CLAIMS

1. A messenger ribonucleic acid (mRNA) vaccine comprising:

(a) an mRNA comprising an open reading frame encoding a fusion protein comprising a receptor binding domain (RBD) of a SARS-CoV-2 Spike protein and a protein transmembrane domain; and

(b) a lipid nanoparticle having a molar ratio of about 20-60 mol% ionizable cationic lipid, 5-25 mol% non-cationic lipid, 25-55 mol% sterol, and 0.5-15 mol% PEG-modified lipid,

wherein the mRNA comprises at least one chemical modification, wherein the at least one chemical modification is selected from the group consisting of pseudouridine (ψ), 1-methyl-pseudouridine (m1ψ), 1-ethyl-pseudouridine (e1ψ), 5-methoxy-uridine (mo5U), 5-methyl-cytidine (m5C), 5-methoxymethyl uridine, 5-methylthio uridine, 1-methoxymethyl pseudouridine, 5-methyl cytidine, and/or 5-methoxy cytidine.

2. The mRNA vaccine of claim 1, wherein the transmembrane domain is an influenza hemagglutinin transmembrane domain.

3. A messenger ribonucleic acid (mRNA) vaccine comprising:

(a) an mRNA comprising an open reading frame encoding:

(i) a fusion protein comprising a receptor binding domain (RBD) of a SARS-CoV-2 Spike protein and a protein transmembrane domain, wherein the open reading frame comprises a nucleotide sequence having at least 70% identity to the nucleotide sequence of SEQ ID NO: 76; or

(ii) a receptor binding domain (RBD) of a SARS-CoV-2 Spike protein, wherein the RBD is soluble; and

(b) a lipid nanoparticle having a molar ratio of about 20-60 mol% ionizable cationic lipid, 5-25 mol% non-cationic lipid, 25-55 mol% sterol, and 0.5-15 mol% PEG-modified lipid, wherein the mRNA comprises at least one chemical modification.

4. The mRNA vaccine of claim 3, wherein the open reading frame comprises a nucleotide sequence having at least 75%, at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the nucleotide sequence of SEQ ID NO: 76.

5. A messenger ribonucleic acid (mRNA) comprising an open reading frame (ORF) that encodes at least two domains of a SARS-CoV-2 Spike protein, and less than the full length spike protein, wherein the first domain is a receptor binding domain (RBD) of a SARS-CoV-2 Spike protein, and wherein the second domain is an N-terminal domain (NTD) of a SARS-CoV-2 Spike protein.

6. The mRNA of claim 5, wherein the ORF encodes a transmembrane domain (TD) linked to the NTD and/or RBD, optionally wherein (i) the TD is an influenza hemagglutinin transmembrane domain, and/or (ii) the ORF comprises NTD - RBD - TM.

7. The mRNA of claim 5 or claim 6, wherein the ORF encodes a signal peptide, optionally wherein the signal peptide is linked to the RBD.

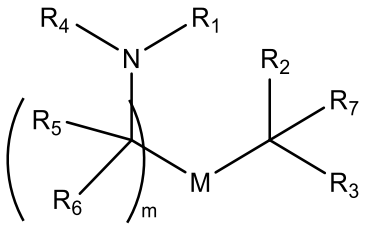
8. The mRNA of claim 7, wherein the signal peptide is heterologous to SARS-CoV-2.

9. The mRNA of any one of claims 5-8, wherein the mRNA comprises at least one chemical modification.

10. The mRNA vaccine of any one of claims 3, 4 or 9, wherein the at least one chemical modification is selected from the group consisting of pseudouridine (ψ), 1-methyl-pseudouridine (m1ψ), 1-ethyl-pseudouridine (e1ψ), 5-methoxy-uridine (mo5U), 5-methyl-cytidine (m5C), 5-methoxymethyl uridine, 5-methylthio uridine, 1-methoxymethyl pseudouridine, 5-methyl cytidine, and/or 5-methoxy cytidine.

11. The mRNA of any one of claims 5-10, wherein the mRNA is in an mRNA vaccine further comprising a lipid nanoparticle having a molar ratio of about 20-60% ionizable cationic lipid: about 5-25% non-cationic lipid: about 25-55% sterol; and about 0.5-15% PEG-modified lipid.

12. The mRNA vaccine of any one of claims 1-4 or 11, wherein the ionizable cationic lipid comprises a compound of Formula (I):



(I),

or a salt or isomer thereof, wherein:

R_1 is selected from the group consisting of C_{5-30} alkyl, C_{5-20} 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} carbocycle, $-(CH_2)_nQ$, $-(CH_2)_nCHQR$, -CHQR, $-CQ(R)_2$, and unsubstituted C_{1-6} alkyl, where Q is selected from a carbocycle, heterocycle, -OR, $-O(CH_2)_nN(R)_2$, -C(O)OR, -OC(O)R, $-CX_3$, $-CX_2H$, $-CXH_2$, -CN, $-N(R)_2$, $-C(O)N(R)_2$, -N(R)C(O)R, $-N(R)S(O)_2R$, $-N(R)C(O)N(R)_2$, $-N(R)C(S)N(R)_2$, $-N(R)R_8$, $-O(CH_2)_nOR$, $-N(R)C(=NR_9)N(R)_2$, $-N(R)C(=CHR_9)N(R)_2$, $-OC(O)N(R)_2$, -N(R)C(O)OR, -N(OR)C(O)R, $-N(OR)S(O)_2R$, -N(OR)C(O)OR, $-N(OR)C(O)N(R)_2$, $-N(OR)C(S)N(R)_2$, $-N(OR)C(=NR_9)N(R)_2$, $-N(OR)C(=CHR_9)N(R)_2$, $-C(=NR_9)N(R)_2$, $-C(=NR_9)R$, -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;

each R_5 is independently selected from the group consisting of C_{1-3} alkyl, C_{2-3} alkenyl, and H;

each R_6 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;

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, NO_2, 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 C_{1-3} alkyl, C_{2-3} alkenyl, and H;

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

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_{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.

13. Use of the mRNA vaccine of any one of claims 1-12 in the manufacture of a medicament for inducing an antigen specific immune response in a subject.

14. Use of the mRNA vaccine of any one of claims 1-12 in the manufacture of a medicament for preventing and/or treat a coronavirus infection.

15. The mRNA vaccine of any one of claims 1-12, for use as a medicament.