faster than conventional vaccine production, which can require the use of chicken eggs or other mammalian cells. In addition, mRNA vaccines have the potential to streamline vaccine discovery and development, and facilitate a rapid response to emerging infectious diseases [Maruggi *et al., Mol Ther.* 2019; 27(4): 757-772

Preclinical and clinical trials have shown that mRNA vaccines provide a safe and long-lasting immune response in animal models and humans. mRNA vaccines against infectious diseases may be developed as prophylactic or therapeutic treatments. mRNA vaccines expressing antigens of infectious pathogens have been shown to induce potent T cell and humoral immune responses [Pardi *et al.,Nat Rev Drug Discov.* 2018; 17: 261–279.]. The production procedure to generate mRNA vaccines is cell-free, simple, and rapid, compared to production of whole microbe, live attenuated, and subunit vaccines. This fast and simple manufacturing process makes mRNA a promising bio-product that can potentially fill the gap between emerging infectious disease and the desperate need for effective vaccines.

SUMMARY

In one aspect, the present disclosure provides a composition comprising an effective amount of a messenger ribonucleic acid (mRNA) that comprises an open reading frame (ORF) encoding a 2019-nCoV protein or protein fragment formulated in a pharmaceutically acceptable carrier, wherein said mRNA and said carrier form a polymeric nanoparticle. In another aspect, the present disclosure provides a method of making the composition as described herein, comprising expressing said ORF in a linear *in vitro* transcription (IVT) system, or using a plasmid DNA (pDNA) vector delivery system. In another aspect, the present disclosure provides a method of making a composition as described herein, comprising contacting a composition comprising said ORF with an HKP, said mRNA and said HKP self-assemble into nanoparticles.

In a further aspect, the present disclosure provides a use of the composition as described herein in the manufacture of a medicament for treating a subject with a 2019-nCoV infection. In yet another aspect, the present disclosure provides the composition as described

herein for use in therapy. Compositions are provided containing an effective amount of a messenger ribonucleic acid (mRNA) that contains an open reading frame (ORF) encoding a 2019-nCoV protein or protein fragment formulated in a pharmaceutically acceptable carrier, where the mRNA and the carrier form a polymeric nanoparticle. The 2019-nCoV protein may be a spike (S) protein or spike (S) subunit. The ORF may be an mRNA encoding a peptide such as the peptides having a sequence of selected from SEQ ID 14 to 31, or 50-66. The ORF may contain for example, an mRNA have a sequences as shown in SEQ ID Nos. 32 to 49 or SEQ ID No.91 to 107. The ORF may be selected from mRNA molecules encoding the amino acid sequence selected from SEQ ID No. 11, 13, 68, 70, 72, 74 and 90. The ORF may have a sequence such as SEQ ID No. 1-4, 10, 12, 67, 69, 71, 73 or 89.

These composition may also contain an mRNA containing all or part of orf1a and/or orf1b, where the mRNA encodes a 2019-nCoV non-structural protein polymerase and/or RdRp. The ORF may be an mRNA having a sequence such as SEQ ID NO:. 5 or 6. The

WHAT IS CLAIMED IS:

1. A composition comprising an effective amount of a messenger ribonucleic acid (mRNA) that comprises an open reading frame (ORF) encoding a 2019-nCoV protein or protein fragment formulated in a pharmaceutically acceptable carrier, wherein said mRNA and said carrier form a polymeric nanoparticle.

2. The composition of claim 1, wherein the 2019-nCoV protein is a spike (S) protein or spike (S) subunit.

3. The composition of claim 1 or claim 2, wherein the ORF encoding the 2019-nCoV protein or protein fragment is selected from the group consisting of mRNA molecules encoding the protein or fragment selected from SEQ ID NOs: 11, 13 to 31, 50 to 66, 68, 70, 72, or 74, or an mRNA molecule encoding the protein or fragment thereof of the amino acid sequence:

MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLF
LPFFSNVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLD
SKTQSLLIVNNATNVVIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANN
CTFEYVSQPFLMDLEGKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGF
SALEPLVDLPIGINITRFQTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFL
LKYNENGTITDAVDCALDPLSETKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNIT
NLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGVSPTKL
NDLCFTNVYADSFVIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNL
DSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYG
FQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKNKCVNFNFNGLTGTG
VLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVSVITPGTNTSNQ
VAVLYQGVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNNSYE
CDIPIGAGICASYQTQTNSPSRAGSVASQSIIAYTMSLGAENSVAYSNNSIAIPTNF
TISVTTEILPVSMTKTSVDCTMYICGDSTECSNLLLQYGSFCTQLNRALTGIAVEQ
DKNTQEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLAD
AGFIKQYGDCLGDIAARDLICAQKFNGLTVLPPLLTDEMIAQYTSALLAGTITSG
WTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYENQKLIANQFNSAIGKIQDSLS
STASALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRLDPPEAEVQID
RLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDFCGKGYH
LMSFPQSAPHGVVFLHVTYVPAQEKNFTTAPAICHDGKAHFPREGVFVSNGTHW
FVTQRNFYEPQIITTDNTFVSGNCDVVIGIVNNTVYDPLQPELDSFKEELDKYFKN
HTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYIKWP
WYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDEDDSEPVLKGV
KLHYT.

4. The composition of any one of claims 1-3, wherein the 2019-nCoV protein or protein fragment is encoded by any one of SEQ ID NOs: 1-4, 10, 12, 32 to 49, 67, 69, 71, 73, 89, or 91 to 95, or by the sequence TACTACCACAAGAACAACAAGAGCTGGATGGAGAGCGAGTTCAGG.

5. The composition of any one of claims 1-4, wherein said ORF encoding the 2019-nCoV protein or protein fragment comprises any one of SEQ ID NOs: 96 to 106.

6. The composition of any one of claims 1-5, further comprising an mRNA comprising all or part of orf1a or orf1b or both, wherein said mRNA encodes a 2019-nCoV non-structural protein polymerase or RdRp or both.

7. The composition of claim 6 wherein the 2019-nCoV non-structural protein polymerase is encoded by SEQ ID NO: 5 and wherein the 2019-nCoV non-structural RdRp is encoded by SEQ ID NO: 6.

8. The composition of any one of claims 1-7, wherein said ORF encodes all or part of the 2019 nCoV encoding envelope (E), membrane (M), nucleocapsid (N) protein, or any combination thereof, or wherein the composition further comprises one or more Mrna sequences encoding all or part of the 2019 nCoV encoding envelope (E), membrane (M), nucleocapsid (N) protein, or any combination thereof.

9. The composition of claim 8, wherein the M protein is encoded by SEQ ID NO. 7, the N protein is encoded by SEQ ID NO: 8, and the E protein is encoded by SEQ ID NO: 9.

10. The composition according to any one of claims 1-9, wherein any one or more or all uridine residues in the mRNA are N1-methyl pseudouridine or pseudouridine.

11. The composition of any one of claims 1-10, wherein the mRNA molecule further comprises a 3'-UTR-and a 5'-UTR and optionally further comprises additional elements that (a) stabilize the composition and (b) enhance expression of the polypeptide encoded by said ORF.

12. The composition of claim 11, wherein the 5'-UTR comprises an m7G cap structure and a start codon, or wherein the 3’-UTR comprises a stop codon and a poly A tail, or both.

13. A method of making the composition according to any one of claims 1-12, comprising expressing said ORF in a linear *in vitro* transcription (IVT) system, or using a plasmid DNA (pDNA) vector delivery system.

14. The composition of any one of claims 1-12, wherein the composition comprises more than one ORF and encodes at least two polypeptides.

15. The composition of any one of claims 1-12 or 14, wherein the polymeric nanoparticle carrier comprises a Histidine-Lysine co-polymer (HKP), or a lipid or both.

16. The composition of claim 15, wherein the HKP is selected from the group consisting of polymers having side chains selected from SEQ ID NOs:75-88, or wherein said lipid is a cationic lipid, or both.

17. A method of making a composition according to claim 15 or claim 16, comprising contacting a composition comprising said ORF with an HKP, said mRNA and said HKP self-assemble into nanoparticles.

18. Use of the composition of any one of claims 1-12 or 14-16 in the manufacture of a medicament for treating a subject with a 2019-nCoV infection.

19. The use of claim 18, wherein the composition is atomized by a nebulizer inhalation system prior to or during administration, and optionally wherein the nebulizer system is a portable nebulizer for whole respiratory tract drug delivery.

20. The use of claim 18, wherein the composition is to be administered by a method comprising a subcutaneous injection, or an intramuscular injection, or an intraperitoneal injection (i.p).

21. The composition of any one of claims 1-12 or 14-16 for use in therapy.