CLAIMS

1. A purified mRNA comprising:

(a) a 5’ cap structure;

(b) a heterologous 5’ untranslated region (UTR);

(c) a coding sequence encoding a SARS-CoV-2 spike protein (S) at least 95% identical to SEQ ID NO: 10 that is a pre-fusion stabilized spike protein (S_stab) comprising K986P and V987P stabilizing substitutions and further comprising a D614G amino acid substitution relative to SEQ ID NO: 10; and

(d) a heterologous 3’ UTR,

wherein the mRNA optionally comprises a nucleotide substitution at one or more uracil position(s) selected from a 1-methylpseudouridine or a pseudouridine substitution.

2. The purified mRNA of claim 1, wherein the 3’ UTR comprises at least one poly(A) sequence comprising 30 to 200 adenosine nucleotides.

3. The purified mRNA of claim 2, wherein the 5’ cap is a m7G, cap0, cap1, cap2, a modified cap0 or a modified cap1 structure.

4. The purified mRNA of claim 3, wherein the 5’ cap is a cap1 structure.

5. The purified mRNA of claim 2, wherein the mRNA comprises a terminal poly(A) sequence of 30 to 200 adenosine nucleotides.

6. The purified mRNA of claim 2, wherein the at least one coding sequence of the mRNA has a G/C content of at least about 50%.

7. The purified mRNA of claim 6, wherein the mRNA comprises an RNA sequence at least 80% identical to SEQ ID NO: 23092.

8. The purified mRNA of claim 2, wherein the spike protein comprises the D614G amino acid substitution and a E484K amino acid substitution relative to SEQ ID NO: 10.

9. The purified mRNA of claim 8, comprising at least one of the following amino acid substitutions relative to SEQ ID NO: 10: L18F, D80A, D215G, delL242, delA243, delL244, R246I, K417N, N501Y and/or A701V.

10. The purified mRNA of claim 9, wherein the spike protein comprises the following amino acid substitutions relative to SEQ ID NO: 10: L18F, D80A, D215G, delL242, delA243, delL244, R246I, K417N, E484K, N501Y, D614G and A701V.

11. The purified mRNA of claim 2, wherein the mRNA comprises a 1-methylpseudouridine nucleotide substitution at one or more uracil position(s).

12. The purified mRNA of claim 11, wherein 100% of the uracil positions in the coding sequence are replaced with 1-methylpseudouridine.

13. The purified mRNA of claim 2, wherein the mRNA is a purified mRNA that has been purified by RP-HPLC and/or TFF.

14. A pharmaceutical composition comprising the purified mRNA of claim 1 and at least one pharmaceutically acceptable carrier.

15. The composition of claim 14, wherein the composition comprises at least two different mRNA encoding at least two different SARS-CoV-2 spike proteins.

16. The composition of claim 15, wherein the at least two different SARS-CoV-2 spike proteins are each at least 95% identical to SEQ ID NO: 10 and comprise the K986P and V987P stabilizing substitutions.

17. The composition of claim 16, wherein the at least two different SARS-CoV-2 spike proteins are from different SARS CoV-2 variants.

18. The composition of claim 14, wherein the mRNA is complexed or associated with lipid nanoparticles (LNPs).

19. The composition of claim 18, wherein the LNPs comprises:

(i) at least one cationic lipid;

(ii) at least one neutral lipid;

(iii) at least one steroid or steroid analogue; and

(iv) at least one PEG-lipid,

wherein (i) to (iv) are in a molar ratio of about 20-60% cationic lipid, 5-25% neutral lipid, 25-55% sterol, and 0.5-10% PEG-lipid.

20. The composition of claim 19, wherein the at least one PEG-lipid is present in the LNPs in a molar ratio of about 0.5% to 5%.

21. The composition of claim 20, wherein the at least one PEG-lipid comprises PEG-DMG or PEG-cDMA.

22. (Original) The composition of claim 21, wherein the at least one PEG-lipid comprises PEG-2000-DMG.

23. The composition of claim 18, wherein the LNPs have a mean diameter of from about 60nm to 200nm.

24. The composition of claim 18, wherein the composition has a lipid to RNA molar ratio (N/P ratio) of from about 2 to about 12.

25. The composition of claim 20, further comprising sucrose.

26. A composition comprising:

(I) a purified mRNA comprising:

(a) a 5’ cap structure;

(b) a heterologous 5’ untranslated region (UTR);

(c) a coding sequence encoding a SARS-CoV-2 spike protein (S) at least 95% identical to SEQ ID NO: 10 that is a pre-fusion stabilized spike protein (S_stab) comprising K986P and V987P stabilizing substitutions and further comprising a D614G amino acid substitution relative to SEQ ID NO: 10; and

(d) a heterologous 3’ UTR, comprising a terminal poly(A) sequence of 30 to 200 adenosine nucleotides,

wherein 100% of the uracil positions in the mRNA are replaced with 1-methylpseudouridine; and

(II) at least one pharmaceutically acceptable carrier,

wherein the mRNA is complexed or associated with lipid nanoparticles (LNPs).

27. The composition of claim 26, wherein the LNPs comprises:

(i) at least one cationic lipid;

(ii) at least one neutral lipid;

(iii) at least one steroid or steroid analogue; and

(iv) at least one PEG-lipid,

wherein (i) to (iv) are in a molar ratio of about 20-60% cationic lipid, 5-25% neutral lipid, 25-55% sterol, and 0.5-5% PEG-lipid.

28. The composition of claim 27, wherein the at least one PEG-lipid comprises PEG-2000-DMG.

29. The composition of claim 27, wherein the spike protein comprises the D614G substitution and a E484K substitution relative to SEQ ID NO: 10.

30. Use of an effective amount of a composition according to claim 27 in the manufacture of a medicament for stimulating an immune response to a coronavirus spike protein in a subject, wherein the said medicament is to be administered to the subject.