Claims

1. A nucleic acid comprising a nucleotide sequence encoding a modified influenza H1 hemagglutinin (HA) protein, the HA protein comprising an amino acid sequence comprising at least one substitution when compared to a corresponding wildtype amino acid sequence, said at least one substitution being at one or more than one amino acid corresponding to amino acid at position 390, 429, 97, or 374 of H1 A/Michigan/45/15 HA.

2. The nucleic acid of claim 1, wherein:

(i) the at least one substitution of the amino acid corresponding to the amino acid at position 97 of H1 A/Michigan/45/15 HA is to a non-asparagine, such as to an aspartic acid or a conserved substitution of aspartic acid;

(ii) the at least one substitution of the amino acid corresponding to the amino acid at position 374 of H1 A/Michigan/45/15 HA is to a non-lysine, such as to a glutamic acid or a conserved substitution of glutamic acid;

(iii) the at least one substitution of the amino acid corresponding to the amino acid at position 390 of H1 A/Michigan/45/15 HA is to a non-phenylalanine, such as to an aspartic acid or a conserved substitution of aspartic acid; and/or

(iv) the at least one substitution of the amino acid corresponding to the amino acid at position 429 of H1 A/Michigan/45/15 HA is to a non-leucine, such as to a methionine or a conserved substitution of methionine.

3. The nucleic acid of claim 2, wherein the at least one substitution of the amino acid corresponding to the amino acid at position 429 of H1 A/Michigan/45/15 HA is to a non-leucine, such as to a methionine or a conserved substitution of methionine,

the nucleic acid further comprising a second substitution, said second substitution being at an amino acid corresponding to amino acid at position 380 of H1 A/Michigan/45/15 HA, said second substitution being to a non-asparagine, such as to an alanine or a conserved substitution of alanine.

4. The nucleic acid of claim 1, comprising

a first substitution at the amino acid corresponding to amino acid at position 390 of H1 A/Michigan/45/15 HA, said substitution being to a non-phenylalanine, such as to an aspartic acid or a conserved substitution of aspartic acid, and

a second substitution at the amino acid corresponding to amino acid at position 429 of H1 A/Michigan/45/15 HA, said substitution being to a non-leucine, such as to a methionine or a conserved substitution of methionine.

5. The nucleic acid of claim 1, comprising

a first substitution at the amino acid corresponding to amino acid at position 97 of H1 A/Michigan/45/15 HA, said substitution being to a non-asparagine, such as to an aspartic acid or a conserved substitution of aspartic acid, and

a second substitution at the amino acid corresponding to amino acid at position 374 of the H1 A/Michigan/45/15 HA, said substitution being to a non-lysine, such as to a glutamic acid or a conserved substitution of glutamic acid.

6. The nucleic acid of claim 1, comprising

a first substitution at the amino acid corresponding to amino acid at position 97 of H1 A/Michigan/45/15 HA, said substitution being to a non-asparagine, such as to an aspartic acid or a conserved substitution of aspartic acid;

a second substitution at the amino acid corresponding to amino acid at position 390 of H1 A/Michigan/45/15 HA, said substitution being to a non-phenylalanine, such as to an aspartic acid or a conserved substitution of aspartic acid, and

a third substitution at the amino acid corresponding to amino acid at position 429 of H1 A/Michigan/45/15 HA, said substitution being to a non-leucine, such as to a methionine or a conserved substitution of methionine.

7. The nucleic acid of claim 1, comprising

a first substitution at the amino acid corresponding to amino acid at position 374 of H1 A/Michigan/45/15 HA, said substitution being to a non-lysine, such as to a glutamic acid or a conserved substitution of glutamic acid;

a second substitution at the amino acid corresponding to amino acid at position 390 of H1 A/Michigan/45/15 HA, said substitution being to a non-phenylalanine, such as to an aspartic acid or a conserved substitution of aspartic acid, and a third substitution at the amino acid corresponding to amino acid at position 429 of H1 A/Michigan/45/15 HA, said substitution being to a non-leucine, such as to a methionine or a conserved substitution of methionine.

8. The nucleic acid of claim 1, comprising

a first substitution at the amino acid corresponding to amino acid at position 97 of H1 A/Michigan/45/15 HA, said substitution being to a non-asparagine, such as to an aspartic acid or a conserved substitution of aspartic acid;

a second substitution at the amino acid corresponding to amino acid at position 374 of H1 A/Michigan/45/15 HA, said substitution being to a non-lysine, such as to a glutamic acid or a conserved substitution of glutamic acid;

a third substitution at the amino acid corresponding to amino acid at position 390 of H1 A/Michigan/45/15 HA, said substitution being to a non-phenylalanine, such as to an aspartic acid or a conserved substitution of aspartic acid; and

a fourth substitution at the amino acid corresponding to amino acid at position 429 of H1 A/Michigan/45/15 HA, said substitution being to a non-leucine, such as to a methionine or a conserved substitution of methionine.

9. The nucleic acid of any one of claim 2 to 8, 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.

10. A modified influenza H1 hemagglutinin (HA) protein encoded by the nucleic acid of any one of claims 1 to 9.

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

12. 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 any one of claims 1 to 9 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 any one of claims 1 to 9;
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.

13. A VLP produced by the method of claim 12, optionally 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.

14. A plant, portion of the plant, or plant cell comprising the nucleic acid of any one of claims 1 to 9, the HA protein of claim 10, or the VLP of claim 11 or 13.

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

16. The VLP of claims 11 or 13 for use in inducing immunity to an influenza infection in a subject, optionally wherein the VLP is administered to the subject orally, intranasally, intramuscularly, intraperitoneally, intravenously or subcutaneously.

17. 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 any one of claims 1 to 9 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 any one of claims 1 to 9;

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.

18. A modified influenza H1 hemagglutinin (HA) protein, the HA protein comprising an amino acid sequence comprising at least one substitution when compared to a corresponding wildtype amino acid sequence, said at least one substitution being at one or more than one amino acid corresponding to amino acid at position 390, 429, 97, or 374 of H1 A/Michigan/45/15 HA.