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 acid corresponding to amino acids at positions 382, 384, 392, 431, 524, 525, 526 or 528 of A/Hong Kong/4801/14 HA.

2. The nucleic acid of claim 1, comprising

a first substitution at the amino acid corresponding to amino acid at position 382 of A/Hong Kong/4801/14 HA, said substitution being to a non-asparagine, such as to an alanine or a conserved substitution of alanine,

a second substitution at the amino acid corresponding to amino acid at position 524 of A/Hong Kong/4801/14 HA, said substitution being to a non-cysteine, such as to a serine or a conserved substitution of serine, and

a third substitution at the amino acid corresponding to amino acid at position 528 of A/Hong Kong/4801/14 HA, said substitution being to a non-cysteine, such as to a leucine or a conserved substitution of leucine.

3. The nucleic acid of claim 1, comprising

a first substitution at the amino acid corresponding to amino acid at position 384 of A/Hong Kong/4801/14 HA, said substitution being to a non-leucine, such as to a valine or a conserved substitution of valine,

a second substitution at the amino acid corresponding to amino acid at position 524 of A/Hong Kong/4801/14 HA, said substitution being to a non-cysteine, such as to a serine or a conserved substitution of serine, and

a third substitution at the amino acid corresponding to amino acid at position 528 of A/Hong Kong/4801/14 HA, said substitution being to a non-cysteine, such as to a leucine or a conserved substitution of leucine.

4. The nucleic acid of claim 1, comprising

a first substitution at the amino acid corresponding to amino acid at position 392 of A/Hong Kong/4801/14 HA, said substitution being to a non-phenylalanine, such as to a aspartic acid or a conserved substitution of aspartic acid,

a second substitution at the amino acid corresponding to amino acid at position 524 of A/Hong Kong/4801/14 HA, said substitution being to a non-cysteine, such as to a serine or a conserved substitution of serine, and

a third substitution at the amino acid corresponding to amino acid at position 528 of A/Hong Kong/4801/14 HA, said substitution being to a non-cysteine, such as to a leucine or a conserved substitution of leucine.

5. The nucleic acid of claim 1, comprising

a first substitution at the amino acid corresponding to amino acid at position 431 of A/Hong Kong/4801/14 HA, said substitution being to a non-leucine, such as to a methionine or a conserved substitution of methionine,

a second substitution at the amino acid corresponding to amino acid at position 524 of A/Hong Kong/4801/14 HA, said substitution being to a non-cysteine, such as to a serine or a conserved substitution of serine, and

a third substitution at the amino acid corresponding to amino acid at position 528 of A/Hong Kong/4801/14 HA, said substitution being to a non-cysteine, such as to a leucine or a conserved substitution of leucine.

6. The nucleic acid of claim 1, comprising

a first substitution at the amino acid corresponding to amino acid at position 382 of A/Hong Kong/4801/14 HA, said substitution being to a non-asparagine, such as to an alanine or a conserved substitution of alanine,

a second substitution at the amino acid corresponding to amino acid at position 384 of A/Hong Kong/4801/14 HA, said substitution being to a non-leucine, such as to a valine or a conserved substitution of valine,

a third substitution at the amino acid corresponding to amino acid at position 524 of A/Hong Kong/4801/14 HA, said substitution being to a non-cysteine, such as to a serine or a conserved substitution of serine, and

a fourth substitution at the amino acid corresponding to amino acid at position 528 of A/Hong Kong/4801/14 HA, said substitution being to a non-cysteine, such as to a leucine or a conserved substitution of leucine.

7. The nucleic acid of any one of claims 1 to 6, wherein the HA protein further comprises a substitution at amino acids corresponding to amino acids at positions 525, 526 or 525 and 526 of A/Hong Kong/4801/14 HA, wherein the substitution of the amino acid at position 525 is to a non-

phenylalanine, such as to a leucine or a conserved substitution of leucine, and the substitution of the amino acid at position 526 is to a non-leucine, such as to a valine or a conserved substitution of valine.

8. The nucleic acid of any one of claims 1 to 7, 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.

9. A modified influenza H3 hemagglutinin (HA) protein encoded by the nucleic acid of any one of claims 1 to 8.

10. A virus-like particle (VLP) comprising the HA protein encoded by the nucleic acid of any one of claims 1 to 8.

11. 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 8 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 any one of claims 1 to 8, 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.

12. A VLP produced by the method of claim 11, optionally 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.

13. A plant, portion of the plant, or plant cell comprising the recombinant nucleic acid of any one of claims 1 to 9, the HA protein of claim 10 or the VLP of claims 10 or 12.

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

15. The VLP of any one of claims 10 or 12, for use in inducing immunity to an influenza infection in a subject, wherein the VLP is optionally administered to the subject orally, intranasally, intramuscularly, intraperitoneally, intravenously or subcutaneously.

16. 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 any one of claims 1 to 8 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 any one of claims 1 to 10; 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.

17. 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 acid corresponding to amino acids at positions 382, 384, 392, 431, 524, 525, 526 or 528 of A/Hong Kong/4801/14 HA.