Claims

1. A group 1 influenza A hemagglutinin (HA) stem polypeptide, comprising an HA1 and a HA2 domain, said HA stem polypeptide comprising an amino acid sequence which comprises:

(i) a deletion of the head region in the HA1 domain;

(ii) a modification of the trimerization region in the HA2 domain;

(iii) at least 2 cysteine residues forming an intramonomeric disulphide bridge;

(iv) at least 2 cysteine residues forming an intermonomeric disulphide bridge;

wherein the amino acid corresponding to the amino acid at position 392 is P, R or Y, preferably P or R, and the amino acid corresponding to the amino acid at position 434 is Q, and wherein the numbering of the amino acid positions is based on SEQ ID NO: 15.

2. Polypeptide according to claim 1, wherein said stem polypeptides comprise an amino acid sequence which comprises:

(i) a deletion of the head region in the HA1 domain, said deletion comprising at least the amino acid sequence from the amino acid corresponding to the amino acid at position 53 up to and including the amino acid corresponding to the amino acid at position 302;
(ii) a modification of the trimerization region in the HA2 domain, preferably a modification of the trimerization region in the C-helix, said trimerization region comprising the amino acid sequence from the amino acid corresponding to the amino acid at position 405 up to and including the amino acid corresponding to the amino acid at position 419;
(iii) a cysteine at the amino acid position corresponding to position 310 and a cysteine at the position corresponding to position 422;
(iv) a cysteine at the position corresponding to position 397 in combination with a cysteine at the position corresponding to position 405; or a cysteine at the position corresponding to position 396 in combination with a cysteine at the position corresponding to position 408; or or a cysteine at the position corresponding to position 399 in combination with a cysteine at position 405;

wherein the amino acid at the position corresponding to position 392 is P, R or Y, preferably P or R, and wherein the amino acid at the position corresponding to position 434 is Q.

3. Polypeptide according to claim 1 or 2, wherein the deletion in the HA1 domain comprises at least the amino acid sequence from the amino acid at position 47 up to and including the amino acid at position 306.

4. Polypeptide according to claim 1, 2 or 3, wherein the modification of the trimerization domain comprises the introduction of a heterologous trimerization domain in the C-helix.

5. Polypeptide according to claim 4, wherein the heterologous trimerization domain is a GCN4 sequence.

6. Polypeptide according to claim 1, 2 or 3, wherein the modification of the trimerization domain comprises an optimization of the heptad repeat sequence in the C-helix.

7. Polypeptide according to any of the preceding claims, wherein the amino acid corresponding to the amino acid 392 is Y, P or R and the amino acid corresponding to the amino acid at position 434 is Q and the amino acid at the position corresponding to position 442 is A.

8. Polypeptide according to any one of the preceding claims, comprising a cysteine at the position corresponding to position 397 in combination with a cysteine at the position corresponding to position 405.

9. Polypeptide according to any one of the preceding claims, wherein:

- the amino acid at the position corresponding to position 395 is I;
- the amino acid at the position corresponding to position 399 is Y or C, preferably Y;
- the amino acid at the position corresponding to position 400 is P;
- the amino acid at the position corresponding to position 401 is K;
- the amino acid at the position corresponding to position 402 is S; and/or
- the amino acid at the position corresponding to position 404 is R or Q.

10. Polypeptide according to any one of the preceding claims, wherein the amino acid corresponding to the amino acid at position 323 is K and/or the amino acid corresponding to the amino acid at position 326 is K.

11. Polypeptide according to any one of the preceding claims, wherein the amino acid corresponding to the amino acid at position 339 is T.

12. Polypeptide according to anyone of the preceding claims, wherein the polypeptide does not comprise a protease cleavage site.

13. Polypeptide according to claim 12, wherein the amino acid at position 329 is not arginine (R), preferably wherein the amino acid at position 329 is glutamine (Q).

14. Polypeptide according to anyone of the preceding claims 1-11, wherein the polypeptide comprises a natural cleavage site or a polybasic cleavage site.

15. Polypeptide according to any one of the preceding claims, wherein the polypeptide comprises (part) of a a signal sequence.

16. Polypeptide according to any one of the preceding claims, comprising a truncated HA2 domain.

17. Polypeptide according to claim 16, wherein the polypeptide does not comprise a transmembrane and cytoplasmic domain.

18. Polypeptide according to any one of the preceding claims, wherein at least the C-terminal part of the HA2 domain starting with the amino acid corresponding to the amino acid at position 516 has been deleted.

19. Polypeptide according to anyone of the preceding claims, wherein the deletion in the HA1 domain has been replaced by a linking sequence of 1-10 amino acids.

20. Nucleic acid encoding a polypeptide according to any one of the precding claims.

21. Vector comprising a nucleic acid molecule encoding a group 1 HA stem polypeptide according to any one of the claims 1-19.

22. Vector according to claim 21, wherein the vector is a recombinant adenoviral vector.

23. Pharmaceutical composition comprising a polypeptide according to any one of claims 1 to 19 and/or a nucleic acid according to claim 20, and/or a vector according to claim 21 or 22, and a pharmaceutically acceptable carrier.

24. Polypeptide according to any one of claims 1 to 19, a nucleic acid according to claim 20, and/or a vector according to claim 21 or 22, for use in inducing an immune response against an influenza virus.

25. Polypeptide according to any one of claims 1 to 19 and/or a nucleic acid according to claim 20, and/or a vector according to claim 21 or 22 for use as a vaccine.