

Claims

What is claimed is:

1. A chimeric influenza virus hemagglutinin (HA) polypeptide, comprising one or more stem domain sequence, each having at least 60% homology with a stem domain consensus sequence of H1 subtype HA (H1 HA) and/or H5 subtype HA (H5 HA), fused with one or more globular head domain sequence, each having at least 60% homology with a globular head domain consensus sequence of H1 subtype HA (H1 HA) or H5 subtype HA (H5 HA).
2. The polypeptide of claim 1, wherein the HA is an influenza A HA, an influenza B HA, or an influenza C HA.
3. The polypeptide of claim 1, wherein the homology is at least 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%.
4. The polypeptide of claim 1, wherein the stem domain sequence is an N-terminal stem segment of H1 HA or a C-terminal stem segment of H1 HA; an N-terminal stem segment of H1 HA or a C-terminal stem segment of H1+H5 HA sequences; or an N-terminal stem segment of H5 HA or a C-terminal stem segment of H1+H5 HA sequences.
5. The polypeptide of claim 1, wherein the stem domain consensus sequence of H1 HA comprises an amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 9, or SEQ ID NO: 10.
6. The polypeptide of claim 1, wherein the globular head domain consensus sequence of H5 HA comprises an amino acid sequence of SEQ ID NO: 3, SEQ ID NO: 7, or SEQ ID NO: 11.
7. The polypeptide of claim 1, which comprises an amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 8, or SEQ ID NO: 12.

8. The polypeptide of claim 1, wherein one or more glycosites on HA are monoglycosylated, wherein the monoglycosylated HA has only N-Acetylglucosamine (GlcNAc) on each glycosite.

9. The polypeptide of claim 1, wherein the chimeric influenza virus HA polypeptide is
5 used as an immunogen.

10. An immunogenic composition comprising the chimeric influenza virus HA polypeptide of any of claims 1 to 9 and an adjuvant.

11. The immunogenic composition of claim 10, wherein the adjuvant is a glycolipid adjuvant.

10 12. A method of immunizing a subject against influenza virus or preventing an influenza virus disease comprising administering an effective amount of a chimeric influenza virus hemagglutinin (HA) polypeptide of any of claims 1 to 9 or an immunogenic composition of claims 10 to the subject.

13. The method of claim 12, wherein the method elicits CD4⁺ and CD8⁺ T-cell
15 immune responses.

14. The method of claim 12, wherein the method induces stem-specific antibodies, with higher antibody-dependent cellular cytotoxicity (ADCC), better neutralizing and stronger cross-protection activities against H1, H3, H5 and H7 strains and subtypes.

15. The method of claim 12, wherein the method enhances the vaccine efficacy with
20 more IFN- γ , IL-4 and CD8⁺ memory T cells produced.

16. A recombinant polynucleotide comprising a nucleic acid sequence encoding the polypeptide of any of claims 1 to 9 and optionally a nucleic acid sequence encoding a signal peptide.

17. The recombinant polynucleotide of claim 16, wherein the signal peptide
25 comprises a sequence of SEQ ID NO: 13 or SEQ ID NO: 14.

18. A vector comprising the recombinant polynucleotide of claim 17.

19. A host cell comprising the vector of claim 18.