

CLAIMS:

1. A non-replicating recombinant adeno-associated virus (rAAV) having an AAV capsid having packaged therein a vector genome which comprises AAV inverted terminal repeat sequences and at least one nucleic acid sequence encoding an immunoglobulin region (a), (b), (c) and (d), wherein each of immunoglobulin regions (a), (b), (c) and (d) is expressed from the rAAV, wherein

(a) is a first immunoglobulin region having the amino acid sequence of SEQ ID NO:1: (Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Ile Ser Ile Phe Asp Ile Tyr Ala Met Asp Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Leu Val Ala Val Ser Phe Arg Asp Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys His Val Ser Leu Tyr Arg Asp Pro Leu Gly Val Ala Gly Gly Ile Gly Val Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser);

(b) a second immunoglobulin region having an amino acid sequence of SEQ ID NO: 2: (Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Tyr Ala Met Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Glu Phe Val Ala Ala Ile Asn Ala Leu Gly Thr Arg Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Thr Ala Gln Gly Gln Trp Arg Ala Ala Pro Val Ala Val Ala Ala Glu Tyr Glu Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser);

(c) a third immunoglobulin region having an amino acid sequence of SEQ ID NO: 3: (Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Glu Asn Lys Ala Ile Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Glu Gly Val Leu Cys Ile Ser Lys Ser Gly Ser Trp Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Val Tyr Leu Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala Thr Thr Thr Ala Gly Gly Gly Leu Cys Trp Asp Gly Thr Thr Phe Ser Arg Leu Ala Ser Ser Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser);

and

(d) a fourth immunoglobulin region having an amino acid sequence of SEQ ID NO:4: (Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Ser Trp Met Tyr Trp Leu Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser Val Ile Asn Thr Asp Gly Gly Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Asp Trp Gly Gly Pro Glu Pro Thr Arg Gly Gln Gly Thr Leu Val Thr Val Ser Ser).

2. The rAAV according to claim 1, wherein the first, second, third and/or fourth immunoglobulin regions are in a fusion construct which further comprises an Fc region, wherein there is optionally a linking sequence joining the four immunoglobulin regions and the Fc region.
3. The rAAV according to claim 2, wherein the fusion construct further comprises the linking sequence located between two or more of the immunoglobulin regions.
4. The rAAV according to claim 2 or 3, wherein each linking sequence is independently selected.
5. The rAAV according to any of claims 2 to 4, wherein at least one linking sequence is GGGGSGGGGS (SEQ ID NO: 7).
6. The rAAV according to any one of claims 1 to 5, wherein the vector genome comprises a signal peptide from a source exogenous to the immunoglobulin at the amino terminus of the first immunoglobulin.
7. The rAAV according to claim 6, wherein the signal peptide is a human interleukin-2 signal peptide.

8. The rAAV according to any one of claims 1 to 7, wherein the vector genome comprises a monocistronic expression cassette.
9. The rAAV according to any one of claims 1 to 7, wherein the vector genome comprises a bicistronic expression cassette.
10. The rAAV according to claim 9, wherein two of the immunoglobulin regions are linked to a first Fc to form a first chain and the other two immunoglobulin regions are linked to a second Fc to form a second chain.
11. The rAAV according to claim 9 or 10, wherein the vector genome comprises an IRES or an F2A sequence.
12. The rAAV according to any one of claims 1 to 11, wherein the vector genome comprises a 5' UTR.
13. The rAAV according to claim 12, wherein the 5' UTR is a fragment of human c-myc 5' UTR.
14. The rAAV according to any one of claims 1 to 13, wherein the vector genome comprises a single- stranded AAV 5' inverted terminal repeat and an AAV 3' inverted terminal repeat.
15. The rAAV according to any one of claims 1 to 14, wherein the vector genome encodes an anti-influenza fusion construct having the amino acid sequence of SEQ ID NO: 27, SEQ ID NO: 12, or SEQ ID NO: 30.
16. The rAAV according to any one of claims 1 to 15, wherein the vector genome comprises a nucleic acid sequence selected from the group consisting of: SEQ ID NO: 21, SEQ ID NO: 19; SEQ ID NO: 15, SEQ ID NO: 14, SEQ ID NO: 5, SEQ ID NO: 26, SEQ ID NO: 20, SEQ ID NO: 13, SEQ ID NO: 31 and SEQ ID NO: 32.

17. The rAAV according to any one of claims 1 to 16, wherein the rAAV has an AAVhu68 capsid, wherein the AAVhu68 capsid comprises:

a heterogenous population of AAVhu68 vp1 proteins selected from: vp1 proteins produced by expression from a nucleic acid sequence which encodes the predicted amino acid sequence of 1 to 736 of SEQ ID NO:16, vp1 proteins produced from SEQ ID NO: 18, or vp1 proteins produced from a nucleic acid sequence at least 70% identical to SEQ ID NO:18 which encodes the predicted amino acid sequence of 1 to 736 of SEQ ID NO:16,

a heterogenous population of AAVhu68 vp2 proteins selected from: vp2 proteins produced by expression from a nucleic acid sequence which encodes the predicted amino acid sequence of at least about amino acids 138 to 736 of SEQ ID NO:16, vp2 proteins produced from a sequence comprising at least nucleotides 412 to 2211 of SEQ ID NO:18, or vp2 proteins produced from a nucleic acid sequence at least 70% identical to at least nucleotides 412 to 2211 of SEQ ID NO:18 which encodes the predicted amino acid sequence of at least about amino acids 138 to 736 of SEQ ID NO:16,

a heterogenous population of AAVhu68 vp3 proteins selected from: vp3 produced by expression from a nucleic acid sequence which encodes the predicted amino acid sequence of at least about amino acids 203 to 736 of SEQ ID NO:16, vp3 proteins produced from a sequence comprising at least nucleotides 607 to 2211 of SEQ ID NO:18, or vp3 proteins produced from a nucleic acid sequence at least 70% identical to at least nucleotides 607 to 2211 of SEQ ID NO:18 which encodes the predicted amino acid sequence of at least about amino acids 203 to 736 of SEQ ID NO:16.

18. The rAAV according to any one of claims 1 to 17, wherein the nucleic acid sequence encoding the proteins is SEQ ID NO: 18, or a sequence at least 80% to at least 99% identical to SEQ ID NO: 18 which encodes the amino acid sequence of SEQ ID NO:16.

19. The rAAV according to any one of claim 17 or 18, wherein the sequence is at least 80% to 97% identical to SEQ ID NO: 18.

20. The rAAV according to any one of claims 1 to 16, wherein the AAV has an AAV9 capsid, wherein said AAV9 capsid comprises vp1 capsid proteins having an amino acid sequence of SEQ ID NO: 17 or an amino acid sequence encoded by SEQ ID NO: 36.
21. A composition comprising a carrier, diluent or excipient and a stock of at least the non-replicating rAAV according to any one of claims 1 to 20.
22. The composition according to claim 21, wherein the composition is formulated for intranasal administration.
23. The composition according to claim 22, wherein the composition is formulated for intramuscular or intravenous administration.
24. The rAAV according to any one of claims 1 to 20 or a composition according to any one of claims 21 to 23 for use in vaccinating or immunizing human patients against influenza.
25. The rAAV or composition according to claim 24 adapted for dosing a patient intranasally with about 10^9 to about 7×10^{13} GC of rAAV.
26. The rAAV according to any one of claims 1 to 20 or a composition according to any one of claims 21 to 25 for use in protecting human patients against influenza.
27. Use of the rAAV according to any one of claim 1 to 20 or a composition according to any one of claims 21 to 25 in the preparation of a medicament for immunizing human patients against influenza..
28. The use according to claim 27, wherein the patient is to be administered a dose intranasally in an amount of about 10^9 to about 7×10^{13} GC of rAAV.
29. A product which comprises a container comprising a rAAV according to any one of claims 1 to 20, optional diluent, and instructions for administration.