Claims

What is claimed is:

1. A polypeptide whose sequence includes an element corresponding to a reference sequence element, which reference sequence element comprises residues 130-228 of a reference H5 HA that does not mediate significant human infectivity,

wherein the polypeptide's sequence element shows at least 80% overall sequence identity with the reference sequence element but is not identical to the reference sequence element in that it includes at least one of:

i. a first feature that is a deletion of the amino acid corresponding to amino acid 130 of the reference H5 HA;

ii. a second feature selected from the group consisting of:

i. Xaa_{226} + ser228,

ii. Lys_{224} + Xaa_{226}

iii. Xaa_{137} + Xaa_{226}+ ser228,

iv. Xaa_{226} + gly227 + ser228,

v. Xaa_{137} + pro221 + Xaa_{226}+ ser228, and

vi. Xaa_{137} + thr155 + pro221 + Xaa_{226} + gly227 + ser228;

iii. a third feature selected from the group consisting of:

i. glu188 + Xaa_{192} + Xaa_{193},

ii. asp187 + Xaa_{193}, and

iii. Xaa_{193}; and

iv. a fourth feature selected from the group consisting of:

i. ala160,

ii. asn158 + ala160, and

iii. asn158 + thr160,

wherein the position of the amino acids of the second, third, and fourth features correspond to the referenced position of the reference H5 HA, and wherein Xaa_{226} is selected from the group Leu, Ile, Val, Met, and Ala, Xaa_{137} is selected from the group Arg, Lys, Gln, Glu, His, and Asn, Xaa_{192} is selected from the group Arg, Thr, Ala, Val, Leu, and Ile, and Xaa_{193} is selected from the group Thr, Ala, Lys, Arg, and His.

2. The polypeptide of claim 1, wherein the polypeptide includes at least two features.

3. The polypeptide of claim 1, wherein the polypeptide includes at least three features.

4. The polypeptide of claim 1, wherein the polypeptide includes all four features.

5. The polypeptide of claim 1, wherein the polypeptide is between 98 amino acids and 400 amino acids in length, inclusive.

6. The polypeptide of claim 1, wherein the peptide's sequence element is between 98 amino acids and 230 amino acids in length, inclusive.

7. A vaccine composition comprising at least one antigen comprising

a polypeptide whose sequence includes an element corresponding to a reference sequence element, which reference sequence element comprises residues 130-228 of a reference H5 HA that does not mediate significant human infectivity,

wherein the polypeptide's sequence element shows at least 80% overall sequence identity with the reference sequence element but is not identical to the reference sequence element in that it includes at least one of:

a first feature that is a deletion of the amino acid corresponding to amino acid 130 of the reference H5 HA;

a second feature selected from the group consisting of:

i. Xaa_{226} + ser228,
ii. Lys_{224} + Xaa_{226}
iii. Xaa_{137} + Xaa_{226} + ser228,
iv. Xaa1 + gly227 + ser228,
v. Xaa_{137} + pro221 + Xaa_{226} + ser228, and
vi. Xaa_{137} + thr155 + pro221 + Xaa_{226} + gly227 + ser228;

a third feature selected from the group consisting of:

iv. glu188 + Xaa_{192} + Xaa_{193},

v. asp187 + Xaa_{193}, and

vi. Xaa_{193}; and

a fourth feature selected from the group consisting of:

iv. ala160,

v. asn158 + ala160, and

vi. asn158 + thr160,

wherein the position of the amino acids of the second, third, and fourth features correspond to the referenced position of the reference H5 HA, and wherein Xaa_{226} is selected from the group Leu, Ile, Val, Met, and Ala, Xaa_{137} is selected from the group Arg, Lys, Gln, Glu, His, and Asn, Xaa_{192} is selected from the group Arg, Thr, Ala, Val, Leu, and Ile, and Xaa_{193} is selected from the group Thr, Ala, Lys, Arg, and His; and

a pharmaceutically acceptable carrier.

8. The vaccine composition of claim 7, wherein the polypeptide includes at least two features.

9. The vaccine composition of claim 7, wherein the polypeptide includes at least three features.

10. The vaccine composition of claim 7, wherein the polypeptide includes all four features.

11. The vaccine composition of claim 7, wherein the polypeptide is between 98 amino acids and 400 amino acids in length, inclusive.

12. The vaccine composition of claim 7, wherein the peptide's sequence element is between 98 amino acids and 230 amino acids in length, inclusive.

13. A method of providing a vaccine comprising

providing at least one antigen comprising a polypeptide whose sequence includes an element corresponding to a reference sequence element, which reference sequence element comprises residues 130-228 of a reference H5 HA that does not mediate significant human infectivity,

wherein the polypeptide's sequence element shows at least 80% overall sequence identity with the reference sequence element but is not identical to the reference sequence element in that it includes at least one of:

a first feature that is a deletion of the amino acid corresponding to amino acid 130 of the reference H5 HA;

a second feature selected from the group consisting of:

i. Xaa_{226} + ser228,
ii. Lys_{224} + Xaa_{226}
iii. Xaa_{137} + Xaa_{226} + ser228,
iv. Xaa_{226} + gly227 + ser228,
v. Xaa_{137} + pro221 + Xaa_{226} + ser228, and
vi. Xaa_{137} + thr155 + pro221 + Xaa_{226} + gly227 + ser228;

a third feature selected from the group consisting of:

i. glu188 + Xaa_{192} + Xaa_{193},
ii. asp187 + Xaa_{193}, and
iii. Xaa_{193}; and

a fourth feature selected from the group consisting of:

i. ala160,
ii. asn158 + ala160, and
iii. asn 158 + thr160,

wherein the position of the amino acids of the second, third, and fourth features correspond to the referenced position of the reference H5 HA, and wherein Xaa_{226} is selected from the group Leu, Ile, Val, Met, and Ala, Xaa_{137} is selected from the group Arg, Lys, Gln, Glu, His, and Asn, Xaa_{192} is selected from the group Arg, Thr, Ala, Val, Leu, and Ile, and Xaa_{193} is selected from the group Thr, Ala, Lys, Arg, and His; and

formulating the provided at least one antigen into a vaccine composition.

14. The method of claim 13, wherein the polypeptide includes at least two features.

15. The method of claim 13, wherein the polypeptide includes at least three features.

16. The method of claim 13, wherein the polypeptide includes all four features.

17. The method of claim 13, wherein the polypeptide is between 98 amino acids and 400 amino acids in length, inclusive.

18. The method of claim 13, wherein the peptide's sequence element is between 98 amino acids and 230 amino acids in length, inclusive.

19. A diagnostic kit for determining pandemic risk in a strain of H5 influenza, the kit comprising

at least one antibody that binds to a polypeptide whose sequence includes an element corresponding to a reference sequence element, which reference sequence element comprises residues 130-228 of a reference H5 HA that does not mediate significant human infectivity,

wherein the polypeptide's sequence element shows at least 80% overall sequence identity with the reference sequence element but is not identical to the reference sequence element in that it includes at least one of:

a first feature that is a deletion of the amino acid corresponding to amino acid 130 of the reference H5 HA;

a second feature selected from the group consisting of:

i. Xaa_{226} + ser228,

ii. Lys_{224} + Xaa_{226}

iii. Xaa_{137} + Xaa_{226} + ser228,

iv. Xaa_{226} + gly227 + ser228,

v. Xaa_{137} + pro221 + Xaa_{226} + ser228, and

vi. Xaa_{137} + thr155 + pro221 + Xaa_{226} + gly227 + ser228;

a third feature selected from the group consisting of:

i. glu188 + Xaa_{192} + Xaa_{193},

ii. asp187 + Xaa_{193}, and

iii. Xaa_{193}; and

a fourth feature selected from the group consisting of:

i. ala160,

ii. asn158 + ala160, and

iii. asn158 + thr160,

wherein the position of the amino acids of the second, third, and fourth features correspond to the referenced position of the reference H5 HA, and wherein Xaa_{226} is selected from the group Leu, Ile, Val, Met, and Ala, Xaa_{137} is selected from the group Arg, Lys, Gln, Glu, His, and Asn, Xaa_{192} is selected from the group Arg, Thr, Ala, Val, Leu, and Ile, and Xaa_{193} is selected from the group Thr, Ala, Lys, Arg, and His.

20. The diagnostic kit of claim 19, wherein the polypeptide includes at least two features.

21. The diagnostic kit of claim 19, wherein the polypeptide includes at least three features.

22. The diagnostic kit of claim 19, wherein the polypeptide includes all four features.

23. The diagnostic kit of claim 19, wherein the polypeptide is between 98 amino acids and 400 amino acids in length, inclusive.

24. The diagnostic kit of claim 19, wherein the peptide's sequence element is between 98 amino acids and 230 amino acids in length, inclusive.

25. The diagnostic kit of claim 19, wherein the reference sequence element is not glycosylated at position 158.

26. The diagnostic kit of claim 19, further comprising an antibody that binds to a reference H5 HA that does not infect humans.

27. A method of monitoring influenza in a sample:

a. obtaining a sample from a source suspected to contain influenza;

b. contacting the sample with one or more agents that specifically binds to an H5 HA polypeptide of claim 1;

c. detecting binding of the agent with the sample, so that presence and/or level of the H5 HA in the sample is determined.

28. The method of claim 27, wherein the source is an environmental source.

29. The method of claim 27, wherein the source is a human patient.

30. The method of claim 27, wherein the obtaining, contacting and detecting steps are repeated at least once after a period of time has elapsed since the first obtaining, contacting and detecting steps were completed.

31. The method of claim 27, further comprising contacting a sample from the source with one or more agents that specifically bind to an H5 HA that does not infect humans.

32. A polypeptide whose sequence includes an element corresponding to a reference sequence element, which reference sequence element comprises residues 130-228 of a reference H5 HA that does not mediate significant human infectivity,

wherein the polypeptide's sequence element shows at least 80% overall sequence identity with the reference sequence element but is not identical to the reference sequence element in that it includes at least one of:

a first feature that is a deletion of the amino acid corresponding to amino acid 130 of the reference H5 HA;

a second feature that is arg137 + thr155 + pro221 + leu226 + gly227 + ser228;

a third feature that is glu188 + arg192 + ala193; and

a fourth feature that is asn 158 + thr160,

wherein the position of the amino acids of the second, third, and fourth features correspond to the referenced position of the reference H5 HA.

33. A polypeptide whose sequence includes an element corresponding to a reference sequence element, which reference sequence element comprises residues 130-228 of a reference H5 HA that does not mediate significant human infectivity,

wherein the polypeptide's sequence element shows at least 80% overall sequence identity with the reference sequence element but is not identical to the reference sequence element in that it includes at least one of:

a first feature that is a deletion of the amino acid corresponding to amino acid 130 of the reference H5 HA;

a second feature that is arg137 + lys226 + ser228,

a third feature that is asp187 + thr193; and

a fourth feature that is asn158 + ala160,

wherein the position of the amino acids of the second, third, and fourth features correspond to the referenced position of the reference H5 HA.

Claims

What is claimed is:

1. An engineered polypeptide whose sequence, includes an element corresponding to a reference sequence element, which reference sequence element comprises residues 130-228 of a reference H5 hemagglutinin (HA), including residues 127-136 (the "130 loop"), using positions based on the canonical H3 numbering system, which reference H5 HA is selected from the group consisting of wild type A/Egypt/N03450/2009 ("Egy09") and A/duck/Egypt/10185SS/2010 ("Egy10"),

wherein the polypeptide's sequence element shows at least 80% overall sequence identity with the reference sequence element but is not identical to the reference sequence element and comprises each of:

a first feature that is a deletion of an amino acid corresponding to an amino acid in the 130 loop of the reference H5 HA;

a second feature that is Lys_{224} + Leu_{226}

a third feature selected from the group consisting of:

i. Asp_{187} + Arg_{193}, and

ii. Arg_{193};

a fourth feature selected from the group consisting of:

i. Ala_{160}, and

ii. Asn_{158} + Ala_{160};

wherein the position of the amino acids of the features correspond to the referenced position of the reference H5 HA, and

which engineered HA polypeptide is characterized by increased preference for binding to α2-6 topology over α2-3 topology glycans relative to that preference displayed by the reference H5 HA polypeptide.

2. The polypeptide of claim 1, wherein the polypeptide is between 98 amino acids and 400 amino acids in length, inclusive.

3. The polypeptide of claim 1, wherein the peptide's sequence element is between 98 amino acids and 230 amino acids in length, inclusive.

4. A vaccine composition comprising at least one antigen that is
a polypeptide of claim 1 and
a pharmaceutically acceptable carrier.

5. The vaccine composition of claim 4, wherein the polypeptide is between 98 amino acids and 400 amino acids in length, inclusive.

6. The vaccine composition of claim 4, wherein the peptide's sequence element is between 98 amino acids and 230 amino acids in length, inclusive.

7. A method of providing a vaccine comprising
providing at least one antigen comprising a polypeptide of claim 1 and
formulating the provided at least one antigen into a vaccine composition.

8. The method of claim 7, wherein the polypeptide is between 98 amino acids and 400 amino acids in length, inclusive.

9. The method of claim 7, wherein the peptide's sequence element is between 98 amino acids and 230 amino acids in length, inclusive.

10. A diagnostic kit for determining pandemic risk in a strain of H5 influenza, the kit comprising
at least one antibody that binds to a polypeptide of claim 1.

11. The diagnostic kit of claim 10, wherein the polypeptide is between 98 amino acids and 400 amino acids in length, inclusive.

12. The diagnostic kit of claim 10, wherein the peptide's sequence element is between 98 amino acids and 230 amino acids in length, inclusive.

13. The diagnostic kit of claim 10, wherein the reference sequence element is not glycosylated at position 158.

14. The diagnostic kit of claim 10, further comprising an antibody that binds to a reference H5 HA that does not infect humans.

15. A method of monitoring influenza in a sample:

a. obtaining a sample from a source suspected to contain influenza;

b. contacting the sample with one or more agents that specifically binds to an H5 HA polypeptide of claim 1;

c. detecting binding of the agent with the sample, so that presence and/or level of the H5 HA in the sample is determined.

16. The method of claim 15, wherein the source is an environmental source.

17. The method of claim 15, wherein the source is a human patient.

18. The method of claim 15, wherein the obtaining, contacting and detecting steps are repeated at least once after a period of time has elapsed since the first obtaining, contacting and detecting steps were completed.

19. The method of claim 15, further comprising contacting a sample from the source with one or more agents that specifically bind to an H5 HA that does not infect humans.

20. An engineered polypeptide whose sequence, includes an element corresponding to a reference sequence element, which reference sequence element comprises residues 130-228 of a reference hemagglutinin H5 HA, including residues 127-136 (the "130 loop"), using positions based on the canonical H3 numbering system, which reference H5 HA is Egy09,

wherein the polypeptide's sequence element shows at least 80% overall sequence identity with the reference sequence element but is not identical to the reference sequence element and comprises each of:

a first feature that is a deletion of an amino acid corresponding to an amino acid in the 130 loop of the reference H5 HA;

a second feature that is Lys_{224} + Leu_{226};

a third feature selected from the group consisting of:

i. Asp_{187} + Arg_{193}, and

ii. Xaa_{193};

a fourth feature that is Asn_{158} + Ala_{160},

wherein the position of the amino acids of the features correspond to the referenced position of the reference H5 HA, and

which engineered HA polypeptide is characterized by increased preference for binding to α2-6 topology over α2-3 topology glycans relative to that preference displayed by the reference H5 HA polypeptide.

21. An engineered polypeptide whose sequence, includes an element corresponding to a reference sequence element, which reference sequence element comprises residues 130-228 of a reference hemagglutinin H5 HA including residues 127-136 (the "130 loop"), using positions based on the canonical H3 numbering system, which reference H5 HA is Egy09,

wherein the polypeptide's sequence element shows at least 80% overall sequence identity with the reference sequence element but is not identical to the reference sequence element and comprises each of:

a first feature that is a deletion of an amino acid corresponding to an amino acid in the 130 loop of the reference H5 HA;

a second feature that is Lys_{224} + Leu_{226},

a third feature that is Asp_{187} + Arg_{193}; and

a fourth feature that is Asn_{158} + Ala_{160},

wherein the position of the amino acids of the features correspond to the referenced position of the reference H5 HA, and

which engineered HA polypeptide is characterized by increased preference for binding to α2-6 topology over α2-3 topology glycans relative to that preference displayed by the reference H5 HA polypeptide.

22. An engineered polypeptide whose sequence, includes an element corresponding to a reference sequence element, which reference sequence element comprises residues 130-228 of a reference H5 HA, including residues 127-136 (the "130 loop"), using positions based on the canonical H3 numbering system, which reference H5 HA is Egy10,

wherein the polypeptide's sequence element shows at least 80% overall sequence identity with the reference sequence element but is not identical to the reference sequence element and comprises each of:

a first feature that is a deletion of an amino acid corresponding to an amino acid in the 130 loop of the reference H5 HA;

a second feature that is Lys_{224} + Leu_{226},

a third feature that is Asp_{187} + Arg_{193}; and

a fourth feature that is Ala_{160},

wherein the position of the amino acids of the features correspond to the referenced position of the reference H5 HA, and

which engineered HA polypeptide is characterized by increased preference for binding to α2-6 topology over α2-3 topology glycans relative to that preference displayed by the reference H5 HA polypeptide.