CLAIMS

What is claimed is:

1. An mRNA vaccine comprising:

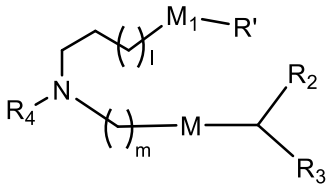
(a) an mRNA comprising an open reading frame encoding a stabilized prefusion form of a human respiratory syncytial virus (hRSV) F glycoprotein, wherein the hRSV F protein consists of the amino acid sequence of SEQ ID NO: 8; and

(b) a lipid nanoparticle.

2. An mRNA vaccine comprising:

(a) an mRNA comprising an open reading frame encoding a stabilized prefusion form of a human respiratory syncytial virus (hRSV) F glycoprotein, wherein the hRSV F protein comprises an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 8; and

(b) a lipid nanoparticle comprising an ionizable lipid, optionally wherein the ionizable lipid is a compound of Formula (IA)



(IA),

or a salt or isomer thereof, wherein l 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 $-(CH_2)_nQ$, 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.

3. An mRNA vaccine comprising:

(a) an mRNA comprising an open reading frame encoding a stabilized prefusion form of a human respiratory syncytial virus (hRSV) F glycoprotein, wherein the open reading frame comprises a nucleic acid sequence having at least 80% identity to the nucleic acid sequence of SEQ ID NO: 7; and

(b) a lipid nanoparticle.

4. The mRNA vaccine of any one of claims 1-3, wherein the open reading frame comprises a nucleic acid sequence having at least 90% identity to the nucleic acid sequence of SEQ ID NO: 7

5. The mRNA vaccine of claim 4, wherein the open reading frame comprises the nucleic acid sequence of SEQ ID NO: 7

6. The mRNA vaccine of any one of claims 1-5, wherein the mRNA further comprises a 5' untranslated region (UTR) comprising the nucleic acid sequence of SEQ ID NO: 2 and a 3' UTR comprising the nucleic acid sequence of SEQ ID NO: 4.

7. The mRNA vaccine of any one of claims 1-6, wherein the mRNA comprises a nucleic acid sequence having at least 80%, at least 90%, or 100% identity to the nucleic acid sequence of SEQ ID NO: 15.

8. An mRNA vaccine comprising:

(a) an mRNA comprising an open reading frame encoding a stabilized prefusion form of a human respiratory syncytial virus (hRSV) F glycoprotein, wherein the hRSV F protein comprises an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 8;

(b) an mRNA comprising an open reading frame encoding a human metapneumovirus (hMPV) F glycoprotein; and

(b) a lipid nanoparticle.

9. The mRNA vaccine composition of any one of claims 2-8, wherein the hRSV F glycoprotein variant comprises a modification, relative to a wild-type hRSV F glycoprotein, selected from the group consisting of: a P102X substitution, a substitution of amino acids 104-144 with a linker molecule, an A149X substitution, an S155X substitution, an S190X substitution, a V207X substitution, an S290X substitution, a L373X substitution, an I379X substitution, an M447X substitution, and a Y458X substitution, wherein X is any amino acid.

10. The mRNA vaccine composition of claim 9, wherein the hRSV F glycoprotein variant comprises a modification, relative to a wild-type hRSV F glycoprotein, selected from the group consisting of: a P102A substitution, a substitution of amino acids 104-144 with a linker molecule, an A149C substitution, an S155C substitution, an S190F substitution, a V207L substitution, an S290C substitution, a L373R substitution, an I379V substitution, an M447V substitution, and a Y458C substitution.

11. The mRNA vaccine composition of claim 10, wherein the hRSV F glycoprotein variant comprises the following modifications, relative to a wild-type hRSV F glycoprotein: a P102A substitution, a substitution of amino acids 104-144 with a linker molecule, an A149C substitution, an S155C substitution, an S190F substitution, a V207L substitution, an S290C substitution, a L373R substitution, an I379V substitution, an M447V substitution, and a Y458C substitution.

12. The mRNA vaccine composition of any one of claims 9-11, wherein the wild-type hRSV F glycoprotein comprises the sequence of SEQ ID NO: 1.

13. The mRNA vaccine composition of any one of the preceding claims, wherein the hRSV RNA comprises a chemical modification.

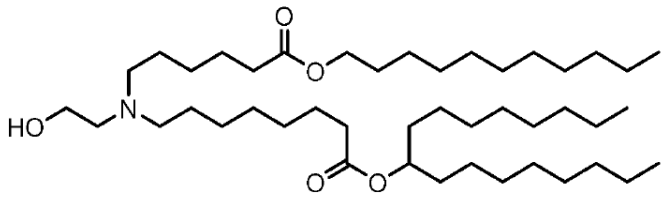
14. The mRNA vaccine composition of claim 13, wherein the chemical modification is 1-methylpseudouridine.

15. The mRNA vaccine composition of any one of the preceding claims, wherein the lipid nanoparticle comprises an ionizable lipid, a neutral lipid, a sterol, and a PEG-modified lipid.

16. The mRNA vaccine composition of claim 15, wherein the lipid nanoparticle comprises 20-60 mol% ionizable lipid, 5-25 mol% neutral lipid, 25-55 mol% sterol, and 0.5-15 mol% PEG-modified lipid.

17. The mRNA vaccine composition of claim 16, wherein the lipid nanoparticle comprises 40-50 mol% ionizable lipid, 10-20 mol% neutral lipid, 35-45 mol% sterol, and 1-5 mol% PEG-modified lipid.

18. The mRNA vaccine composition of any one of claims 15-17, wherein the neutral lipid is 1,2 distearoyl-sn-glycero-3-phosphocholine (DSPC), the sterol is cholesterol, the PEG-modified lipid is 1,2 dimyristoyl-sn-glycerol, methoxypolyethyleneglycol (PEG2000 DMG), and the ionizable lipid is Compound 1:



(Compound 1).

19. Use of the mRNA vaccine composition of any one of claims 1-18 in the manufacture of a medicament to induce a neutralizing antibody response against hRSV in the subject.

20. The use of claim 19, wherein the subject is immunocompromised and/or has a pulmonary disease.