lys | Met | Ala 190 | Val | Ser |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser |
| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 |
| Ile | Lys | Leu | Met | Leu 245 | Glu | Asn | Arg | Ala | Met 250 | Val | Arg | Arg | Lys | Gly 255 | Phe |
| Gly | Ile | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu | Pro | Ile 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Cys | Trp | Ile 285 | Val | Lys | Ala |
| Ala | Pro 290 | Ser | Сүз | Ser | Glu | Lys 295 | Lys | Gly | Asn | Tyr | Ala 300 | Сув | Leu | Leu | Arg |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Суз | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro | Asn | Glu | Lys | Asp 325 | Суз | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Сув 335 | Asp |
| Thr | Ala | Ala | Gly 340 | | Asn | Val | Ala | Glu 345 | Gln | Ser | Гүз | Glu | Сув 350 | Asn | Ile |
| Asn | Ile | Ser 355 | Thr | Thr | Asn | Tyr | P ro 360 | Сув | Гуз | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Суз |
| Tyr 385 | Lys | Gly | Val | Ser | Суз 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| Lys | Gln | Leu | Asn | Lуз 405 | Gly | Суя | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr | Val | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Гλа | Val 430 | Glu | Gly |
| Glu | Gln | His 435 | Val | Ile | Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Aab | Pro |
| Ile | Lys 450 | Phe | Pro | Glu | Asn | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Asn | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lys 515 | Lys | Thr | Lys | Lys | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
| Gly | Val 530 | Thr | Asn | Asn | Gly | Phe 535 | Ile | Pro | His | Asn | | | | | |
| <21(|)> SH | 50 II | D NO | 93 | | | | | | | | | | | |
| | L> LH | | | 39 | | | | | | | | | | | |
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| |)> FI | | | | | | _ | | | | | | | | |
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| His | Gly | Leu | Lys 20 | Glu | Ser | Tyr | Leu | Glu 25 | Glu | Ser | Сув | Ser | Thr 30 | Ile | Thr |
| Glu | Gly | Tyr 35 | Leu | Ser | Val | Leu | Arg 40 | Thr | Gly | Trp | Tyr | Thr 45 | Asn | Val | Phe |
| Thr | Leu 50 | Glu | Val | Gly | Asp | Val 55 | Glu | Asn | Leu | Thr | Сүз 60 | Ser | Asp | Gly | Pro |
| Ser 65 | Leu | Ile | Lys | Thr | Glu 70 | Leu | Aab | Leu | Leu | Lys 75 | Ser | Ala | Leu | Arg | Glu 80 |
| Leu | Lys | Thr | Val | Ser 85 | Ala | Asp | Gln | Leu | Ala 90 | Arg | Glu | Glu | Gln | Ile 95 | Glu |
| Asn | Pro | Gly | Ser 100 | Gly | Ser | Phe | Val | Leu 105 | Gly | Ala | Ile | Ala | Leu 110 | Gly | Val |
| Ala | Ala | Ala 115 | Ala | Ala | Val | Thr | Ala 120 | Gly | Val | Ala | Ile | Ala 125 | Гла | Thr | Ile |
| Arg | Leu 130 | Glu | Ser | Glu | Val | Thr 135 | Ala | Ile | Asn | Asn | Ala 140 | Leu | Гуз | ГАа | Thr |
| Asn 145 | Glu | Ala | Val | Ser | Thr 150 | Leu | Gly | Asn | Gly | Val 155 | Arg | Val | Leu | Ala | Thr 160 |
| Ala | Val | Arg | Glu | Leu 165 | Гуа | Asp | Phe | Val | Ser 170 | Lys | Asn | Leu | Thr | Arg 175 | Ala |
| Ile | Asn | Гуз | Asn 180 | Гла | Сув | Asp | Ile | Asp 185 | Asp | Leu | Гүз | Met | Ala 190 | Val | Ser |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser |
| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 |
| Ile | Гуз | Leu | Met | Leu 245 | Glu | Asn | Arg | Ala | Met 250 | Val | Arg | Arg | Гуз | Gly 255 | Phe |
| Gly | Ile | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu | Pro | Ile 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Суя | Trp | Ile 285 | Val | ГЛа | Ala |
| Ala | Pro 290 | Ser | Суз | Ser | Glu | Lys 295 | Lys | Gly | Asn | Tyr | Ala 300 | Сув | Leu | Leu | Arg |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Сув | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro | Asn | Glu | ГЛа | Asp 325 | Суз | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Суа 335 | Asp |
| Thr | Ala | Ala | Gly 340 | Ile | Asn | Val | Ala | Glu 345 | Gln | Ser | Lys | Glu | Суя 350 | Asn | Ile |
| Asn | Ile | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Суз | Lys | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Cys |
| Tyr 385 | Lys | Gly | Val | Ser | Сув 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| ГЛа | Gln | Leu | Asn | Lys 405 | Gly | Суз | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr | Val | Thr | Ile | Asp | Asn | Thr | Val | Tyr | Gln | Leu | Ser | Lys | Val | Glu | Gly |
| | | | | | | | | | | | | | | | |

| | | | | | | | | | | | | con | C I III | uea | |
|------------------------------|----------------------------------|------------|-----------------------------|------------|------------|----------------|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|
| _ | _ | _ | 420 | _ | _ | _ | _ | 425 | _ | _ | _ | _ | 430 | _ | _ |
| Glu | Gln | His 435 | Val | Ile | Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| Ile | Lys 450 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Asn | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lys 515 | Lys | Thr | Lys | Lys | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| Glu | Gly | Tyr 35 | Leu | Ser | Val | Leu | Arg 40 | Thr | Gly | Trp | Tyr | Thr 45 | Asn | Val | Phe |
| Thr | Leu 50 | Glu | Val | Gly | Asp | Leu 55 | Glu | Asn | Leu | Thr | 60 СУв | Ser | Asp | Gly | Pro |
| Ser 65 | Leu | Ile | Гла | Thr | Glu 70 | Leu | Asp | Leu | Thr | Lys 75 | Ser | Ala | Leu | Arg | Glu 80 |
| Leu | Lys | Thr | Val | Ser 85 | Ala | Aab | Gln | Leu | Ala 90 | Arg | Glu | Glu | Gln | Ile 95 | Glu |
| Asn | Pro | Gly | Ser 100 | Gly | Ser | Phe | Val | Leu 105 | Gly | Ala | Ile | Ala | Leu 110 | Gly | Val |
| Ala | Ala | Ala 115 | Ala | Ala | Val | Thr | Ala 120 | Gly | Val | Ala | Ile | Ala 125 | Lys | Thr | Ile |
| Arg | Leu 130 | Glu | Ser | Glu | Val | Thr 135 | Ala | Ile | Asn | Asn | Ala 140 | Leu | Lys | Lys | Thr |
| Asn 145 | Glu | Ala | Val | Ser | Thr 150 | Leu | Gly | Asn | Gly | Val 155 | Arg | Val | Leu | Ala | Thr 160 |
| Ala | Val | Arg | Glu | Leu 165 | - | Asp | Phe | Val | Ser 170 | Lys | Asn | Leu | Thr | Arg 175 | Ala |
| Ile | Asn | Lys | Asn 180 | Гла | Суз | Aap | Ile | Asp 185 | Asp | Leu | Гуз | Met | Ala 190 | Val | Ser |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser |
| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp |
| Ala 225 | | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | | Ser | Ala | Gly | Gln 240 |
| | | | | | | | | | | | | | | | |

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe

| | | | | | | | | | | | | con | tin | ued | |
|------------------------------|-------------------------------------|------------|-----------------------------|------------|------------|----------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | | | 245 | | | | | 250 | | | | | 255 | |
| Gly | Ile | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu | Pro | Ile 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Суя | Trp | Ile 285 | Val | Гла | Ala |
| Ala | Pro 290 | Ser | Сүз | Ser | Glu | Lys 295 | Lys | Gly | Asn | Tyr | Ala 300 | Сув | Leu | Leu | Arg |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Суз | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro | Asn | Glu | ГАа | Азр 325 | Суз | Glu | Thr | Arg | Gly 330 | Aap | His | Val | Phe | СУа 335 | Asp |
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| Leu | Ser | Ser | Ala | Glu 485 | гуз | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
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| Thr | Leu 50 | Glu | Val | Gly | Asp | Val 55 | Glu | Asn | Leu | Thr | Суз 60 | Ser | Asp | Gly | Pro |
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| Ala | Ala | Ala 115 | Ala | Ala | Val | Thr | Ala 120 | | Val | Ala | Ile | Ala 125 | Lуs | Thr | Ile |
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| Thr | Val | Thr | | | Asn | Thr | Val | - | | Leu | Ser | Lys | | | Gly |
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| Ile | Lys | 435 Phe | Pro | Glu | Asp | Gln | 440 Phe | Gln | Val | Ala | Leu | 445 Asp | Gln | Val | Phe |
| Glu | 450 Asn | Ile | Glu | Asn | Ser | 455 Gln | Ala | Leu | Val | Aso | 460 Gln | Ser | Asn | Ara | Ile |
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| Pro As | n Glu | Lys | Asp 325 | Cys | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Cys 335 | Asp |
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| Pro Il 37 | | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Сув |
| Tyr Ly 385 | s Gly | Val | Ser | Cys 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| Lys Gl | n Leu | Asn | Lys 405 | Gly | Суя | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr Va | l Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Гуз | Val 430 | Glu | Gly |
| Glu Gl | n His 435 | Val | Ile | Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| Ile Ly 45 | | Pro | Glu | Asp | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
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| Leu Se | r Ser | Ala | Glu 485 | Гла | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu Il | e Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile Il | e Lys 515 | Lys | Thr | гла | Гла | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| Glu Gl | y Tyr 35 | Leu | Ser | Val | Leu | Arg 40 | Thr | Gly | Trp | Tyr | Thr 45 | Asn | Val | Phe |
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| 65 | s Thr | Val | Ser 85 | 70 Ala | Asp | Gln | Leu | 90 | Arg | | | | 95 | Glu |
| 65 Leu Ly | s Thr o Gly | Val Ser 100 | Ser 85 Gly | 70 Ala Ser | Asp Phe | Gln Val | Leu Leu 105 | 90 Gly | Arg Ala | Ile | Ala | Leu 110 | 95 Gly | Glu Val |

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| Ile | Asn | Гуз | Asn 180 | Гүз | Сув | Asp | Ile | Asp 185 | Asp | Leu | Lys | Met | Ala 190 | Val | Ser |
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| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 |
| Ile | Lys | Leu | Met | Leu 245 | Glu | Asn | Arg | Ala | Met 250 | Val | Arg | Arg | Lys | Gly 255 | Phe |
| Gly | Ile | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu | Pro | Ile 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Сув | Trp | Ile 285 | Val | ГЛа | Ala |
| Ala | Pro 290 | Ser | Суз | Ser | Glu | Lys 295 | Lys | Gly | Asn | Tyr | Ala 300 | Суз | Leu | Leu | Arg |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Сув | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro | Asn | Glu | гүз | Asp 325 | Cys | Glu | Thr | Arg | Gly 330 | Aab | His | Val | Phe | Сув 335 | Asp |
| Thr | Ala | Ala | Gly 340 | Ile | Asn | Val | Ala | Glu 345 | Gln | Ser | Lys | Glu | Сув 350 | Asn | Ile |
| Asn | Ile | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Суз | Lys | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Сув |
| Tyr 385 | Lys | Gly | Val | Ser | Cys 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| ГЛа | Gln | Leu | Asn | Lys 405 | Gly | Сув | Ser | Tyr | 11e 410 | Thr | Asn | Gln | Asp | Ala 415 | Aap |
| Thr | Val | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly |
| Glu | Gln | His 435 | Val | Ile | Гла | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| Ile | Lys 450 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
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| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lys 515 | ГАа | Thr | Lys | Lys | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| Glu | Gly | Tyr 35 | Leu | Ser | Val | Leu | Arg 40 | Thr | Gly | Trp | Tyr | Thr 45 | Asn | Val | Phe | | | |
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| Leu | Гув | Thr | Val | Ser 85 | Ala | Asp | Gln | Leu | Ala 90 | Arg | Glu | Glu | Gln | Ile 95 | Glu | | | |
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| Arg | Leu 130 | Glu | Ser | Glu | Val | Thr 135 | Ala | Ile | Asn | Asn | Ala 140 | Leu | Lys | Lys | Thr | | | |
| Asn 145 | Glu | Ala | Val | Ser | Thr 150 | Leu | Gly | Asn | Gly | Val 155 | Arg | Val | Leu | Ala | Thr 160 | | | |
| Ala | Val | Arg | Glu | Leu 165 | Lys | Asp | Phe | Val | Ser 170 | Lys | Asn | Leu | Thr | Arg 175 | Ala | | | |
| Ile | Asn | Lys | Asn 180 | Lys | Cys | Asp | Ile | Asp 185 | Asp | Leu | Lys | Met | Ala 190 | Val | Ser | | | |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser | | | |
| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp | | | |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 | | | |
| Ile | Lys | Leu | Met | Leu 245 | Glu | Asn | Arg | Ala | Met 250 | Val | Arg | Arg | Lys | Gly 255 | Phe | | | |
| Gly | Ile | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln | | | |
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| Ala | Pro 290 | Ser | Сүз | Ser | Glu | Lys 295 | Lys | Gly | Asn | Tyr | Ala 300 | Cys | Leu | Leu | Arg | | | |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Суа | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 | | | |
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| Ile | Lys 450 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Asn | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lys 515 | ГЛа | Thr | Lys | Гла | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| Ala | Ala | Ala 115 | Ala | Ala | Val | Thr | Ala 120 | Gly | Val | Ala | Ile | Ala 125 | Lys | Thr | Ile |
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| Asn 145 | Glu | Ala | Val | Ser | Thr 150 | Leu | Gly | Asn | Gly | Val 155 | Arg | Val | Leu | Ala | Thr 160 |
| Ala | Val | Arg | Glu | Leu 165 | Lys | Aab | Phe | Val | Ser 170 | Lys | Asn | Leu | Thr | Arg 175 | Ala |
| Ile | Asn | Lys | Asn 180 | Lys | Cys | Asp | Ile | Pro 185 | Asp | Leu | Lys | Met | Ala 190 | Val | Ser |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser |
| | | | | | | | | | | | | | | | |

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| Gly I | le | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu Pi | | 11e 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Сув | Trp | Ile 285 | Val | Lys | Ala |
| Ala Pr 29 | ro 90 | Ser | Cys | Ser | Glu | Lys 295 | Lys | Gly | Asn | Tyr | Ala 300 | Суз | Leu | Leu | Arg |
| Glu A: 305 | ab | Gln | Gly | Trp | Tyr 310 | Cys | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
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| Thr A | la | Ala | Gly 340 | Ile | Asn | Val | Ala | Glu 345 | Gln | Ser | ГЛа | Glu | Сув 350 | Asn | Ile |
| Asn II | | Ser 355 | Thr | Thr | Asn | Tyr | Pro 360 | Суз | Lys | Val | Ser | Thr 365 | Gly | Arg | His |
| Pro II 3 | le 70 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Сув |
| Tyr Ly 385 | γs | Gly | Val | Ser | Сув 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| Lys G | ln | Leu | Asn | Lys 405 | Gly | Сув | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | deV |
| Thr Va | al | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly |
| Glu G | | His 435 | Val | Ile | Гλа | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
| Ile L ₃ 49 | 78 50 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
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| Leu I | le | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile I | | Lys 515 | Lya | Thr | Lys | Lys | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| Leu | Гуз | Thr | Val | Ser 85 | Ala | Asp | Gln | Leu | Ala 90 | Arg | Glu | Glu | Gln | Ile 95 | Glu |
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| Ala | Ala | Ala 115 | Ala | Ala | Val | Thr | Ala 120 | Gly | Val | Ala | Ile | Ala 125 | Lys | Thr | Ile |
| Arg | Leu 130 | Glu | Ser | Glu | Val | Thr 135 | Ala | Ile | Asn | Asn | Ala 140 | Leu | Lys | Lys | Thr |
| Asn 145 | Glu | Ala | Val | Ser | Thr 150 | Leu | Gly | Asn | Gly | Val 155 | Arg | Val | Leu | Ala | Thr 160 |
| Ala | Val | Arg | Glu | Leu 165 | Lys | Yab | Phe | Val | Ser 170 | Lys | Asn | Leu | Thr | Arg 175 | Ala |
| Ile | Asn | Lys | Asn 180 | Lys | Cys | Pro | Ile | Asp 185 | Asp | Leu | Lys | Met | Ala 190 | Val | Ser |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser |
| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 |
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| Leu | Pro | Ile 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Суя | Trp | Ile 285 | Val | Lys | Ala |
| Ala | Pro 290 | Ser | Суа | Ser | Glu | Lys 295 | ГЛа | Gly | Asn | Tyr | Ala 300 | Суз | Leu | Leu | Arg |
| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Суа | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | T yr 320 |
| Pro | Asn | Glu | Lys | Asp 325 | Сув | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Сув 335 | Asp |
| Thr | Ala | Ala | Gly 340 | Ile | Asn | Val | Ala | Glu 345 | Gln | Ser | Гуз | Glu | Cys 350 | Asn | Ile |
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| Tyr 385 | Гла | Gly | Val | Ser | Cys 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| Lys | Gln | Leu | Asn | Lys 405 | Gly | Суя | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
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| Glu | Gln | | | Ile | Lys | Gly | - | | Val | Ser | Ser | | | Asp | Pro |
| Ile | Lys | 435 Phe | Pro | Glu | Asp | Gln | 440 Phe | Gln | Val | Ala | Leu | 445 Asp | Gln | Val | Phe |
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| Glu 305 | Asp | Gln | Gly | Trp | Tyr 310 | Суа | Gln | Asn | Ala | Gly 315 | Ser | Thr | Val | Tyr | Tyr 320 |
| Pro | Asn | Glu | Гүз | Asp 325 | Суз | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Сув 335 | Asp |
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| Glu | Gln | His 435 | Val | Ile | Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Asp | Pro |
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| Glu 465 | Asn | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lys 515 | Lys | Thr | Гуз | Гуз | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| Glu | Gly | Tyr 35 | Leu | Ser | Val | Leu | Arg 40 | Thr | Gly | Trp | Tyr | Thr 45 | Asn | Val | Phe |
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| Asn 145 | Glu | Ala | Val | Ser | Thr 150 | Leu | Gly | Asn | Gly | Val 155 | Arg | Val | Leu | Ala | Thr 160 |
| Ala | Val | Arg | Glu | Leu 165 | Гла | Aab | Phe | Val | Ser 170 | Lys | Asn | Leu | Thr | Arg 175 | Ala |
| Ile | Asn | Lys | Asn 180 | ГЛа | Суз | Yab | Ile | Asp 185 | Asp | Leu | ГЛа | Met | Ala 190 | Val | Ser |
| Phe | Ser | Gln 195 | Phe | Asn | Arg | Arg | Phe 200 | Leu | Asn | Val | Val | Arg 205 | Gln | Phe | Ser |
| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 |
| Ile | Lys | Leu | Met | Leu 245 | Glu | Asn | Arg | Ala | Met 250 | Val | Arg | Arg | Lys | Gly 255 | Phe |
| Gly | Ile | Leu | Ile 260 | Gly | Val | Tyr | Gly | Ser 265 | Ser | Val | Ile | Tyr | Met 270 | Val | Gln |
| Leu | Pro | Ile 275 | Phe | Gly | Val | Ile | Asp 280 | Thr | Pro | Суз | Trp | Ile 285 | Val | Гλа | Ala |
| Ala | Pro 290 | Ser | САа | Ser | Glu | Lys 295 | ГÀа | Gly | Asn | Tyr | Ala 300 | Суз | Leu | Leu | Arg |
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| Pro | Asn | Glu | ГЛа | Asp 325 | Cys | Glu | Thr | Arg | Gly 330 | Asp | His | Val | Phe | Сув 335 | Asp |
| Thr | Ala | Ala | Gly 340 | Ile | Asn | Val | Ala | Glu 345 | Gln | Ser | Lys | Glu | Сув 350 | Asn | Ile |
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| Tyr 385 | Гуз | Gly | Val | Ser | Сув 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| Гүз | Gln | Leu | Asn | Lys 405 | Gly | Суя | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr | Val | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Гла | Val 430 | Glu | Gly |
| Glu | Gln | His 435 | Val | Ile | Lys | Gly | Arg 440 | Pro | Val | Ser | Ser | Ser 445 | Phe | Pro | Pro |
| Ile | Lys 450 | Phe | Pro | Glu | Asp | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
| Glu 465 | Asn | Ile | Glu | Asn | Ser 470 | Gln | Ala | Leu | Val | Asp 475 | Gln | Ser | Asn | Arg | Ile 480 |
| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lys 515 | | Thr | Гуз | Гуз | Pro 520 | | Gly | Ala | Pro | Pro 525 | | Leu | Ser |
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| Asn | | | | | | | | | | | | | | | |
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| Pro | Ile 370 | Ser | Met | Val | Ala | Leu 375 | Ser | Pro | Leu | Gly | Ala 380 | Leu | Val | Ala | Суз |
| Tyr 385 | Гла | Gly | Val | Ser | Сув 390 | Ser | Ile | Gly | Ser | Asn 395 | Arg | Val | Gly | Ile | Ile 400 |
| Lys | Gln | Leu | Asn | Lys 405 | Gly | Cys | Ser | Tyr | Ile 410 | Thr | Asn | Gln | Asp | Ala 415 | Asp |
| Thr | Val | Thr | Ile 420 | Asp | Asn | Thr | Val | Tyr 425 | Gln | Leu | Ser | Lys | Val 430 | Glu | Gly |
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| Ile | Lys 450 | Phe | Pro | Glu | Asn | Gln 455 | Phe | Gln | Val | Ala | Leu 460 | Asp | Gln | Val | Phe |
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| Leu | Ser | Ser | Ala | Glu 485 | Lys | Gly | Asn | Thr | Gly 490 | Phe | Ile | Ile | Val | Ile 495 | Ile |
| Leu | Ile | Ala | Val 500 | Leu | Gly | Ser | Ser | Met 505 | Ile | Leu | Val | Ser | Ile 510 | Phe | Ile |
| Ile | Ile | Lуя 515 | Гла | Thr | Гла | Lys | Pro 520 | Thr | Gly | Ala | Pro | Pro 525 | Glu | Leu | Ser |
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| 661 | |
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| Asp | Asn 210 | Ala | Gly | Ile | Thr | Pro 215 | Ala | Ile | Ser | Leu | Asp 220 | Leu | Met | Thr | Asp |
| Ala 225 | Glu | Leu | Ala | Arg | Ala 230 | Val | Pro | Asn | Met | Pro 235 | Thr | Ser | Ala | Gly | Gln 240 |
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| cotaacgaga aggactgoga gacaagaggo gaccacgtgt totgtgatac ogoogotgga 102 atcaatgtgg oogagoagag caaagagtgo aacatcaaca toagcaccac caactatooo 108 tgoaaggtgt coacoggoag geacoctatt totatggtgg ototgtotoo totgggagoo 114 otggtggott gitataaggg ogigtootgt agoatoggoa geaacagagi gggcatcato 120 aagcagotga acaagggotg cagotacato accaaccagg acgoogatac ogigaccato 126 gacaacacog igiatcagot gagcaaggig gaaggogaac agoacgigat caagggoaga 132 | | 900 |
| atcaatgtgg cogagcagag caaagagtge aacatcaaca teagcaceae caactateee 106 tgeaaggtgt eeaeeggeag geaeeetatt tetatggtgg etetgtetee tetgggagee 114 etggtggett gttataaggg egtgteetgt ageateggea geaacagagt gggeateate 120 aageagetga acaagggetg eagetacate aceaaceagg aegeegatae egtgaceate 126 gacaacaeeg tgtateaget gagcaaggtg gaaggegaae ageaegtgat eaagggeaga 132 | getga gagaggaeca aggetggtat tgteagaaeg eeggeageae egtgtaetae | 960 |
| tgcaaggtgt ccaccggcag gcaccctatt totatggtgg ototgtotoo totgggagoo 114 otggtggott gttataaggg ogtgtootgt agcatoggca gcaacagagt gggcatcato 120 aagcagotga acaagggotg cagotacato accaaccagg acgoogatac ogtgaccato 126 gacaacacog tgtatcagot gagcaaggtg gaaggogaac agcacgtgat caagggoaga 132 | cgaga aggactgoga gacaagaggo gaccaogtgt totgtgatad ogoogotgga – 1 | 1020 |
| ctggtgggtt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 120 aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 126 gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 132 | tgtgg cogagoagag caaagagtgo aacatoaaca toagoacoad caactatooo 1 | 1080 |
| aagcagetga acaagggetg cagetacate aceaaceagg aegeegatae egtgaeeate 126 gaeaacaeeg tgtateaget gageaaggtg gaaggegaae ageaegtgat eaagggeaga 132 | ggtgt ccaceggeag geacectatt tetatggtgg etetgtetee tetgggagee - 1 | 1140 |
| gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 132 | ggett gitataaggg egigteeigt agealeggea geaacagagi gggealeale - 1 | 1200 |
| | getga acaagggetg cagetacate aceaaceagg acgeegatae egtgaecate - 1 | 1260 |
| | caccy tytatcayct gagcaaggty gaagycgaac agcacytyat caagyycaga 1 | 1320 |
| cctgtgtoca gcagettega cectateaag tteeetgagg ateagtteaa egtggeeetg 138 | gtoca gragettega rectatraag tteeetgagg ateagttraa rgtggeretg - 1 | 1380 |

| ~ | _ | 1 |
|---|---|---|
| n | 1 | |
| v | | |

| gaccaggtgt tcgagaacat | cgagaattcc | caggetetgg | tggaccagtc | caacagaatc | 1440 |
|--|------------|------------|------------|------------|------|
| ctgtctagcg ccgagaaggg | aaacaccggc | tteateateg | tgatcatcct | gategeegtg | 1500 |
| ctgggcaget ccatgateet | ggtgtccatc | ttcatcatta | tcaagaagac | caagaagccc | 1560 |
| accggcgctc ctccagaact | gageggagtg | accaacaatg | getteateee | tcacaac | 1617 |
| <210> SEQ ID NO 107 <211> LENGTH: 1617 <212> TYPE: DNA <213> ORGANISM: Artifi <220> FEATURE: <223> OTHER INFORMATIO | - | | eotide | | |

<400> SEQUENCE: 107

| 60 | cggcctgaaa | cacctcagca | ctgctgatca | catetteage | aggtggtcat | atgagetgga |
|------|------------|------------|------------|------------|------------|------------|
| 120 | tgtgctgaga | gctacctgtc | atcacagagg | ctgcagcacc | tggaagagtc | gagagetacc |
| 180 | tctgacatgc | acgtcgagaa | gaagtgggcg | gttcacactg | acaccaacgt | accggctggt |
| 240 | cctgagagaa | ccaagagcgc | ctggatctga | caagaccgag | ctagectgat | tctgatggcc |
| 300 | tcctggcage | agatcgagaa | agagaggaac | tcagctggcc | tgtctgccga | ctcaagaccg |
| 360 | tgttacagca | ctgctgcagc | ggagtggctg | cattgctctt | tgetgggage | ggcagetttg |
| 420 | caacaacgcc | tgaccgccat | gaaagcgaag | catcagactg | tetgeaagae | ggcgtggcca |
| 480 | getggeeaca | gcgttagagt | ctcggcaatg | cgtcagcaca | caaacgaggc | ctgaagaaga |
| 540 | taacaagaac | cacgggccat | aagaacctga | cttcgtgtcc | agetgaagga | gccgtgcgcg |
| 600 | ccggcggttt | gccagttcaa | gtgtccttta | gaagatggcc | tcgacgacct | aagtgegaca |
| 660 | cageetggae | caccagccat | gccggaatca | tagcgacaac | tgeggeagtt | ctgaacgtcg |
| 720 | tgeeggeeag | tgeetacate | gtgcctaaca | ggetagagee | atgetgaget | ctgatgacag |
| 780 | cattetgtgt | aaggettegg | gteegaegga | tagagccatg | tgetegagaa | atcaagetga |
| 840 | cgtgatcgac | ctatettegg | gtgcagetgc | gatctatatg | gcagcagcgt | ggcgtgtacg |
| 900 | caattacgcc | agaagaaggg | agetgtageg | ggccgctcct | ggattgtgaa | acaccetget |
| 960 | cgtgtactac | ccggcagcac | tgtcagaacg | aggetggtat | gagaggacca | tgeetgetga |
| 1020 | cgccgctgga | tctgtgatac | gaccacgtgt | gacaagaggc | aggactgcga | cctaacgaga |
| 1080 | caactateee | tcagcaccac | aacatcaaca | caaagagtgc | ccgagcagag | atcaatgtgg |
| 1140 | tetgggagee | ctctgtctcc | tctatggtgg | gcaccctatt | ccaccggcag | tgcaaggtgt |
| 1200 | gggcatcatc | gcaacagagt | agcatcggca | cgtgtcctgt | gttataaggg | ctggtggctt |
| 1260 | cgtgaccatc | acgeegatae | accaaccagg | cagctacatc | acaagggctg | aagcagctga |
| 1320 | caagggcaga | agcacgtgat | gaaggcgaac | gagcaaggtg | tgtatcagct | gacaacaccg |
| 1380 | tgtggccctg | accagtggca | tteeetgage | ccctatcaag | gcagettega | cctgtgtcca |
| 1440 | caacagaatc | tggaccagtc | caggetetgg | cgagaattcc | tcgagaacat | gaccaggtgt |
| 1500 | gategeegtg | tgatcatcct | ttcatcatcg | aaacaccggc | ccgagaaggg | ctgtctagcg |
| 1560 | caagaagccc | tcaagaagac | ttcatcatta | ggtgtccatc | ccatgateet | ctgggcaget |
| 1617 | tcacaac | getteateee | accaacaatg | gageggagtg | ctccagaact | accggcgctc |
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<210> SEQ ID NO 108 <211> LENGTH: 1617 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE:

<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 108

| atgagetgga aggtggteat catetteage etgetgatea caeeteagea eggeetgaaa | 60 | | | | | | |
|---|------|--|--|--|--|--|--|
| gagagetaee tggaagagte etgeageaee ateaeagagg getaeetgte tgtgetgaga | 120 | | | | | | |
| accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc | 180 | | | | | | |
| tetgatggee etageetgat caagacegag etggatetge teaagagege eetgagagaa | 240 | | | | | | |
| ctcaagaceg tgtetgeega teagetggee agagaggaae agategagaa teetggeage | 300 | | | | | | |
| ggcagetttg tgetgggage cattgetett ggagtggetg etgetgeage tgttaeagea | 360 | | | | | | |
| ggegtggeea tegetaagae cateagaetg gaaagegaag tgaeegeeat caacaaegee | 420 | | | | | | |
| ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca | 480 | | | | | | |
| gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac | 540 | | | | | | |
| aagtgegaea teeetgaeet gaagatggee gtgteettta geeagtteaa eeggeggttt | 600 | | | | | | |
| ctgaacgteg tgeggeagtt tagegacaae geeggaatea caceageeat cageetggae | 660 | | | | | | |
| ctgatgacag atgetgaget ggetagagee gtgeetaaca tgeetacate tgeeggeeag | 720 | | | | | | |
| atcaagetga tgetegagaa tagageeatg gteegaegga aaggettegg cattetgatt | 780 | | | | | | |
| ggegtgtaeg geageagegt gatetatatg gtgeagetge etatettegg egtgategae | 840 | | | | | | |
| acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc | 900 | | | | | | |
| tgeetgetga gagaggaeea aggetggtat tgteagaaeg eeggeageae egtgtaetae | 960 | | | | | | |
| cctaacgaga aggactgoga gacaagaggo gaccacgtgt tetgtgatac cgccgctgga | 1020 | | | | | | |
| atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc | 1080 | | | | | | |
| tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc | 1140 | | | | | | |
| ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc | 1200 | | | | | | |
| aagcagetga acaagggetg eagetacate aceaaceagg acgeegatae egtgaceate | 1260 | | | | | | |
| gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga | 1320 | | | | | | |
| cetgtgteea geagettega ecetateaag tteeetgagg ateagtteea ggtggeeetg | 1380 | | | | | | |
| gaccaggtgt tegagaacat egagaattee caggetetgg tggaccagte caacagaate | 1440 | | | | | | |
| ctgtctageg cegagaaggg aaacacegge tteateateg tgateateet gategeegtg | 1500 | | | | | | |
| ctgggcagct ccatgatect ggtgtccate tteateatta teaagaagae caagaageee | 1560 | | | | | | |
| aceggegete etecagaaet gageggagtg aceaacaatg getteateee teacaae | 1617 | | | | | | |
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| gagagetaee tggaagagte etgeageaee ateacagagg getaeetgte tgtgetgaga | 120 | | | | | | |
| accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc | 180 | | | | | | |
| tetgatggee etageetgat caagaeegag etggatetge teaagagege eetgagagaa | 240 | | | | | | |
| ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc | 300 | | | | | | |
| ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca | 360 | | | | | | |
| | - | | | | | | |

675

676

| ggcgtggcca | tcgctaagac | catcagactg | gaaagcgaag | tgaccgecat | caacaacgcc | 420 |
|---|--|--|---|--|---|--|
| ctgaagaaga | caaacgaggc | cgtcagcaca | ctcggcaatg | gcgttagagt | getggeeaea | 480 |
| geegtgegeg | agetgaagga | cttcgtgtcc | aagaacctga | cacgggccat | taacaagaac | 540 |
| aagtgcgaca | tccctgacct | gaagatggcc | gtgtccttta | gccagttcaa | ccggcggttt | 600 |
| ctgaacgtcg | tgcggcagtt | tagcgacaac | gccggaatca | caccagccat | cageetggae | 660 |
| ctgatgacag | atgctgagct | ggetagagee | gtgcctaaca | tgcctacatc | tgeeggeeag | 720 |
| atcaagctga | tgetegagaa | tagagecatg | gteegaegga | aaggettegg | cattetgatt | 780 |
| ggegtgtaeg | gcagcagcgt | gatetatatg | gtgeagetge | ctatettegg | cgtgatcgac | 840 |
| acaccetget | ggattgtgaa | ggeegeteet | agetgtageg | agaagaaggg | caattacgcc | 900 |
| tgeetgetga | gagaggacca | aggetggtat | tgtcagaacg | ccggcagcac | cgtgtactac | 960 |
| cctaacgaga | aggactgcga | gacaagaggc | gaccacgtgt | tctgtgatac | cgccgctgga | 1020 |
| atcaatgtgg | ccgagcagag | caaagagtgc | aacatcaaca | teageaceac | caactatccc | 1080 |
| tgcaaggtgt | ccaccggcag | geaccetatt | tetatggtgg | etetgtetee | tetgggagee | 1140 |
| ctggtggett | gttataaggg | cgtgtcctgt | agcatoggca | gcaacagagt | gggcatcatc | 1200 |
| aagcagctga | acaagggetg | cagetacate | accaaccagg | acgeegatae | cgtgaccatc | 1260 |
| gacaacaccg | tgtatcaget | gagcaaggtg | gaaggcgaac | agcacgtgat | caagggcaga | 1320 |
| cetgtgteea | gcagettega | ccctatcaag | tteeetgaga | accagttcca | ggtggccctg | 1380 |
| gaccaggtgt | tcgagaacat | cgagaattcc | caggetetgg | tggaccagtc | caacagaatc | 1440 |
| ctgtctagcg | ccgagaaggg | aaacaccggc | ttcatcatcg | tgatcatcct | gategeegtg | 1500 |
| ataggagagt | | | | | | |
| crgggcager | ccatgateet | ggtgtccatc | ttcatcatta | tcaagaagac | caagaagccc | 1560 |
| | ctecagaact | | | | | 1560 1617 |
| accggcgctc <210> SEQ : <211> LENG <212> TYPE <213> ORGAI <220> FEAT | ctccagaact ID NO 110 IH: 1617 : DNA NISM: Artif: | gagcggagtg icial Seque | accaacaatg nce | gcttcatccc | | |
| accggcgctc <210> SEQ : <211> LENG <212> TYPE <213> ORGAI <220> FEAT | ctccagaact ID NO 110 IH: 1617 : DNA NISM: Artif: URE: R INFORMATI(| gagcggagtg icial Seque | accaacaatg nce | gcttcatccc | | |
| accggcgctc <210> SEQ : <211> LENG <212> TYPE <213> ORGAI <220> FEAT <223> OTHEI <400> SEQUI | ctccagaact ID NO 110 IH: 1617 : DNA NISM: Artif: URE: R INFORMATI(| gagcggagtg icial Sequen DN: Synthet: | accaacaatg nce ic Polynucle | gcttcatccc eotide | tcacaac | |
| accggcgctc <210> SEQ <211> LENG <212> TYPE <213> ORGAI <220> FEAT <223> OTHEI <400> SEQU atgagctgga | Ctccagaact ID NO 110 TH: 1617 : DNA NISM: Artif: URE: R INFORMATIC ENCE: 110 | gagoggagtg icial Sequen DN: Synthet: catottcago | accaacaatg nce ic Polynucle ctgctgatca | getteatece eotide caceteagea | tcacaac | 1617 |
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| accggcgctc <210> SEQ 3 <211> LENG <212> TYPE <213> ORGAI <220> FEAT <223> OTHEI <400> SEQU atgagctgga gagagctacc accggctggt | ctccagaact ID NO 110 IH: 1617 : DNA NISM: Artif: URE: R INFORMATIC ENCE: 110 aggtggtcat tggaagagtc | gageggagtg icial Sequer DN: Synthet: catetteage etgeageace gtteacaetg | accaacaatg nce ic Polynucle ctgctgatca atcacagagg gaagtgggcg | getteatece eotide caceteagea getacetgte aegtegagaa | tcacaac cggcctgaaa tgtgctgaga tctgacatgc | 1617 60 120 |
| accggcgctc <210> SEQ <211> LENG <212> TYPE <213> ORGA <220> FEAT <223> OTHE <400> SEQU atgagctgga gagagctacc accggctggt tctgatggcc | ctccagaact ID NO 110 IH: 1617 : DNA NISM: Artif: URE: R INFORMATIC ENCE: 110 aggtggtcat tggaagagtc acaccaacgt | gageggagtg icial Sequen DN: Synthet: catetteage etgeageace gtteacaetg caagaeegag | accaacaatg nce ic Polynucle ctgctgatca atcacagagg gaagtgggcg ctggatctgc | getteatece eotide caceteagea getacetgte aegtegagaa teaagagege | tcacaac cggcctgaaa tgtgctgaga tctgacatgc cctgagagaa | 1617 60 120 180 |
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| ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac | 840 |
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| tgeetgetga gagaggaeea aggetggtat tgteagaaeg eeggeageae egtgtaetae | 960 |
| cctaacgaga aggactgoga gacaagaggo gaccaogtgt totgtgatac ogoogotgga | 1020 |
| atcaatgtgg cogagcagag caaagagtgc aacatcaaca tcagcaccac caactatocc | 1080 |
| tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc | 1140 |
| ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc | 1200 |
| aagcagetga acaagggetg cagetacate aceaaceagg acgeegatae egtgaceate | 1260 |
| gacaacaccg tgtatcagct gagcaaggtg gaaggogaac agcacgtgat caagggcaga | 1320 |
| cctgtgteca gcagettega cectateaag tteeetgagg ateagtteea ggtggeeetg | 1380 |
| gaccaggtgt tegagaacat egagaattee eaggetetgg tggaccagte caacagaate | 1440 |
| ctgtctageg cegagaaggg aaacacegge tteateateg tgateateet gategeegtg | 1500 |
| ctgggcaget ceatgateet ggtgteeate tteateatta teaagaagae caagaageee | 1560 |
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| accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc | 180 |
| tetgatggee etageetgat caagacegag etggatetge teaagagege eetgagagaa | 240 |
| ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc | 300 |
| ggcagetttg tgetgggage cattgetett ggagtggetg etgetgeage tgttaeagea | 360 |
| ggegtggeea tegetaagae cateagaetg gaaagegaag tgaeegeeat caacaaegee | 420 |
| ctgaagaaga caaacgagge egteageaea eteggeaatg gegttagagt getggeeaea | 480 |
| geegtgegeg agetgaagga ettegtgett aagaaeetga eaegggeeat taacaagaae | 540 |
| aagtgegaca teeetgaeet gaagatggee gtgteettta geeagtteaa eeggeggttt | 600 |
| ctgaacgteg tgeggeagtt tagegacaac geeggaatea caecageeat cageetggae | 660 |
| ctgatgacag atgetgaget ggetagagee gtgeetaaca tgeetaeate tgeeggeeag | 720 |
| atcaagetga tgetegagaa tagageeatg gteegaegga aaggettegg eattetgatt | 780 |
| ggegtgtaeg geageagegt gatetatatg gtgeagetge etatettegg egtgategae | 840 |
| acaccotgot ggattgtgaa ggoogotoot agotgtagog agaagaaggg caattaogoo | 900 |
| tgeetgetga gagaggaeea aggetggtat tgteagaaeg eeggeageae egtgtaetae | 960 |
| cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga | 1020 |
| atcaatgtgg cogagoagag caaagagtgo aacatcaaca toagoaccao caactatooo | 1080 |
| tgeaaggtgt ceaeeggeag geaeeetatt tetatggtgg etetgtetee tetgggagee | 1140 |
| ctggtggett gttataaggg egtgteetgt ageateggea geaacagagt gggeateate | 1200 |
| aagcagetga acaagggetg cagetacate aceaaceagg acgeegatae egtgaceate | 1260 |
| | |

| | | | | d. | |
|--|--|--|--|----|--|
| | | | | | |
| | | | | | |

| | | | -contin | | | |
|--|------------|------------|------------|------------|------------|--|
| gacaacaccg tgtatcagct g | Jagcaaggtg | gaaggegaae | agcacgtgat | caagggcaga | 1320 | |
| cctgtgteca gcagettega e | cctatcaag | tteeetgaga | accagttcca | ggtggccctg | 1380 | |
| gaccaggtgt tcgagaacat c | gagaattee | caggetetgg | tggaccagtc | caacagaatc | 1440 | |
| ctgtctagcg ccgagaaggg a | laacacegge | ttcatcatcg | tgatcatcct | gategeegtg | 1500 | |
| ctgggcagct ccatgatect g | gtgtccatc | ttcatcatta | tcaagaagac | caagaagccc | 1560 | |
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| tetgatggee etageetgat e | | | | | 240 | |
| ctcaagaccg tgtctgccga t | | | | | 300 | |
| ggcagctttg tgctgggagc c | | | | | 360 | |
| ggegtggeea tegetaagae e | | | | | 420 | |
| ctgaagaaga caaacgagge c | | | | | 480 | |
| geegtgegeg agetgaagga e | | | | | 540 | |
| aagtgegaea tegaegaeet g | | | | | 600 | |
| ctgaacgtcg tgcggcagtt t | | | - | | 660 720 | |
| ctgatgacag atgetgaget g | | | | | 720 | |
| atcaagetga tgetegagaa t | | | | | 840 | |
| ggegtgtaeg geageagegt g acaecetget ggattgtgaa g | | | | | 900 | |
| tgeetgetga gagaggacca a | | | | | 960 | |
| cotaacgaga aggactgoga g | | | | | 1020 | |
| atcaatgtgg cogagcagag d | | | | | 1020 | |
| tgcaaggtgt ccaccggcag g | | | | | 1140 | |
| ctggtggctt gttataaggg c | | | | | 1200 | |
| aagcagetga acaagggetg c | | | | | 1260 | |
| gacaacaccg tgtatcaget g | | | | | 1320 | |
| cetgtgteca geagettega o | | | | | 1380 | |
| gaccaggtgt tcgagaacat c | | | | | 1440 | |
| ctgtctagcg ccgagaaggg a | | | | | 1500 | |
| | | | | | 1560 | |
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tetgatggee etageetgat caagacegag etggatetge teaagagege eetgagagaa

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| ctcaagaccg | tgtctgccga | tcagetggee | agagaggaac | agatcgagaa | teetggeage | 300 |
|------------|-----------------------------------|------------|------------|------------|------------|------|
| ggcagetttg | tgctgggagc | cattgetett | ggagtggctg | ctgctgcagc | tgttacagca | 360 |
| ggcgtggcca | tcgctaagac | catcagactg | gaaagcgaag | tgaccgccat | caacaacgcc | 420 |
| ctgaagaaga | caaacgaggc | cgtcagcaca | ctcggcaatg | gcgttagagt | getggeeaca | 480 |
| gccgtgcgcg | agctgaagga | cttcgtgtcc | aagaacctga | cacgggccat | taacaagaac | 540 |
| aagtgcgaca | tcgacgacct | gaagatggcc | gtgtccttta | gccagttcaa | ceggeggttt | 600 |
| ctgaacgtcg | tgcggcagtt | tagcgacaac | gccggaatca | caccagecat | cagcetggae | 660 |
| ctgatgacag | atgetgaget | ggetagagee | gtgcctaaca | tgeetacate | tgccggccag | 720 |
| atcaagctga | tgctcgagaa | tagagccatg | gteegaegga | aaggettegg | cattetgatt | 780 |
| ggcgtgtacg | gcagcagcgt | gatctatatg | gtgcagetge | ctatettegg | cgtgatcgac | 840 |
| acaccctgct | ggattgtgaa | ggccgctcct | agetgtageg | agaagaaggg | caattacgcc | 900 |
| tgeetgetga | gagaggacca | aggetggtat | tgtcagaacg | ccggcagcac | cgtgtactac | 960 |
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| ctggtggctt | gttataaggg | cgtgtcctgt | agcatcggca | gcaacagagt | gggcatcatc | 1200 |
| aagcagetga | acaagggctg | cagctacatc | accaaccagg | acgccgatac | cgtgaccatc | 1260 |
| gacaacaccg | tgtatcagct | gagcaaggtg | gaaggcgaac | agcacgtgat | caagggcaga | 1320 |
| cctgtgtcca | gcagettega | ccctatcaag | ttccctgagg | atcagttcca | ggtggccctg | 1380 |
| gaccaggtgt | tcgagaacat | cgagaattcc | caggetetgg | tggaccagtc | caacagaatc | 1440 |
| ctgtctagcg | ccgagaaggg | aaacaccggc | ttcatcatcg | tgatcatcct | gategeegtg | 1500 |
| ctgggcagct | ccatgateet | ggtgtccatc | ttcatcatta | tcaagaagac | caagaagccc | 1560 |
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| accggctggt | acaccaacgt | gttcacactg | gaagtgggcg | acetegagaa | tetgacatge | 180 |
| tctgatggcc | ctagcctgat | caagaccgag | ctggatctga | ccaagagege | cctgagagaa | 240 |
| ctcaagaccg | tgtctgccga | tcagctggcc | agagaggaac | agatcgagaa | tcetggeage | 300 |
| ggcagetttg | tgctgggagc | cattgctctt | ggagtggetg | ctgctgcagc | tgttacagca | 360 |
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| geegtgegeg | agetgaagga | cttcgtgtcc | aagaacctga | cacgggccat | taacaagaac | 540 |
| aagtgcgaca | tegaegaeet | gaagatggcc | gtgtccttta | gccagttcaa | ccggcggttt | 600 |
| ctgaacgtcg | tgeggeagtt | tagcgacaac | gccggaatca | caccagccat | cageetggae | 660 |
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| -cont | inued |
|-------|--------|
| COILC | THUCU. |

| | | | | -contir | nued | | |
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| atcaagctga t | gctcgagaa | tagagccatg | gtccgacgga | aaggettegg | cattetgatt | 780 | |
| ggegtgtaeg g | cagcagcgt | gatetatatg | gtgcagetge | ctatcttcgg | cgtgatcgac | 840 | |
| acaccctgct g | gattgtgaa | ggeegeteet | agetgtageg | agaagaaggg | caattacgcc | 900 | |
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| ctgggcaget c | catgateet | ggtgtccatc | ttcatcatta | tcaagaagac | caagaagccc | 1560 | |
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| accggctggt a | caccaacgt | gttcacactg | gaagtgggcg | acgtcgagaa | tetgacatge | 180 | |
| tetgatggee e | tageetgat | caagaccgag | ctggatetga | ccaagagege | cctgagagaa | 240 | |
| ctcaagaccg t | gtetgeega | tcagetggee | agagaggaac | agategagaa | tcetggeage | 300 | |
| ggcagetttg t | getgggage | cattgetett | ggagtggetg | ctgetgeage | tgttacagca | 360 | |
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| geegtgegeg a | gctgaagga | ettegtgett | aagaacctga | cacgggccat | taacaagaac | 540 | |
| aagtgcgaca t | cgacgacct | gaagatggcc | gtgtccttta | gecagtteaa | ccggcggttt | 600 | |
| ctgaacgteg t | | | | | | 660 | |
| ctgatgacag a | | | | | | 720 | |
| atcaagetga t | gctcgagaa | tagagecatg | gtccgacgga | aaggettegg | cattetgatt | 780 | |
| ggcgtgtacg g | cagcagcgt | gatctatatg | gtgcagetgc | ctatcttcgg | cgtgatcgac | 840 | |
| | | | | | | 000 | |
| acaccctgct g | gattgtgaa | ggeegeteet | agetgtageg | agaagaaggg | caattacgee | 900 | |
| acaccctgct g tgcctgctga g | | | | | | 960 | |
| | agaggacca | aggetggtat | tgtcagaacg | ccggcagcac | cgtgtactac | | |
| tgeetgetga g | agaggacca ggactgcga | aggetggtat gacaagagge | tgtcagaacg gaccacgtgt | ccggcagcac tctgtgatac | cgtgtactac cgccgctgga | 960 | |
| tgcctgctga g cctaacgaga a | agaggacca ggactgcga cgagcagag | aggctggtat gacaagaggc caaagagtgc | tgtcagaacg gaccacgtgt aacatcaaca | ccggcagcac tctgtgatac tcagcaccac | cgtgtactac cgccgctgga caactatccc | 960 1020 | |

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| ctggtggctt | gttataaggg | cgtgtcctgt | agcatcggca | gcaacagagt | gggcatcatc | 1200 |
|------------|------------|------------|------------|------------|------------|------|
| aagcagetga | acaagggetg | cagetacate | accaaccagg | acgccgatac | cgtgaccatc | 1260 |
| gacaacaccg | tgtatcagct | gagcaaggtg | gaaggcgaac | agcacgtgat | caagggcaga | 1320 |
| cctgtgtcca | gcagcttcga | ccctatcaag | tteeetgagg | atcagttcca | ggtggccctg | 1380 |
| gaccaggtgt | tcgagaacat | cgagaattcc | caggetetgg | tggaccagtc | caacagaatc | 1440 |
| ctgtctagcg | ccgagaaggg | aaacaccggc | ttcatcatcg | tgatcatcct | gategeegtg | 1500 |
| ctgggcagct | ccatgatect | ggtgtccatc | ttcatcatta | tcaagaagac | caagaagccc | 1560 |
| accggcgctc | ctccagaact | gageggagtg | accaacaatg | getteateee | tcacaac | 1617 |

<210> SEQ ID NO 117 <211> LENGTH: 1617 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 117

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| accggegete etecagaact gageggagtg accaacaatg getteateee teacaac | 1617 |
|---|------|
| <210> SEQ ID NO 118 <211> LENGTH: 1617 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide | |
| <400> SEQUENCE: 118 | |
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| gagagetace tggaagagte etgeageace ateacagagg getacetgte tgtgetgaga | 120 |
| accggctggt acaccaacgt gttcacactg gaagtgggcg acctcgagaa tctgacatgc | 190 |
| totgatggoo otagootgat caagacogag otggatotgo toaagagogo ootgagagaa | 240 |
| ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc | 300 |
| ggcagetttg tgetgggage cattgetett ggagtggetg etgetgeage tgttacagea | 360 |
| ggegtggeea tegetaagae cateagaetg gaaagegaag tgaeegeeat caacaaegee | 420 |
| ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca | 480 |
| gccgtgcgcg agctgaagga cttcgtgctt aagaacctgt ggcgggccat taacaagaac | 540 |
| aagtgegaca tegaegaeet gaagatggee gtgteettta geeagtteaa eeggeggttt | 600 |
| ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac | 660 |
| ctgatgacag atgetgaget ggetagagee gtgeetaaca tgeetacate tgeeggeeag | 720 |
| atcaagetga tgetegagaa tagageeatg gteegaegga aaggettegg eattetgatt | 780 |
| ggogtgtaog goagoagogt gatotatatg gtgoagotgo otatottogg ogtgatogao | 840 |
| acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc | 900 |
| tgeetgetga gagaggaeca aggetggtat tgteagaaeg eeggeageae egtgtaetae | 960 |
| cctaacgaga aggactgega gacaagagge gaccaegtgt tetgtgatae egeegetgga | 1020 |
| atcaatgtgg cogagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc | 1080 |
| tgcaaggtgt ccaceggeag geacectatt tetatggtgg etetgtetee tetgggagee | 1140 |
| ctggtggett gttataaggg egtgteetgt ageateggea geaacagagt gggeateate | 1200 |
| aagcagetga acaagggetg cagetacate aceaaceagg acgeegatae egtgaceate | 1260 |
| gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga | 1320 |
| cetgtgteca geagettega ecctateaag tteeetgagg ateagtteea ggtggeeetg | 1380 |
| gaccaggtgt tegagaacat egagaattee caggetetgg tggaccagte caacagaate | 1440 |
| ctgtctageg cogagaaggg aaacacogge tteateateg tgateateet gategeegtg | 1500 |
| ctgggcaget ceatgateet ggtgteeate tteateatta teaagaagae eaagaageee | 1560 |
| accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac | 1617 |
| <210> SEQ ID NO 119 <211> LENGTH: 1617 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 119 | |
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| gagagetace tggaagagte etgeageace ateaeagagg getaeetgte tgtgetgaga | 120 |

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accggctggt acaccaacgt gttcacactg cctgtgggcg acgtcgagaa tctgacatgc

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180

| totgatggoo otagootgat caagacogag otggatotga ocaagagogo ootgagagaa 240 |) |
|--|---|
| ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcage 300 |) |
| ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360 |) |
| ggegtggeea tegetaagae cateagaetg gaaagegaag tgaeegeeat caacaaegee 420 |) |
| ctgaagaaga caaacgagge egteageaca eteggeaatg gegttagagt getggeeaca 480 |) |
| gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540 |) |
| aagtgegaea tegaegaeet gaagatggee gtgteettta geeagtteaa eeggeggttt 600 |) |
| ctgaacgtog tgoggoagtt tagogacaac googgaatca caccagocat cagootggac 660 |) |
| ctgatgacag atgetgaget ggetagagee gtgeetaaca tgeetacate tgeeggeeag 720 |) |
| atcaagetga tgetegagaa tagageeatg gteegaegga aaggettegg eattetgatt 780 |) |
| ggegtgtaeg geageagegt gatetatatg gtgeagetge etatettegg egtgategae 840 |) |
| acaceetget ggattgtgaa ggeegeteet agetgtageg agaagaaggg caattaegee 900 |) |
| tgeetgetga gagaggaeca aggetggtat tgteagaaeg eeggeageae egtgtaetae 960 |) |
| cctaacgaga aggactgoga gacaagaggo gaccacgtgt totgtgatac ogoogotgga 1020 |) |
| atcaatgtgg cegageagag caaagagtge aacatcaaca teageaceae caactateee 1080 |) |
| tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagce 1140 |) |
| ctggtggett gttataaggg cgtgteetgt ageateggea geaacagagt gggeateate 1200 |) |
| aagcagetga acaagggetg cagetacate aceaaceagg aegeegatae egtgaceate 1260 |) |
| gacaacaccg tgtatcaget gagcaaggtg gaaggegaac agcaegtgat caagggeaga 1320 |) |
| cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380 |) |
| gaccaggtgt tegagaacat egagaattee caggetetgg tggaccagte caacagaate 1440 |) |
| ctgtctageg cegagaaggg aaacacegge tteateateg tgateateet gategeegtg 1500 |) |
| ctgggcaget ceatgateet ggtgteeate tteateatta teaagaagae caagaageee 1560 |) |
| accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 1617 | 7 |
| <210> SEQ ID NO 120 <211> LENGTH: 1617 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide | |
| <400> SEQUENCE: 120 | |
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| gagagetace tggaagagte etgeageace ateaeagagg getaeetgte tgtgetgaga 120 |) |
| accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180 |) |
| tetgatggee etageetgat caagacegag etggatetga ecaagagege eetgagagaa 240 |) |
| ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcage 300 |) |
| ggcagetttg tgetgggage cattgetett ggagtggetg etgetgeage tgttacagea 360 |) |
| ggogtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420 |) |
| ctgaagaaga caaacgagge egteageaca eteggeaatg gegttagagt getggeeaca 480 |) |
| geegtgegeg agetgaagga ettegtgtee aagaaeetga eaegggeeat taacaagaae 540 |) |
| | |

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| | | | | CONCIN | 1404 | | |
|----------------------------|---|-----------------------------|------------|------------|------------|------|--|
| aagtgcgaca | teeetgaeet | gaagatggcc | gtgtccttta | gccagttcaa | ccggcggttt | 600 | |
| ctgaacgtcg | tgcggcagtt | tagcgacaac | gccggaatca | caccagecat | cagcctggac | 660 | |
| ctgatgacag | atgetgaget | ggetagagee | gtgcctaaca | tgeetacate | tgeeggeeag | 720 | |
| atcaagctga | tgetegagaa | tagagccatg | gteegaegga | aaggettegg | cattetgatt | 780 | |
| ggcgtgtacg | gcagcagcgt | gatctatatg | gtgcagetgc | ctatcttcgg | cgtgatcgac | 840 | |
| acaccetget | ggattgtgaa | ggeegeteet | agetgtageg | agaagaaggg | caattacgcc | 900 | |
| tgeetgetga | gagaggacca | aggetggtat | tgtcagaacg | ccggcagcac | cgtgtactac | 960 | |
| cctaacgaga | aggactgcga | gacaagaggc | gaccacgtgt | tetgtgatae | cgccgctgga | 1020 | |
| atcaatgtgg | ccgagcagag | caaagagtgc | aacatcaaca | tcagcaccac | caactatccc | 1080 | |
| tgcaaggtgt | ccaccggcag | gcaccctatt | tctatggtgg | ctctgtctcc | tetgggagee | 1140 | |
| ctggtggctt | gttataaggg | cgtgtcctgt | agcatcggca | gcaacagagt | gggcatcatc | 1200 | |
| aagcagetga | acaagggctg | cagctacatc | accaaccagg | acgccgatac | cgtgaccatc | 1260 | |
| gacaacaccg | tgtatcagct | gagcaaggtg | gaaggegaae | agcacgtgat | caagggcaga | 1320 | |
| cctgtgtcca | gcagettega | ccctatcaag | tteeetgagg | atcagttcca | ggtggccctg | 1380 | |
| gaccaggtgt | tcgagaacat | cgagaattcc | caggetetgg | tggaccagtc | caacagaatc | 1440 | |
| ctgtctagcg | ccgagaaggg | aaacaccggc | ttcatcatcg | tgatcatcct | gategeegtg | 1500 | |
| ctgggcaget | ccatgateet | ggtgtccatc | ttcatcatta | tcaagaagac | caagaagccc | 1560 | |
| accggcgctc | ctccagaact | gagcggagtg | accaacaatg | getteateee | tcacaac | 1617 | |
| <220> FEATU <223> OTHER | TH: 1617 : DNA NISM: Artif: JRE: R INFORMATIC | icial Seque ON: Synthet: | | eotide | | | |
| <400> SEQUE | ENCE: 121 | | | | | | |
| atgagetgga | aggtggtcat | catcttcage | ctgctgatca | cacctcagca | cggcctgaaa | 60 | |
| gagagetace | tggaagagtc | ctgcageace | atcacagagg | getacetgte | tgtgctgaga | 120 | |
| accggctggt | acaccaacgt | gttcacactg | gaagtgggcg | acgtegagaa | tetgaeatge | 180 | |
| tetgatggee | ctageetgat | caagaccgag | ctggatctga | ccaagagege | cctgagagaa | 240 | |
| | | tcagetggee | | | | 300 | |
| ggcagetttg | tgetgggage | cattgetett | ggagtggetg | ctgctgcagc | tgttacagca | 360 | |
| ggcgtggcca | tegetaagae | catcagactg | gaaagcgaag | tgacegecat | caacaacgcc | 420 | |
| | | cgtcagcaca | | | | 480 | |
| | | cttegtgtee | | | - | 540 | |
| aagtgcccta | tcgacgacct | gaagatggcc | gtgtccttta | gccagttcaa | ccggcggttt | 600 | |
| ctgaacgtcg | tgcggcagtt | tagcgacaac | gccggaatca | caccagecat | cageetggae | 660 | |
| ctgatgacag | atgetgaget | ggetagagee | gtgeetaaca | tgeetacate | tgeeggeeag | 720 | |
| atcaagctga | tgetegagaa | tagagecatg | gteegaegga | aaggettegg | cattetgatt | 780 | |
| ggcgtgtacg | gcagcagcgt | gatctatatg | gtgcagetge | ctatettegg | cgtgatcgac | 840 | |
| acaccctgct | ggattgtgaa | ggeegeteet | agetgtageg | agaagaaggg | caattacgcc | 900 | |
| tgeetgetga | gagaggacca | aggetggtat | tgtcagaacg | ccggcagcac | cgtgtactac | 960 | |
| cctaacgaga | aggactgcga | gacaagaggc | gaccacgtgt | tetgtgatae | cgccgctgga | 1020 | |
| | | | | | | | |

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| atcaatgtgg | ccgagcagag | caaagagtgc | aacatcaaca | teageaceac | caactateee | 1080 |
|-------------|------------|------------|------------|------------|------------|------|
| tgcaaggtgt | ccaccggcag | gcaccctatt | tctatggtgg | ctctgtctcc | tetgggagee | 1140 |
| ctggtggett | gttataaggg | cgtgtcctgt | agcatcggca | gcaacagagt | gggcatcatc | 1200 |
| aagcagetga | acaagggctg | cagctacatc | accaaccagg | acgccgatac | cgtgaccatc | 1260 |
| gacaacaccg | tgtatcagct | gagcaaggtg | gaaggcgaac | agcacgtgat | caagggcaga | 1320 |
| cctgtgtcca | gcagettega | ccctatcaag | ttccctgagg | atcagttcca | ggtggccctg | 1380 |
| gaccaggtgt | tcgagaacat | cgagaattcc | caggetetgg | tggaccagtc | caacagaatc | 1440 |
| ctgtctagcg | ccgagaaggg | aaacaccggc | ttcatcatcg | tgatcatcct | gategeegtg | 1500 |
| ctgggcagct | ccatgateet | ggtgtccatc | ttcatcatta | tcaagaagac | caagaagccc | 1560 |
| accggcgctc | ctccagaact | gagcggagtg | accaacaatg | getteateee | tcacaac | 1617 |
| <210> SEO : | ID NO 122 | | | | | |

<210> SEQ ID NO 122
<211> LENGTH: 1617
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Polynucleotide

<400> SEQUENCE: 122

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| -continued | | | | | | | |
|--|------|--|--|--|--|--|--|
| etgtctageg eegagaaggg aaacacegge tteateateg tgateateet gategeegtg | 1500 | | | | | | |
| etgggeaget ceatgateet ggtgteeate tteateatta teaagaagae eaagaageee | 1560 | | | | | | |
| accggcgctc ctocagaact gagcggagtg accaacaatg gcttcatcoc tcacaac | 1617 | | | | | | |
| <210> SEQ ID NO 123 <211> LENGTH: 1617 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide | | | | | | | |
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| gagagetace tggaagagte etgeageace ateacagagg getacetgte tgtgetgaga | 120 | | | | | | |
| accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc | 180 | | | | | | |
| tetgatggee etageetgat caagacegag etggatetga ceaagagege eetgagagaa | 240 | | | | | | |
| ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc | 300 | | | | | | |
| ggcagetttg tgetgggage cattgetett ggagtggetg etgetgeage tgttaeagea | 360 | | | | | | |
| ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc | 420 | | | | | | |
| ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca | 480 | | | | | | |
| gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac | 540 | | | | | | |
| aagtgegaca tegacgacet gaagatggee gtgteettta geeagtteaa eeggeggttt | 600 | | | | | | |
| ctgaacgtog tgoggeagtt tagogacaac googgaatca caccagocat cagootggac | 660 | | | | | | |
| ctgatgacag atgetgaget ggetagagee gtgeetaaca tgeetacate tgeeggeeag | 720 | | | | | | |
| atcaagetga tgetegagaa tagageeatg gteegaegga aaggettegg cattetgatt | 780 | | | | | | |
| ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac | 840 | | | | | | |
| acaccetget ggattgtgaa ggeegeteet agetgtageg agaagaaggg caattaegee | 900 | | | | | | |
| tgeetgetga gagaggacea aggetggtat tgteagaaeg eeggeageae egtgtaetae | 960 | | | | | | |
| cctaacgaga aggactgcga gacaagaggc gaccacgtgt totgtgatac cgccgctgga | 1020 | | | | | | |
| atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc | 1080 | | | | | | |
| tgeaaggtgt ceaceggeag geacectatt tetatggtgg etetgtetee tetgggagee | 1140 | | | | | | |
| etggtggett gttataaggg egtgteetgt ageateggea geaacagagt gggeateate | 1200 | | | | | | |
| aagcagetga acaagggetg cagetacate accaaceagg acgeegatae egtgaceate | 1260 | | | | | | |
| gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga | 1320 | | | | | | |
| cetgtgteca geagettece acctateaag tteeetgagg ateagtteea ggtggeeetg | 1380 | | | | | | |
| gaccaggtgt tegagaacat egagaattee eaggetetgg tggaccagte eaacagaate | 1440 | | | | | | |
| ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg | 1500 | | | | | | |
| ctgggcagct ccatgatect ggtgtecate tteateatta teaagaagae caagaageee | 1560 | | | | | | |
| accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac | 1617 | | | | | | |
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699

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60

700

| gagagetaee tggaagagte | ctgcagcacc | atcacagagg | gctacctgtc | tgtgctgaga | 120 |
|--|------------|------------|------------|------------|------|
| accggctggt acaccaacgt | gttcacactg | gaagtgggcg | acgtcgagaa | tetgacatge | 180 |
| tetgatggee ctageetgat | caagaccgag | ctggatctga | ccaagagcgc | cctgagagaa | 240 |
| ctcaagaccg tgtctgccga | tcagctggcc | agagaggaac | agatcgagaa | tcctggcagc | 300 |
| ggcagetttg tgetgggage | cattgetett | ggagtggetg | ctgctgcagc | tgttacagca | 360 |
| ggegtggeea tegetaagae | catcagactg | gaaagcgaag | tgaccgccat | caacaacgcc | 420 |
| ctgaagaaga caaacgaggo | cgtcagcaca | ctcggcaatg | gcgttagagt | getggeeaca | 480 |
| geegtgegeg agetgaagga | cttcgtgtcc | aagaacctga | cacgggccat | taacaagaac | 540 |
| aagtgegaca tegaegaeet | gaagatggcc | gtgtccttta | gccagttcaa | ccggcggttt | 600 |
| ctgaacgtcg tgcggcagtt | tagegacaac | gccggaatca | caccagccat | cageetggae | 660 |
| ctgatgacag atgetgaget | ggetagagee | gtgcctaaca | tgeetacate | tgeeggeeag | 720 |
| atcaagetga tgetegagaa | tagagecatg | gtccgacgga | aaggettegg | cattetgatt | 780 |
| ggcgtgtacg gcagcagcgt | gatetatatg | gtgcagetge | ctatettegg | cgtgatcgac | 840 |
| acaccctgct ggattgtgaa | ggeegeteet | agetgtageg | agaagaaggg | caattacgcc | 900 |
| tgeetgetga gagaggaeea | aggetggtat | tgtcagaacg | ccggcagcac | cgtgtactac | 960 |
| cctaacgaga aggactgcga | gacaagaggc | gaccacgtgt | tctgtgatac | cgccgctgga | 1020 |
| atcaatgtgg ccgagcagag | caaagagtgc | aacatcaaca | tcagcaccac | caactatccc | 1080 |
| tgcaaggtgt ccaccggcag | gcaccctatt | tctatggtgg | ctctgtctcc | tetgggagee | 1140 |
| ctggtggctt gttataaggg | cgtgtcctgt | agcatcggca | gcaacagagt | gggcatcatc | 1200 |
| aagcagetga acaagggetg | cagetacate | accaaccagg | acgccgatac | cgtgaccatc | 1260 |
| gacaacaccg tgtatcagct | gagcaaggtg | gaaggcgaac | agcacgtgat | caagggcaga | 1320 |
| cetgtgteea geagettega | ccctatcaag | ttccctgaga | accagttcca | ggtggccctg | 1380 |
| gaccaggtgt tegagaacat | cgagaattcc | caggetetgg | tggaccagtc | caacagaatc | 1440 |
| ctgtctagcg ccgagaaggg | aaacaccggc | ttcatcatcg | tgatcatcct | gategeegtg | 1500 |
| ctgggcaget ccatgateet | ggtgtccatc | ttcatcatta | tcaagaagac | caagaagccc | 1560 |
| accggcgctc ctccagaact | gageggagtg | accaacaatg | getteateee | tcacaac | 1617 |
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| gagagetace tggaagagte | ctgcagcacc | atcacagagg | getacetgte | tgtgctgaga | 120 |
| accggctggt acaccaacgt | gttcacactg | gaagtgggcg | acgtegagaa | tetgacatge | 180 |
| tetgatggee ctageetgat | caagaccgag | ctggatetga | ccaagagcgc | cctgagagaa | 240 |
| ctcaagaccg tgtctgccga | tcagetggee | agagaggaac | agatogagaa | tcctggcagc | 300 |
| ggcagetttg tgetgggage | cattgetett | ggagtggetg | ctgctgcagc | tgttacagca | 360 |
| ggegtggeea tegetaagae | catcagactg | gaaagcgaag | tgaccgccat | caacaacgcc | 420 |
| | | | | | |

701

| ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca | 480 |
|--|---|
| gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac | 540 |
| aagtgegaea tegaegaeet gaagatggee gtgteettta geeagtteaa eeggeggttt | 600 |
| ctgaacgtog tgoggoagtt tagogacaac googgaatca caccagocat cagootggac | 660 |
| ctgatgacag atgetgaget ggetagagee gtgeetaaca tgeetacate tgeeggeeag | 720 |
| atcaagetga tgetegagaa tagageeatg gteegaegga aaggettegg cattetgatt | 780 |
| ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac | 840 |
| acaccetget ggattgtgaa ggeegeteet agetgtageg agaagaaggg caattaegee | 900 |
| tgeetgetga gagaggaeca aggetggtat tgteagaaeg eeggeageae egtgtaetae | 960 |
| cctaacgaga aggactgoga gacaagaggo gaccacgtgt totgtgatac ogoogotgga | 1020 |
| atcaatgtgg cegagcagag caaagagtgc aacatcaaca tcagcaccac caactateee | 1080 |
| tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagec | 1140 |
| ctggtggett gttataaggg egtgteetgt ageateggea geaacagagt gggeateate | 1200 |
| aagcagetga acaagggetg cagetacate aceaaceagg acgeegatae egtgaceate | 1260 |
| gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga | 1320 |
| cetgtgteca geagettega ecetateaag tteeeteagg ateagtteea ggtggeeetg | 1380 |
| gaccaggtgt tegagaacat egagaattee caggetetgg tggaccagte caacagaate | 1440 |
| ctgtctageg eegagaaggg aaacaeegge tteateateg tgateateet gategeegtg | 1500 |
| ctgggcaget ceatgateet ggtgteeate tteateatta teaagaagae caagaageee | 1560 |
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| <211> LENGTH: 1617 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 126 | 60 120 |
| <211> LENGTH: 1617 <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATURE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 126 atgagetgga aggtggteat catetteage etgetgatea caceteagea eggeetgaaa | |
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| <pre><211> LENGTH: 1617 <212> TYPE: DNA <212> TYPE: DNA <213> ORGANISM: Artificial Sequence <220> FEATORE: <223> OTHER INFORMATION: Synthetic Polynucleotide <400> SEQUENCE: 126 atgagetgga aggtggteat catetteage etgetgatea caeeteagea eggeetgaaa gagagetace tggaagagte etgeageace ateaeagagg getaeetgte tgtgetgaga aceggetggt acaecaaegt gtteaeaetg gaagtgggeg acgtegagaa tetgaeatge tetgatggee etageetgat eaagaeegag etggatetga ceaagagege eetgagagaa cteaagaeeg tgtetgeega teagetggee aggaggaae agategagaa teetggeage</pre> | 120 180 240 300 |
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703

704

| - tgeetgetga gagaggaeea aggetggtat tgteagaaeg eeggeageae egtgtaetae 960 | | | | | | |
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| cctaacgaga aggactgoga gacaagaggo gaccaogtgt totgtgatao ogoogotgga 1020 | | | | | | |
| atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080 | | | | | | |
| tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140 | | | | | | |
| ctggtggett gttataaggg egtgteetgt ageateggea geaacagagt gggeateate 1200 | | | | | | |
| aagcagetga acaagggetg cagetacate aceaaceagg acgeegatae egtgaceate 1260 | | | | | | |
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| cctgtgtcca gcagettega eestateaag tteeetgagg ateagtteea ggtggeeetg 1380 | | | | | | |
| gaccaggtgt tegagaacat egagaattee eaggetetgg tggaccagte caacagaate 1440 | | | | | | |
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| ctgggcaget ceatgateet ggtgteeate tteateatta teaagaagae caagaageee 1560 | | | | | | |
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| aceggeuggu acaeeaaegu guucaeaeug gaagugggeg aeguegagaa ueugaeauge 180 | | | | | | |
| ucugauggee cuagecugau caagaeegag cuggaucuga eeaagagege eeugagagaa 240 | | | | | | |
| cucaagaceg ugueugeega ucageuggee agagaggaae agauegagaa uceuggeage 300 | | | | | | |
| ggcageuuug ugeugggage cauugeueuu ggaguggeug eugeugeage uguuacagea 360 | | | | | | |
| ggcguggcca ucugcaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420 | | | | | | |
| cugaagaaga caaacgagge egucageaca cueggeaaug geguuagagu geuggeeuuu 480 | | | | | | |
| gcegugegeg ageugaagga cuucguguee aagaaceuga caegggeeeu gaacaagaae 540 | | | | | | |
| aagugegaea uegaegaeeu gaagauggee gugueeuuua geeaguueaa eeggegguuu 600 | | | | | | |
| cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660 | | | | | | |
| cugaugacag augeugageu ggeuagagee gugeeuaaca ugeeuacaue ugeeggeeag 720 | | | | | | |
| aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugugu 780 | | | | | | |
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| cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200 | | | | | | |
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| cugucuageg cegagaaggg aaacacegge uucaucaueg ugaucaueeu gauegeegug | 1500 |
| cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc | 1560 |
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| ucugauggee cuagecugau caagaeegag cuggaucuga ceaagagege ceugagagaa | 240 |
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| ccuaacgaga aggacugcga gacaagaggo gaccacgugu ucugugauac cgccgcugga | 1020 |
| aucaaugugg cogagcagag caaagagugo aacaucaaca ucagcaccac caacuaucco | 1080 |
| ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc | 1140 |
| cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc | 1200 |
| aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc | 1260 |
| dacaacacca nanancadon dadcaaddna daaddodaac adcacandan caadddcada | 1320 |
| ccugugueca geageuuega eccuaueaag uueccugage accaguggea uguggeecug | 1380 |
| gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc | 1440 |
| cugucuageg cegagaaggg aaacacegge uucaucaueg ugaucaueeu gauegeegug | 1500 |
| cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagcc | 1560 |
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<210> SEQ ID NO 129 <211> LENGTH: 1617 <212> TYPE: RNA <213> ORGANISM: Artificial Sequence

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709

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300

360

420

480

540

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711

712

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| accggcuggu | acaccaacgu | guucacacug | gaagugggcg | acgucgagaa | ucugacaugc | 180 |
| ucugauggee | cuagccugau | caagaccgag | cuggaucugc | ucaagagcgc | ccugagagaa | 240 |
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| ugcaaggugu | ccaccggcag | gcacccuauu | ucuauggugg | cucugucucc | ucugggagcc | 1140 |
| | guuauaaggg | | | | | 1200 |
| 55-555 Au | 5 | J J | 5 | J | | |

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| cugggcageu ceaugaueeu ggugueeaue uueaueauua ueaagaagae caagaageee | 1560 | | | |
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| aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu | 840 |
| acacceuden adamandada adeedenen adenanaede adaadaadda caannaedee | 900 |
| udecendenden abaundanden abeeldenen uderstanden abendende eine eine eine eine eine eine ei | 960 |
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| aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuaucco | 1030 |
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| conditioned a contraction contraction of the second s | 1440 |
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726

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| ucugauggee cuagecugau caagaeegag cuggaucuga ceaagagege ceugagagaa | 240 |
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| cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc | 1560 |
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600

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| | or | | | | |
|--|----|--|--|--|--|
| | | | | | |

| | | | | -contir | nued | | |
|--|--------------------------------------|------------|------------|------------|------------|------|--|
| ccuaacgaga a | aggacugcga | gacaagaggc | gaccacgugu | ucugugauac | cgccgcugga | 1020 | |
| aucaaugugg d | ccgagcagag | caaagagugc | aacaucaaca | ucagcaccac | caacuauccc | 1080 | |
| ugcaaggugu d | ccaccggcag | gcacccuauu | ucuauggugg | cucugucucc | ucugggagee | 1140 | |
| cugguggcuu g | guuauaaggg | cguguccugu | agcaucggca | gcaacagagu | gggcaucauc | 1200 | |
| aagcagcuga a | acaagggcug | cagcuacauc | accaaccagg | acgccgauac | cgugaccauc | 1260 | |
| gacaacaccg u | uguaucagcu | gagcaaggug | gaaggcgaac | agcacgugau | caagggcaga | 1320 | |
| ccugugucca g | gcagcuucga | cccuaucaag | uucccugagg | aucaguucca | gguggeeeug | 1380 | |
| gaccaggugu ı | ucgagaacau | cgagaauucc | caggcucugg | uggaccaguc | caacagaauc | 1440 | |
| cugucuageg o | ccgagaaggg | aaacaccggc | uucaucaucg | ugaucauccu | gaucgccgug | 1500 | |
| cugggcagcu d | ccaugauccu | gguguccauc | uucaucauua | ucaagaagac | caagaagccc | 1560 | |
| accggcgcuc d | cuccagaacu | gagcggagug | accaacaaug | gcuucauccc | ucacaac | 1617 | |
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| accggcuggu a | acaccaacgu | guucacacug | gaagugggcg | acgucgagaa | ucugacaugc | 180 | |
| ucugauggee o | cuagccugau | caagaccgag | cuggaucuga | ccaagagcgc | ccugagagaa | 240 | |
| cucaagaeeg u | igucugcega | ucageuggee | agagaggaac | agaucgagaa | uccuggcagc | 300 | |
| ggcagcuuug u | ugcugggagc | cauugcucuu | ggaguggcug | cugcugcagc | uguuacagca | 360 | |
| ggcguggcca ı | ucgcuaagac | caucagacug | ccuagegaag | ugacegecau | caacaacgcc | 420 | |
| cugaagaaga d | caaacgaggc | cgucagcaca | cucggcaaug | gcguuagagu | gcuggccaca | 480 | |
| geegugegeg a | agcugaagga | cuucgugucc | aagaaccuga | cacgggccau | uaacaagaac | 540 | |
| aagugegaca u | ucgacgaccu | gaagauggee | guguccuuua | gccaguucaa | ccggcgguuu | 600 | |
| cugaacgucg u | ugeggeaguu | uagegacaac | geeggaauca | caccagecau | cagecuggae | 660 | |
| cugaugacag a | augcugagcu | ggcuagagee | gugccuaaca | ugccuacauc | ugeeggeeag | 720 | |
| aucaagcuga u | ugcucgagaa | uagagccaug | guccgacgga | aaggcuucgg | cauucugauu | 780 | |
| ggeguguaeg g | gcagcagcgu | gaucuauaug | gugcagcugc | cuaucuucgg | cgugaucgac | 840 | |
| acacccugcu ç | ggauugugaa | ggeegeueeu | agcuguagcg | agaagaaggg | caauuacgcc | 900 | |
| ugecugeuga g | gagaggacca | aggcugguau | ugucagaacg | ccggcagcac | cguguacuac | 960 | |
| ccuaacgaga a | aggacugcga | gacaagaggc | gaccacgugu | ucugugauac | cgccgcugga | 1020 | |
| aucaaugugg d | ccgagcagag | caaagagugc | aacaucaaca | ucagcaccac | caacuauccc | 1080 | |
| ugcaaggugu d | ccaccggcag | gcacccuauu | ucuauggugg | cucugucucc | ucugggagcc | 1140 | |
| cugguggcuu ç | guuauaaggg | cguguccugu | agcaucggca | gcaacagagu | gggcaucauc | 1200 | |
| aagcagcuga a | acaagggcug | cagcuacauc | accaaccagg | acgeegauae | cgugaccauc | 1260 | |
| gacaacaccg ι | uguaucagcu | gagcaaggug | gaaggcgaac | agcacgugau | caagggcaga | 1320 | |
| ccugugucca g | gcagcuucga | cccuaucaag | uucccugagg | aucaguucca | gguggeeeug | 1380 | |
| gaccaggugu u | | _ | | - | | 1440 | |
| | | 5 5 | 55 | 55 | | | |

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| cugucuageg cegagaaggg | aaacaccggc | uucaucaucg | ugaucauccu | gaucgccgug | 1500 |
|--|-------------|------------|------------|------------|------|
| cugggcagcu ccaugauccu | gguguccauc | uucaucauua | ucaagaagac | caagaagccc | 1560 |
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| gagageuace uggaagague | | | | | 120 |
| accggcuggu acaccaacgu | | | | | 180 |
| ucugauggee cuagecugau | | | | | 240 |
| cucaagaceg ugucugeega | | | | | 300 |
| ggcagcuuug ugcugggagc | | | | | 360 |
| ggcguggcca ucgcuaagac | | | | | 420 |
| cugaagaaga caaacgaggc | | | | | 480 |
| geegugegeg ageugaagga | | | | | 540 |
| aagugegaca uegaegaeeu | | | | | 600 |
| cugaacgucg ugcggcaguu | | | | | 660 |
| cugaugacag augcugagcu | | | | | 720 |
| aucaagcuga ugcucgagaa | | | | | 780 |
| ggcguguacg gcagcagcgu | | | | | 840 |
| acacccugcu ggauugugaa | | | | | 900 |
| ugccugcuga gagaggacca | | | | | 960 |
| ccuaacgaga aggacugcga | | | | | 1020 |
| aucaaugugg ccgagcagag | | | | | 1080 |
| ugcaaggugu ccaccggcag | | | | | 1140 |
| cugguggcuu guuauaaggg | | | | | 1200 |
| aagcagcuga acaagggcug | | | | | 1260 |
| gacaacaccg uguaucagcu | gagcaaggug | gaaggegaae | agcacgugau | caagggcaga | 1320 |
| ccugugueca geageuuece | accuaucaag | uucccugagg | aucaguucca | gguggeeeug | 1380 |
| gaccaggugu ucgagaacau | cgagaauucc | caggeucugg | uggaccaguc | caacagaauc | 1440 |
| cugucuageg cegagaaggg | aaacaccggc | uucaucaucg | ugaucauccu | gauegeegug | 1500 |
| cugggcagcu ccaugauccu | | | | | 1560 |
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| | 7-7-224948 | | Jeastatoo | | |
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| gagagcuacc | uggaagaguc | cugcagcacc | aucacagagg | gcuaccuguc | ugugcugaga | 120 | |
| accggcuggu | acaccaacgu | guucacacug | gaagugggcg | acgucgagaa | ucugacauge | 190 | |
| ucugauggee | cuagccugau | caagaccgag | cuggaucuga | ccaagagcgc | ccugagagaa | 240 | |
| cucaagaccg | ugucugeega | ucagcuggcc | agagaggaac | agaucgagaa | uccuggcagc | 300 | |
| ggcagcuuug | ugcugggagc | cauugcucuu | ggaguggcug | cugcugcagc | uguuacagca | 360 | |
| ggcguggcca | ucgcuaagac | caucagacug | gaaagcgaag | ugacegecau | caacaacgcc | 420 | |
| cugaagaaga | caaacgaggc | cgucagcaca | cucggcaaug | gcguuagagu | gcuggccaca | 480 | |
| geegugegeg | agcugaagga | cuucgugucc | aagaaccuga | cacgggccau | uaacaagaac | 540 | |
| aagugcgaca | ucgacgaccu | gaagauggcc | guguccuuua | gccaguucaa | ccggcgguuu | 600 | |
| cugaacgucg | ugeggeaguu | uagegacaac | gccggaauca | caccagecau | cagccuggac | 660 | |
| cugaugacag | augcugagcu | ggcuagagcc | gugccuaaca | ugccuacauc | ugeeggeeag | 720 | |
| aucaagcuga | ugcucgagaa | uagagccaug | guccgacgga | aaggcuucgg | cauucugauu | 780 | |
| ggeguguaeg | gcagcagcgu | gaucuauaug | gugcagcugc | cuaucuucgg | cgugaucgac | 840 | |
| acacccugcu | ggauugugaa | ggccgcuccu | agcuguagcg | agaagaaggg | caauuacgcc | 900 | |
| ugecugeuga | gagaggacca | aggcugguau | ugucagaacg | ccggcagcac | cguguacuac | 960 | |
| ccuaacgaga | aggacugcga | gacaagaggc | gaccacgugu | ucugugauac | cgccgcugga | 1020 | |
| aucaaugugg | ccgagcagag | caaagagugc | aacaucaaca | ucagcaccac | caacuauccc | 1080 | |
| ugcaaggugu | ccaccggcag | gcacccuauu | ucuauggugg | cucugucucc | ucugggagee | 1140 | |
| cugguggcuu | guuauaaggg | cguguccugu | agcaucggca | gcaacagagu | gggcaucauc | 1200 | |
| aagcagcuga | acaagggcug | cagcuacauc | accaaccagg | acgccgauac | cgugaccauc | 1260 | |
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| gaccaggugu | ucgagaacau | cgagaauucc | caggeucugg | uggaccaguc | caacagaauc | 1440 | |
| cugucuageg | ccgagaaggg | aaacaccggc | uucaucaucg | ugaucauccu | gauegeegug | 1500 | |
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| | uggaagaguc | | | | | 120 | |
| | acaccaacgu | | | | | 180 | |
| | | | | | | 240 | |
| | cuagccugau | | | | | | |
| | ugucugcega | | | | | 300 | |
| ggcagcuuug | ugcugggagc | cauugcucuu | ggaguggcug | cugcugcagc | uguuacagca | 360 | |
| ggeguggeea | ucgcuaagac | caucagacug | gaaagcgaag | ugacegeeau | caacaacgcc | 420 | |

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| cugaagaaga caaacgaggc | cgucagcaca | cucggcaaug | gcguuagagu | gcuggccaca | 480 |
|--|--|--|--|--|------------|
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| aagugegaea uegaegaeeu | gaagauggee | guguccuuua | gccaguucaa | ccggcgguuu | 600 |
| cugaacgucg ugcggcaguu | uagcgacaac | gccggaauca | caccagccau | cagccuggac | 660 |
| cugaugacag augcugagcu | ggcuagagee | gugccuaaca | ugccuacauc | ugccggccag | 720 |
| aucaagcuga ugcucgagaa | uagagccaug | guccgacgga | aaggcuucgg | cauucugauu | 780 |
| ggcguguacg gcagcagcgu | gaucuauaug | gugcagcugc | cuaucuucgg | cgugaucgac | 840 |
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| accggcuggu acaccaacgu | | | | | 180 |
| ucugauggee cuagecugau | | | | | 240 |
| cucaagaccg ugucugccga | ucageuggee | agagaggaac | agaucgagaa | uccuggcage | 300 |
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What is claimed is:

1. A composition, comprising: a messenger ribonucleic acid (mRNA) comprising an open reading frame encoding a betacoronavirus (BetaCoV) S protein or S protein subunit formulated in a lipid nanoparticle.

2. The composition of claim 1, wherein the open reading ³⁰ frame encodes a BetaCoV S protein.

3. The composition of claim 1, wherein the open reading frame encodes an S protein subunit selected from an S1 subunit and an S2 subunit.

4. The composition of claim **1**, wherein the mRNA further 35 comprising a 5' untranslated region (UTR) and a 3' UTR.

5. The composition of claim 4, wherein the mRNA further comprises a poly(A) tail.

6. The composition of claim 4, wherein the mRNA further comprises a 5' cap analog.

7. The composition of claim 6, wherein the 5' cap analog is 7mG(5')ppp(5')NImpNp.

8. The composition of claim 1, wherein the mRNA comprises a chemical modification.

9. The composition of claim **8**, wherein the chemical 45 modification is a 1-methylpseudouridine modification or a 1-ethylpseudouridine modification.

10. The composition of claim 8, wherein at least 80% of the uracil in the open reading frame has a chemical modification.

11. The composition of claim 1, wherein the lipid nanoparticle comprises an ionizable cationic lipid, a neutral lipid, a sterol, and a PEG-modified lipid.

12. The composition of claim 11, wherein the lipid nanoparticle comprises 20-60% ionizable cationic lipid, 55 5-25% neutral lipid, 25-55% cholesterol, and 0.5-15% PEG-modified lipid.

13. The composition of claim 12, wherein the lipid nanoparticle comprises 50% ionizable cationic lipid, 10% neutral lipid, 38.5% sterol, and 1.5% PEG-modified lipid.

14. The composition of claim 11, wherein the ionizable cationic lipid is Compound 25.

15. The composition of claim **11**, wherein the neutral lipid is 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), the sterol is cholesterol, and the PEG-modified lipid is 1,2-65 dimyristoyl-racalycero-3-methoxypolyethylene glycol-2000 (PEG-DMG) or PEG-cDMA.

16. A composition, comprising: a messenger ribonucleic acid (mRNA) comprising a 5' untranslated region (UTR), an open reading frame encoding a betacoronavirus (BetaCoV) S protein or S protein subunit, a 3' UTR, and a poly(A) tail, formulated in a lipid nanoparticle that comprises 20-60% ionizable cationic lipid, 5-25% neutral lipid, 25-55% cholesterol, and 0.5-15% PEG-modified lipid.

17. The composition of claim 16, wherein the open reading frame encodes a BetaCoV S protein.

18. The composition of claim 16, wherein the open reading frame encodes an S protein subunit selected from an S1 subunit and an S2 subunit.

19. The composition of claim **16**, wherein the mRNA further comprises 5' cap analog 7mG(5')ppp(5')NlmpNp.

20. The composition of claim **16**, wherein at least 80% of the uracil in the open reading frame has a chemical modification.

21. The composition of claim **20**, wherein the chemical modification is a 1-methylpseudouridine modification or a 1-ethylpseudouridine modification.

22. The composition of claim 16, wherein the ionizable cationic lipid is Compound 25.

23. The composition of claim **16**, wherein the neutral lipid is DSPC, the sterol is cholesterol, and the PEG-modified lipid is PEG-DMG.

24. A composition, comprising: a messenger ribonucleic acid (mRNA) comprising a 5' cap analog, a 5' untranslated region (UTR), an open reading frame encoding a betacoronavirus (BetaCoV) S protein, a 3' UTR, and a poly(A) tail, formulated in a lipid nanoparticle that comprises 20-60% ionizable cationic lipid, 5-25% DSPC, 25-55% cholesterol, and 0.5-15% PEG-DMG, wherein the ionizable cationic lipid has the structure of Compound 25, and wherein at least 80% of the uracil in the open reading frame has a 1-meth-ylpseudouridine modification.

25. The composition of claim **24**, wherein the 5' cap analog is 7mG(5')ppp(5')NlmpNp.

26. A lipid nanoparticle, comprising: a messenger ribonucleic acid (mRNA) comprising an open reading frame encoding a betacoronavirus (BetaCoV) S protein or S protein subunit; wherein the lipid nanoparticle comprises

20-60% ionizable cationic lipid, 5-25% neutral lipid, 25-55% cholesterol, and 0.5-15% PEG-modified lipid.

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