Claims

1. A modified influenza H1 hemagglutinin (HA) protein comprising an amino acid sequence of a wildtype influenza H1 HA protein and comprising at least one amino acid substitution, said at least one substitution consisting of an amino acid substitution corresponding to position 390 of reference sequence SEQ ID NO: 134, and optionally one or more amino acid substitution at positions 429, 97, and/or 374 of reference sequence SEQ ID NO: 134.

2. The modified influenza H1 HA protein of claim 1, wherein:

(i) the amino acid substitution corresponding to position 97 of reference sequence SEQ ID NO: 134 is to an aspartic acid or a conserved substitution of aspartic acid;

(ii) the amino acid substitution corresponding to position 374 of reference sequence SEQ ID NO: 134 is to a glutamic acid or a conserved substitution of glutamic acid;

(iii) the amino acid substitution corresponding to position 390 of reference sequence SEQ ID NO: 134 is to an aspartic acid or a conserved substitution of aspartic acid; and/or

(iv) the amino acid substitution corresponding to position 429 of reference sequence SEQ ID NO: 134 is to methionine or a conserved substitution of methionine.

3. The modified influenza H1 HA protein of claim 1, wherein the amino acid substitution corresponding to position 390 of reference sequence SEQ ID NO: 134 is to an aspartic acid or a conserved substitution of aspartic acid, and

wherein the at least one amino acid substitution further consists of an amino acid substitution corresponding to position 429 of reference sequence SEQ ID NO: 134, said substitution being to a methionine or a conserved substitution of methionine.

4. The modified influenza H1 HA protein of claim 1, wherein the amino acid corresponding to amino acid at position 390 of reference sequence SEQ ID NO: 134 is to an aspartic acid or a conserved substitution of aspartic acid, and

wherein the at least one amino acid substitution further consists of amino acid substitutions corresponding to positions 97 and 429 of reference sequence SEQ ID NO: 134, said substitution corresponding to position 97 being to an aspartic acid or a conserved substitution of aspartic acid and said substitution corresponding to position 429 being to a methionine or a conserved substitution of methionine.

5. The modified influenza H1 HA protein of claim 1, wherein the amino acid substitution corresponding to position 390 of reference sequence SEQ ID NO: 134 is to an aspartic acid or a conserved substitution of aspartic acid, and

wherein the at least one amino acid substitution further consists of amino acid substitutions corresponding to positions 429 and 374 of reference sequence SEQ ID NO: 134, said substitution corresponding to position 429 being to a methionine or a conserved substitution of methionine and said substitution corresponding to position 374 being to a glutamic acid or a conserved substitution of glutamic acid.

6. The modified influenza H1 HA protein of claim 1, wherein the amino acid substitution corresponding to position 390 of reference sequence SEQ ID NO: 134 is to an aspartic acid or a conserved substitution of aspartic acid; and

wherein the at least one amino acid substitution further consists of amino acid substitutions corresponding to positions 429, 97 and 374 of reference sequence SEQ ID NO: 134, said substitution corresponding to position 429 being to a methionine or a conserved substitution of methionine, said substitution corresponding to position 97 being to an aspartic acid or a conserved substitution of aspartic acid, and said substitution corresponding to position 374 being to glutamic acid or a conserved substitution of glutamic acid.

7. The modified influenza H1 HA protein of any one of claim 2 to 6, wherein:

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

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

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

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

8. A nucleic acid encoding the modified influenza H1 HA protein of any one of claims 1 to 7.

9. A virus-like particle (VLP) comprising the modified influenza H1 hemagglutinin (HA) protein of any one of claims 1 to 7.

10. 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 8 into the plant, portion of the plant, or plant cell; or

ii) providing a plant, portion of a plant, or plant cell comprising the nucleic acid of claim 8;

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, thereby producing the VLP; and

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

11. The VLP of claim 9, 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.

12. A plant, portion of the plant, or plant cell comprising the modified influenza H1 HA protein of any one of claims 1 to 7, the HA protein of claim 8, or the VLP of claim 9 or 11.

13. A composition for inducing an immune response comprising, an effective dose of the VLP of claims 9 or 11, and a pharmaceutically acceptable carrier, adjuvant, vehicle or excipient.

14. The VLP of claims 9 or 11 for use in inducing an immune response in a subject, optionally wherein the VLP is administered to the subject orally, intranasally, intramuscularly, intraperitoneally, intravenously or subcutaneously.

15. 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) i) introducing the nucleic acid of claim 8 into the plant, portion of the plant, or plant cell; or ii) providing a plant, portion of a plant, or plant cell comprising the nucleic acid of claim 8;

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, thereby producing the VLP at a higher yield compared to plant, portion of the plant, or plant cell expressing an unmodified HA protein; and

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

16. An influenza H1 hemagglutinin (HA) protein comprising an amino acid substitution corresponding to position 390 of reference sequence SEQ ID NO: 134, wherein the amino acid substitution is to aspartic acid or a conserved substitution of aspartic acid.