CLAIMS

What is claimed is:

1. A viral vector that encodes a human metapneumovirus (hMPV) F polypeptide antigen that lacks a transmembrane domain, lacks a cytoplasmic tail, and comprises a human rhinovirus 3C (HRV-3C) protease cleavage site.

2. The viral vector of claim 1, comprising a viral vector backbone derived from a parainfluenza virus (PIV), optionally wherein the PIV is a chimeric bovine/human parainfluenza type 3 virus (rB/HPIV3) or a human parainfluenza type 3 virus (HPIV3).

3. The viral vector of claim 1, wherein:

said F polypeptide further comprises a F_0 cleavage site mutation comprising amino acid substitutions Q100R and S101R, replacing glutamine at amino acid position 100 of SEQ ID NO: 1 with arginine, and replacing serine at amino acid position 101 of SEQ ID NO: 1 with arginine;

said F polypeptide comprises a signal peptide;

said F polypeptide further comprises at least one tag sequence that is optionally an 8x His tag and/or a Strep II tag; and/or

said F polypeptide comprises a foldon domain; and/or

the hMPV F polypeptide is a pre-fusion F polypeptide.

4. The viral vector of claim 1, wherein the F polypeptide further comprises:

an amino acid substitution replacing the amino acid at position 160 of SEQ ID NO: 1, and an amino acid substitution replacing the amino acid position 46 of SEQ ID NO: 1;

an amino acid substitution replacing the amino acid at position 160 with phenylalanine, tryptophan, tyrosine, valine, alanine, isoleucine, or leucine;

an amino acid substitution replacing the amino acid position 160 with phenylalanine;

an amino acid substitution replacing the amino acid position 46 with valine, alanine, isoleucine, leucine, phenylalanine, tyrosine, or proline;

an amino acid substitution replacing the amino acid position 46 with valine;

an amino acid substitution replacing the amino acid at position 160 of SEQ ID NO: 1 with phenylalanine, tryptophan, tyrosine, valine, alanine, isoleucine, or leucine and/or an amino acid

substitution replacing the amino acid position 46 of SEQ ID NO: 1 with valine, alanine, isoleucine, leucine, phenylalanine, tyrosine, or proline; and/or

an amino acid substitution replacing threonine at amino acid position 160 of SEQ ID NO: 1, and an amino acid substitution replacing asparagine at amino acid position 46 of SEQ ID NO: 1.

5. The viral vector of claim 1, wherein the viral vector encodes a F polypeptide antigen,

wherein said F polypeptide lacks a transmembrane domain and lacks a cytoplasmic tail, and further comprises:

an F_0 cleavage site mutation comprising amino acid substitutions Q100R and S101R; replacing glutamine at amino acid position 100 of SEQ ID NO: 1 with arginine, and replacing serine at amino acid position 101 of SEQ ID NO: 1 with arginine;

a protease cleavage site;

a heterologous signal peptide;

an 8x His tag and/or a Strep II tag; and

a foldon domain.

6. A viral vector that encodes an F polypeptide antigen, wherein said F polypeptide lacks a transmembrane domain, lacks a cytoplasmic tail, and comprises an amino acid substitution replacing threonine at amino acid position 160 of SEQ ID NO: 1, and an amino acid substitution replacing asparagine at amino acid position 46 of SEQ ID NO: 1.

7. The viral vector of claim 6, wherein said F polypeptide comprises:

an amino acid substitution replacing threonine at amino acid position 160 with phenylalanine, tryptophan, tyrosine, valine, alanine, isoleucine, or leucine;

an amino acid substitution T160F replacing threonine at amino acid position 160 with phenylalanine;

an amino acid substitution replacing asparagine at amino acid position 46 with valine, alanine, isoleucine, leucine, phenylalanine, tyrosine, or proline;

an amino acid substitution N46V replacing asparagine at amino acid position 46 with valine;

at least 95% sequence identity to SEQ ID NO: 7;

an F_0 cleavage site mutation comprising amino acid substitutions Q100R and S101R, replacing glutamine at amino acid position 100 of SEQ ID NO: 1 with arginine, and replacing serine at amino acid position 101 of SEQ ID NO: 1 with arginine;

a signal peptide;

at least one tag sequence that is optionally an 8x His tag and/or a Strep II tag;

a foldon domain;

optionally wherein the hMPV F polypeptide is a pre-fusion F polypeptide; and/or

the viral vector further comprising a hMPV F nucleic acid molecule having at least 95% sequence identity to SEQ ID NO: 8, optionally wherein the nucleic acid molecule comprises SEQ ID NO: 8.

8. The viral vector of claim 6, that encodes an antigenic prefusion F polypeptide, wherein said prefusion F polypeptide lacks a transmembrane domain, lacks a cytoplasmic tail, and comprises:

an amino acid substitution T160F replacing threonine at amino acid position 160 of SEQ ID NO: 1 with phenylalanine, and an amino acid substitution N46V replacing asparagine at amino acid position 46 of SEQ ID NO: 1 with valine;

an F_0 cleavage site mutation comprising amino acid substitutions Q100R and S101R; replacing glutamine at amino acid position 100 of SEQ ID NO: 1 with arginine, and replacing serine at amino acid position 101 of SEQ ID NO: 1 with arginine;

a protease cleavage site;

a signal peptide;

an 8x His tag and/or a Strep II tag; and

a foldon domain.

9. The viral vector of claim 1, wherein

the hMPV F is from A strain hMPV; and/or

the hMPV F is A1 subtype or A2 subtype hMPV.

10. The viral vector of claim 1, wherein the F polypeptide comprises at least 95% sequence identity to SEQ ID NO: 3 or comprising SEQ ID NO: 3.

11. A viral vector encoding an F polypeptide, wherein said F polypeptide comprises at least 95% sequence identity to SEQ ID NO: 7.

12. The viral vector of claim 11, wherein:

the F polypeptide is a prefusion F polypeptide;

the viral vector backbone derived from a PIV, optionally wherein the PIV is a chimeric rB/HPIV3 or a HPIV3;

the F polypeptide comprises amino acid substitution T160F replacing threonine at amino acid position 160 with phenylalanine, and amino acid substitution N46V replacing asparagine at amino acid position 46 with valine;

the F polypeptide comprises SEQ ID NO: 7; and/or

the viral vector further comprising a hMPV F nucleic acid molecule having at least 95% sequence identity to SEQ ID NO: 8, optionally wherein the nucleic acid molecule comprises SEQ ID NO: 8.

13. A live-attenuated virus or a pharmaceutical composition comprising the viral vector of claim 1, optionally wherein the live-attenuated virus or the pharmaceutical composition is comprised in a vaccine.

14. A pharmaceutical composition comprising the vaccine of claim 13 for use in eliciting an immune response to hMPV and/or HPIV3 or protecting a subject against hMPV infection and/or HPIV3 infection, comprising the vaccine of claim 13 to be administered to a subject.

15. The pharmaceutical composition for use claim 14, wherein:

the vaccine is to be co-administered with an adjuvant;

the vaccine is to be administered in combination with an additional vaccine, optionally wherein the additional vaccine is a respiratory syncytial virus (RSV) vaccine or an influenza vaccine;

the subject is human, optionally wherein the human subject is an infant, a toddler, or an older adult; and/or

the vaccine increases the serum concentration of neutralizing antibodies, and wherein the subject has pre-existing hMPV immunity.

16. Use of the viral vector of claim 1, in the manufacture of a medicament for eliciting an immune response to hMPV and HPIV3 or protecting a subject against hMPV infection and HPIV3 infection.

17. A pharmaceutical composition comprising the viral vector of claim 1 for use in:

(A) eliciting an immune response in a subject in need thereof, comprising the subject to be administered, optionally intramuscularly, intranasally, intravenously, subcutaneously, or intradermally, a prophylactically effective amount of the viral vector of claim 1.

(B) preventing an hMPV infection and an HPIV3 infection or reducing one or more symptoms of an hMPV infection and an HPIV3 infection, comprising the subject to be administered, optionally intramuscularly, intranasally, intravenously, subcutaneously, or intradermally, a prophylactically effective amount of the viral vector of claim 1.

18. The viral vector of claim 1, for use in treating a subject in need thereof.

19. A kit comprising a container comprising a single-use or multi-use dosage of the viral vector of claim 1, optionally wherein the container is a vial or a pre-filled syringe or injector.

20. The viral vector of claim 1, wherein the viral vector comprises a hMPV F nucleic acid molecule having at least 95% identity to SEQ ID NO: 8, optionally wherein the nucleic acid molecule comprises SEQ ID NO: 8.