Claims

1. A nucleic acid comprising a nucleotide sequence encoding a modified influenza H3 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 acids corresponding to amino acids at position 382, 384, 392 or 431 of A/Hong Kong/4801/14 HA.

2. The nucleic acid of claim 1, wherein:

the at least one substitution of the amino acid corresponding to the amino acid at position 382 of A/Hong Kong/4801/14 HA is to a non-asparagine; the at least one substitution of the amino acid corresponding to the amino acid at position 382 of A/Hong Kong/4801/14 HA is to an alanine or a conserved substitution of alanine;

the at least one substitution of the amino acid corresponding to the amino acid at position 384 of A/Hong Kong/4801/14 HA is to a non-leucine;

the at least one substitution of the amino acid corresponding to the amino acid at position 384 of A/Hong Kong/4801/14 HA is to a valine or a conserved substitution of valine;

the at least one substitution of the amino acid corresponding to the amino acid at position 392 of A/Hong Kong/4801/14 HA is to a non-phenylalanine; the at least one substitution of the amino acid corresponding to the amino acid at position 392 of A/Hong Kong/4801/14 HA is to an aspartic acid or a conserved substitution of aspartic acid; the at least one substitution of the amino acid corresponding to the amino acid at position 431 of A/Hong Kong/4801/14 HA is to a non-leucine; and/or the at least one substitution of the amino acid corresponding to the amino acid at position 431 of A/Hong Kong/4801/14 HA is to a methionine or a conserved substitution of methionine.

3. The nucleic acid of claim 2, 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.

4. A modified influenza H3 hemagglutinin (HA) protein encoded by the nucleic acid of any one of claims 1 to 3.

5. A virus-like particle (VLP) comprising the modified influenza H3 hemagglutinin (HA) protein encoded by the nucleic acid of any one of claims 1 to 3.

6. 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 3 into the plant, portion of the plant, or plant cell, and optionally further 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 any one of claims 1 to 3, 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 influenza HA protein encoded by the nucleic acid, thereby producing the VLP, and optionally further incubating the plant, portion of the plant, or plant cell under conditions that permit expression of the proton channel protein encoded by the second nucleic acid, and

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

7. A VLP produced by the method of claim 6.

8. The VLP of claim 7, 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.

9. A plant, portion of the plant, or plant cell comprising the nucleic acid of any one of claims 1 to 3.

10. A plant, portion of the plant, or plant cell comprising the HA protein of claim 4 or the VLP of any one of claims 5, 7 or 8.

11. A composition for inducing an immune response comprising, an effective dose of the VLP of any one of claims 5, 7 or 8, and a pharmaceutically acceptable carrier, adjuvant, vehicle or excipient.

12. The VLP of any one of claims 5, 7 or 8, for use in inducing immunity to an influenza infection in a subject.

13. The method of claim 31, wherein the VLP is 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) i) introducing the nucleic acid of any one of claims 1 to 3 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 3; 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, 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 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 acids corresponding to amino acids at position 382, 384, 392 or 431 of A/Hong Kong/4801/14 HA.