CLAIMS

1. An immunogenic composition consisting essentially of a stabilized pre-fusion conformation form of a human metapneumovirus (hMPV) F protein as the only hMPV antigen, wherein the F protein is of the A subgroup, and wherein the prefusion stabilized F protein is characterized by
   a) consisting of a single polypeptide chain stabilized by at least one non-natural disulfide bond,
   b) lacking a protease cleavage site between the F1 and F2 domains relative to a native F protein,
   c) comprising one or more amino acid substitution(s) to cysteine, which introduce one or more non-native disulfide bond(s) that stabilize the prefusion conformation,
   d) comprising a heterologous linker consisting of 1 to 5 amino acid residues including a cysteine residue, wherein the linker replaces amino acid residues at positions 103-118 of the native F protein, wherein the cysteine residue forms a non-natural disulfide bond with an introduced cysteine residue in the F1 domain,
   e) comprising one or more amino acid substitutions at positions corresponding to positions 49, 51, 67, 80, 137, 147, 159, 160, 161, 166, 177, 258, 266, 480 and/or 481 of the native hMPV F protein,
   f) comprising one of the following substitution combinations:
      N97Q, R102G and G294E;
      N97Q, R102G, T160F, I177L and G294E;
      N97Q, R102G, T49M, I67L, A161M, E80N, F258I and G294E;
      N97Q, R102G, T49M, I67L, A161M, E51C, K166C, S266D, G294E, I480C and L481C; or
      N97Q, R102G, T49M, A161M, I137W, A159V, A147V, I177L and G294E, and
   g) comprising a trimerization helper domain (foldon) having a sequence selected from SEQ ID Nos: 23 to 28, or a variant thereof,

   wherein said immunogenic composition cross-neutralizes the hMPV from another subgroup and/or genotype.

2. The composition of claim 1, wherein the stabilized pre-fusion conformation form of the human metapneumovirus (hMPV) F protein or fragment thereof is of the A1 subgroup.

3. The immunogenic composition according to claim 1 or claim 2, wherein the prefusion stabilized F protein comprises or consists of the amino acid sequence provided by SEQ ID NO: 54 (L7F_A1_23), or an immunogenic variant thereof having at least 80%, 90%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO: 54.

4. The immunogenic composition of any one of claims 1 to 3, wherein the composition further comprises one or more adjuvants and/or at least one pharmaceutically acceptable carrier or excipient.

5. The immunogenic composition of any one of claims 1 to 4, wherein the A hMPV prefusion stabilized F protein sequence is derived from the A hMPV strain consisting of NL/1/00, NL/17/00, TN/94-49, NCL174, CAN97-83, as defined by the amino acid sequence provided by SEQ ID NOs: 1-5.

6. The immunogenic composition of any one of claims 1 to 5, wherein the heterologous linker consists of the amino acid sequence CGAGA or CGAGV.

7. The immunogenic composition of any one of claims 1 to 6, wherein the substitution is selected from the group consisting of T49M, E80N, I137W, A147V, A159V, T160F, A161M, I67L, I177L, F258I, S266D, I480C and/or L481C.

8. The immunogenic composition of any one of claims 1 to 7, wherein the pre-fusion F protein comprises or consists of the amino acid sequence of SEQ ID NO: 56 (L7F_A1_23.2).

9. The immunogenic composition of any one of claims 1 to 7, wherein the pre-fusion F protein comprises or consist of the amino acid sequence of SEQ ID NO: 58 (sF_A1_K_L7).

10. The immunogenic composition of any one of claims 1 to 7, wherein the pre-fusion F protein comprises or consists of the amino acid sequence of SEQ ID NO: 59 (L7F_A1_31).

11. The immunogenic composition of any one of claims 1 to 7, wherein the pre-fusion F protein comprises or consists of the amino acid sequence of SEQ ID NO: 60 (L7F_A1_33).

12. The immunogenic composition of any one of claims 1 to 7, wherein the pre-fusion F protein comprises or consists of the amino acid sequence of SEQ ID NO: 61 (L7F_A1_4.2).

13. The immunogenic composition of any preceding claim, wherein the immunogenic composition comprises a further antigen which is not an hMPV antigen, preferably wherein the further antigen is derived from a virus selected from the group consisting of Respiratory Syncytial Virus (RSV), Parainfluenza Virus type 3 (PIV3), Influenza virus, Severe Acute Respiratory Syndrome-Coronavirus (SARS-CoV), SARS-CoV-2 and Middle East Respiratory Syndrome virus (MERS).

14. The immunogenic composition of any preceding claim, wherein the adjuvant is selected from the group consisting of an aluminium salt, CpG, oligo(dIdC)$_{13}$ (SEQ ID NO: 65), KLK peptide (SEQ ID NO: 66), AS03, AS01, QS21, MPL, GLA-SE, GLA-3M-052-LS, 3M-052-alum or combinations thereof.

15. The immunogenic composition of any preceding claim, wherein the immunogenic composition is a vaccine.

16. The immunogenic composition according to any preceding claim for use as a medicament.

17. The immunogenic composition according to any preceding claim for use in the treatment and/or prevention of hMPV infection and associated disease in a subject.

18. The immunogenic composition of claim 17, wherein an effective amount of the immunogenic composition according to any one of claims 1 to 15 is to be administered intramuscularly, intradermally, subcutaneously, mucosally, intrarectally, or orally.

19. The immunogenic composition of claims 17 or 18, wherein the immunogenic composition according to any of claims 1 to 15 is to be administered as a prime-boost regime.

20. A method for producing the immunogenic composition according to any of claims 1 to 19, wherein the method comprises i) expression of the recombinant prefusion F protein from the corresponding nucleic acid molecule inserted in an expression vector in a host cell, ii) purifying the expressed recombinant F protein, and iii) combining the purified recombinant protein with a pharmaceutically acceptable carrier and/or excipient, optionally with an adjuvant.