Claims

1. A modified influenza H3 hemagglutinin (HA) protein comprising an amino acid sequence of a wildtype influenza H3 HA protein and comprising at least one amino acid substitution, said at least one amino acid substitution consisting of amino acid substitutions that correspond to positions 382, 384, 524, and 528 of reference sequence SEQ ID NO: 92, and optionally amino acid substitutions that correspond to positions 392, 431, 525 and/or 526 of reference sequence SEQ ID NO: 92, wherein the amino acid substitutions corresponding to positions 524 and 528 are to a non-cysteine.

2. The modified influenza H3 HA protein of claim 1, wherein:

the amino acid substitution corresponding to position 382 of reference sequence SEQ ID NO: 92 is to an alanine or a conserved substitution of alanine,

the amino acid substitution corresponding to position 384 of reference sequence SEQ ID NO: 92 is to a valine or a conserved substitution of valine,

the amino acid substitution corresponding to position 524 of reference sequence SEQ ID NO: 92 is to a serine or a conserved substitution of serine, and

the amino acid corresponding to amino acid at position 528 of reference sequence SEQ ID NO: 92 is to a leucine or a conserved substitution of leucine.

3. The modified influenza H3 HA protein of claim 1 or claim 2, wherein the amino acid substitution corresponding to position 392 of reference sequence SEQ ID NO: 92 is to a aspartic acid or a conserved substitution of aspartic acid,.

4. The modified influenza H3 HA protein of any one of claims 1 to 3, wherein the amino acid substitution corresponding to position 431 of reference sequence SEQ ID NO: 92 is to a methionine or a conserved substitution of methionine.

5. The modified influenza H3 HA protein of any one of claims 1 to 4, wherein the HA protein further comprises a substitution at amino acids corresponding to amino acids at positions 525, 526 or 525 and 526 of reference sequence SEQ ID NO: 92, wherein the substitution of the amino acid at position 525 is to a leucine or a conserved substitution of leucine, and the substitution of the amino acid at position 526 is to a valine or a conserved substitution of valine.

6. The modified influenza H3 HA protein of any one of claims 2 to 5, wherein:

the conserved substitution of alanine is serine, glycine, threonine, cysteine, or valine;

the conserved substitution of valine is isoleucine, methionine, alanine, or threonine;

the conserved substitution of aspartic acid is glutamic acid, glutamine, or serine;

the conserved substitution of methionine is isoleucine, glutamine, valine or phenylalanine;

the conserved substitution of serine is threonine, alanine, asparagine, aspartic acid, glutamine, glycine, glutamic acid or lysine; and/or

the conserved substitution of leucine is isoleucine, valine, methionine, phenylalanine or valine.

7. A nucleic acid encoding the modified influenza H3 HA protein of any one of claims 1 to 6.

8. A virus-like particle (VLP) comprising the modified influenza H3 HA protein of any one of claims 1 to 6.

9. A method of producing an influenza virus like particle (VLP) in a plant, portion of a plant, or a plant cell, comprising:

a) i) introducing the nucleic acid of claim 7 into the plant, portion of the plant, or plant cell, and optionally introducing a second nucleic acid encoding a proton channel protein such as an influenza A subtype M2 protein; or

ii) providing a plant, portion of a plant, or plant cell comprising the nucleic acid of claim 7, and optionally wherein the plant, portion of the plant, or plant cell further comprises a second nucleic acid encoding a proton channel protein such as an influenza A subtype M2 protein; and

b) incubating the plant, portion of the plant, or plant cell under conditions that permit expression of the HA protein encoded by the nucleic acid and optionally the proton channel protein encoded by the second nucleic acid, thereby producing the VLP; and

c) optionally harvesting the plant, portion of the plant, or plant cell, and purifying the VLP.

10. The VLP of claim 8, further comprising one or more than one lipid derived from the plant, portion of the plant, or plant cell, plant-specific N-glycans, modified N-glycans or a combination thereof.

11. A plant, portion of the plant, or plant cell comprising the recombinant nucleic acid of claim 7, the HA protein of any one of claims 1 to 6 or the VLP of claims 8 or 10.

12. A composition for inducing an immune response comprising, an effective dose of the VLP of any one of claims 8 or 10, and a pharmaceutically acceptable carrier, adjuvant, vehicle or excipient.

13. The VLP of any one of claims 8 or 10, for use in inducing an immune response in a subject, wherein the VLP is optionally administered to the subject orally, intranasally, intramuscularly, intraperitoneally, intravenously or subcutaneously.

14. A method of increasing yield of production of an influenza virus like particle (VLP) in a plant, portion of a plant, or a plant cell, comprising:

a) introducing the nucleic acid of claim 7 into the plant, portion of the plant, or plant cell; or providing a plant, portion of a plant, or plant cell comprising the nucleic acid of claim 7; and

b) incubating the plant, portion of the plant, or plant cell under conditions that permit expression of the modified influenza HA protein encoded by the nucleic acid, thereby producing the VLP at a higher yield compared to plant, portion of the plant, or plant cell expressing an unmodified influenza HA protein, and

c) optionally harvesting the plant, portion of the plant, or plant cell, and purifying the VLP.

15. A modified influenza H3 hemagglutinin (HA) protein comprising amino acid substitutions corresponding to positions 382, 384, 524, and 528 of reference sequence SEQ ID NO: 92, wherein:

the amino acid substitution corresponding to position 382 is to alanine or a conserved substitution of alanine,

the amino substitution corresponding to position 384 is to valine or a conserved substitution of valine;

the amino acid substitution corresponding to position 524 is to serine or a conserved substitution of serine; and

the amino acid substitution corresponding to position 528 is to leucine or a conserved substitution of leucine.