Hemagglutinin protein is the receptor-binding and membrane fusion glycoprotein of influenza virus and the target for infectivity-neutralizing antibodies. The entire hemagglutinin protein (HA) from the H5N1 is composed of 568 amino acids, with a molecular weight of 56 kDa. The HA molecule consists of HA1 and HA2 subunits, with the HA1 subunit mediating initial contact with the cell membrane and HA2 being responsible for membrane fusion (*Chizmadzhev, Bioelectrochemistry 2004, 63(1–2):129-136*).

Baculovirus/insect cell systems have been used to express hemagglutinin genes isolated from avian influenza subtypes (*Babai et al., Vaccine 1999, 17(9–10):1223-1238; Crawford et al., Vaccine 1999, 17(18):2265-2274; Johansson et al., Vaccine 1999, 17(15–16):2073-2080); Nwe et al., BMC Mircobiology 2006, 6(16):doi:10.1186/1471-2180-6-16*). However, the those recombinant proteins seems not to be protective in any case, or only less effective at least for some species (Treanor et al., Vaccine 2001, 19: 1732-1737).

Thus, there is a need to increase availability of improved vaccines and new vaccination approaches to provide better approaches to control influenza infections and to have a positive impact on disease load.

SUMMARY

In one aspect, there is provided a vaccine comprising the haemagglutinin protein of influenza virus subtype 5 (H5 protein) and an adjuvant, wherein the H5 protein has the amino acids 223N, 120N and 155N and the modification 328K+, wherein numbering of the amino acid positions of the H5 protein refers to the amino acid position as exemplarily given in SEQ IN NO:1 and wherein the modification 328K+ means that at amino acid position 328 of H5 protein a second Lysine (K+) is inserted; and wherein the adjuvant is selected from the group consisting of oil-in-water emulsions.

In another aspect, there is provided a method for producing the vaccine as defined above comprising the steps of: a. obtaining a H5 protein having the amino acids 223N, 120N and 155N and the modification 328K+, wherein numbering of the amino acid positions of the H5 protein refers to the amino acid position as exemplarily given in SEQ ID NO:1 and wherein the modification 328K+ means that at amino acid position 328 of H5 protein a second Lysine (K+) is inserted; and b. admixing the H5 protein of step (a) with an adjuvant selected from the group consisting of oil-in-water emulsions.

DESCRIPTION OF THE INVENTION

Before the embodiments of the present invention it shall be noted that as used herein and in the appended claims, the singular forms "a", "an", and "the" include plural reference unless the context clearly dictates otherwise. Thus, for example, reference to "a preparation" includes a plurality of such preparations; reference to the "carrier" is a reference to one or more carriers and equivalents thereof known to those skilled in the art, and so forth. Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. All given ranges and values may vary by 1 to 5 % unless indicated otherwise or known otherwise by the person skilled in the art, therefore, the term "about" was omitted from the description. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods, devices, and materials are now described. All publications mentioned herein are incorporated herein by reference for the purpose of describing and disclosing the substances, excipients, carriers, and methodologies as reported in the publications which might be used in connection with the invention. Nothing

CLAIMS:

1. A vaccine comprising the haemagglutinin protein of influenza virus subtype 5 (H5 protein) and an adjuvant, wherein the H5 protein has the amino acids 223N, 120N and 155N and the modification 328K+, wherein numbering of the amino acid positions of the H5 protein refers to the amino acid position as exemplarily given in SEQ ID NO:1 and wherein the modification 328K+ means that at amino acid position 328 of H5 protein a second Lysine (K+) is inserted; and wherein the adjuvant is selected from the group consisting of oil-in-water emulsions.

2. The vaccine according to claim 1, wherein such H5 protein has the amino acid 94N.

~~3. The vaccine according to claim 1 or 2, wherein such H5 protein has the amino acid 120N.~~

~~4. The vaccine according to any one of claims 1 to 3, wherein such H5 protein has the amino acid 155N.~~

~~5.~~3. The vaccine according to ~~any one of~~ claims 1 ~~to 4~~or 2, wherein such H5 protein has one or more of the following amino acid clusters selected from the group consisting of:

a. aa 93 - 95: GNF
b. aa 123 – 125: SDH
c. aa 128 – 130: SSG
d. aa 138 - 140: GSS
e. aa 226 - 228: MDF
f. aa 270 – 272: EVE
g. aa 309 – 311: NKL.

~~6.~~4. The vaccine according to any one of claims 1 to ~~5~~3, wherein such H5 protein comprises a peptide that comprises:

i. the amino acid sequences of SEQ ID NO:4; SEQ ID NO:5 or SEQ ID NO:6; or

ii. any peptide that has at least 85% sequence homology to the polypeptide of i) and that comprises hemagglutinin inhibition in a standard hemagglutinin inhibition assay; or

iii. any part of the polypeptides of i) or ii) comprising at least 8 contiguous amino acids of any of such peptides of i) or ii) and wherein any of such peptide comprises hemagglutinin inhibition in a standard hemagglutinin inhibition assay; or

iv. any peptide of i), ii) or iii) having one of the amino acids 36T, 36K, 83A, 83T, 83D, 86A, 86V, 120S, 155S, 156A, 156T, 189R, 189K, 212K, 212R, 212E, 263A or 263T; or

v. any peptide of i), ii), iii) or iv) having one or more of the following amino acid clusters selected from the group consisting of:

a. aa 93 - 95: GNF
b. aa 123 – 125: SDH
c. aa 128 – 130: SSG
d. aa 138 - 140: GSS
e. aa 226 - 228: MDF
f. aa 270 – 272: EVE
g. aa 309 – 311: NKL.

~~7.~~5. The vaccine according to any one of claims 1 to ~~6~~4, wherein such H5 protein is originated from an avian influenza virus.

~~8.~~6. The vaccine according to anyone of claims 1 to ~~7~~5, wherein such H5 protein comprises the amino acid sequence of SEQ ID NO:4.

~~9.~~7. The vaccine according to anyone of claims 1 to ~~8~~6 wherein such vaccine further comprises a pharmaceutical acceptable carrier and/or excipients.

~~10~~8. The vaccine according to claim 1, wherein the adjuvant is an Emulsigen-based adjuvant.

~~11~~9. The vaccine according to any one of claims ~~9~~7 to ~~10~~8, wherein the vaccine comprises one or more antigens.

~~12~~10. The vaccine according to claim ~~11~~9, wherein said further antigen is an antigen of a poultry or mammalian pathogen.

~~13~~11. The vaccine according to claim ~~12~~10, wherein the further antigen is the haemagglutinin protein of influenza virus subtype 3, 7, or 9.

~~14~~12. A method for producing the vaccine according to any one of claims 1 to ~~13~~11 comprising the steps of:

a. obtaining a H5 protein having the amino acids 223N, 120N and 155N and the modification 328K+, wherein numbering of the amino acid positions of the H5 protein refers to the amino acid position as exemplarily given in SEQ ID NO:1 and wherein the modification 328K+ means that at amino acid position 328 of H5 protein a second Lysine (K+) is inserted; and
b. admixing the H5 protein of step (a) with an adjuvant selected from the group consisting of oil-in-water emulsions.