Claims

1. A method of producing a virus like particle (VLP) in a plant comprising,

a) introducing a first nucleic acid comprising a first regulatory region active in the plant and operatively linked to a nucleotide sequence encoding an influenza hemagglutinin (HA) protein selected from the group consisting of B and H3 into the plant, or portion of the plant;

b) introducing a second nucleic acid comprising a second regulatory region active in the plant and operatively linked to a nucleotide sequence encoding a proton channel protein, wherein the proton channel protein is M2 or BM2; and

c) incubating the plant or portion of the plant under conditions that permit the expression of the nucleic acids, thereby producing the VLP.

2. The method of claim 1, wherein the proton channel protein comprises the proton channel signature sequence HXXXW.

3. The method of claim 1, wherein one or more proteolytic loop of the influenza HA protein has been deleted.

4. The method of claim 1, wherein the influenza B HA is from influenza B/Brisbane/60/2008, B/Malaysia/2506/2004 or B/Wisconsin/1/2010.

5. The method of claim 4, wherein one or more proteolytic loop of the influenza B HA protein has been deleted.

6. The method of claim 1, wherein the influenza H3 is from influenza A/Perth/16/2009 or from influenza A/Victoria/361/2011.

7. The method of claim 1, wherein the nucleotide sequence encoding the influenza hemagglutinin (HA) protein has at least 70% sequence identity to a sequence selected from the group consisting of SEQ ID NO: 28, SEQ ID NO:51 and SEQ ID NO:61.

8. The method of claim 1, wherein the sequence of the influenza hemagglutinin (HA) protein is as shown as in at least one of SEQ ID NO:30, SEQ ID NO:54 and SEQ ID NO:64.

9. The method of claim 1, wherein the nucleotide sequence encoding the influenza hemagglutinin (HA) protein has at least 70% sequence identity to a sequence selected from the group consisting of SEQ ID NO: 43 and the underlined portion of SEQ ID NO:57.

10. The method of claim 1, wherein the sequence of the influenza hemagglutinin (HA) protein is as shown as in at least one of SEQ ID NO:41 and SEQ ID NO:58.

11. The method of claim 1, wherein the nucleotide sequence encoding the influenza hemagglutinin (HA) protein has at least 70% sequence identity to a sequence selected from the group consisting of SEQ ID NO: 23 and SEQ ID NO:46.

12. The method of claim 1, wherein the sequence of the influenza hemagglutinin (HA) protein is as shown as in at least one of SEQ ID NO:25 and SEQ ID NO:48.

13. The method of claim 1, wherein the first nucleic acid sequence comprises the first regulatory region operatively linked with one or more than one comovirus enhancer, the nucleotide sequence encoding the influenza hemagglutinin (HA) protein, and one or more than one geminivirus amplification element, and a third nucleic acid encoding a geminivirus replicase is introduced into the plant or portion of the plant.

14. The method of claim 13, wherein the one or more than one comovirus enhancer is a comovirus UTR.

15. The method of claim 14, wherein the comovirus UTR is a Cowpea Mosaic Virus (CPMV) UTR.

16. The method of claim 13, wherein the one or more than one geminivirus amplification element is selected from a Bean Yellow Dwarf Virus long intergenic region (BeYDV LIR), and a BeYDV short intergenic region (BeYDV SIR).

17. The method of claim 13, wherein the nucleotide sequence encoding the influenza hemagglutinin (HA) protein has at least 70% sequence identity to a sequence selected from the group consisting of SEQ ID NO: 28, SEQ ID NO: 51 and SEQ ID NO: 61.

18. The method of claim 13, wherein the sequence of the influenza hemagglutinin (HA) protein is as shown as in at least one of SEQ ID NO: 30, SEQ ID NO: 54 and SEQ ID NO: 64.

19. The method of claim 13, wherein the nucleotide sequence encoding the influenza hemagglutinin (HA) protein has at least 70% sequence identity to a sequence selected from the group consisting of SEQ ID NO: 43 and the underlined portion of SEQ ID NO: 57.

20. The method of claim 13, wherein the sequence of the influenza hemagglutinin (HA) protein is as shown as in at least one of SEQ ID NO: 41 and SEQ ID NO: 58.

21. The method of claim 13, wherein the nucleotide sequence encoding the influenza hemagglutinin (HA) protein has at least 70% sequence identity to a sequence selected from the group consisting of SEQ ID NO: 23 and SEQ ID NO: 46.

22. The method of claim 13, wherein the sequence of the influenza hemagglutinin (HA) protein is as shown as in at least one of SEQ ID NO: 25 and SEQ ID NO: 48.

23. The method of claim 1, wherein in the step of introducing (step a), the nucleic acid is transiently expressed in the plant.

24. The method of claim 1, wherein, in the step of introducing (step a), the nucleic acid is stably expressed in the plant.

25. The method of claim 1 further comprising a step of

d) harvesting the plant and purifying the VLPs.

26. The method of claim 1, wherein the VLP does not contain a viral matrix, a core protein or a channel protein.

27. A method of producing a virus like particle (VLP) comprising,

a) providing a plant or portion of the plant comprising a first nucleic acid comprising a first regulatory region active in the plant and operatively linked to a nucleotide sequence encoding an influenza hemagglutinin (HA) protein selected from the group consisting of B and H3, and a second nucleic acid comprising a second regulatory region active in the plant and operatively linked to a nucleotide sequence encoding a proton channel protein, wherein the proton channel protein is M2 or BM2; and

b) incubating the plant or portion of the plant under conditions that permit the expression of the nucleic acids, thereby producing the VLP.

28. The method of claim 27, wherein the proton channel protein comprises the proton channel signature sequence HXXXW.

29. The method of claim 27, wherein one or more proteolytic loop of the influenza HA protein has been deleted.

30. A VLP produced by the method of claim 3.

31. A VLP produced by the method of claim 29.

32. The VLP of claim 30 or 31, further comprising one or more than one lipid derived from a plant.

33. The VLP of claim 30 or 31, wherein one or more virus protein comprises plant-specific N-glycans, or modified N-glycans.

34. A composition comprising an effective dose of the VLP of claim 30 or 31 for inducing an immune response, and a pharmaceutically acceptable carrier.

35. Use of a composition comprising an effective dose of the VLP of claim 30 or 31 in the manufacture of a medicament for inducing immunity to an influenza virus infection in a subject, wherein the VLP of claim 30 or 31 is to be administered.

36. The use of claim 35, wherein the VLP is to be administered to a subject orally, intradermally, intranasally, intramusclarly, intraperitoneally, intravenously, or subcutaneously.

37. A plant matter comprising a VLP produced by the method of claim 1 or 28.

38. The plant matter of claim 37 for use in inducing immunity to an influenza virus infection in a subject.

39. A food supplement comprising the plant matter of claim 38.

40. The method of claim 1, further comprising introducing a third nucleic acid sequence, the third nucleic acid sequence encoding a suppressor of silencing.

41. The method of claim 13, further comprising introducing a fourth nucleic acid sequence, the fourth nucleic acid sequence encoding a suppressor of silencing.

42. The method of claim 40 or 41 wherein the suppressor of silencing is selected from the group HcPro and p19.

43. The method of claim 1 or 27, wherein the VLP does not contain the proton channel protein.

44. The method of claim 1 or 27, wherein the influenza hemagglutinin (HA) protein is an HA0 protein.

45. The method of claim 1, wherein the M2 protein is selected from the group comprising influenza A/Puerto Rico/8/1934 and influenza A/New Caledonia/20/1999.