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(54) IMMUNOPROTECTIVE INFLUENZA ANTIGEN AND ITS USE IN VACCINATION

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References Cited (56)

U.S. PATENT DOCUMENTS

3.919.044 A	11/1075	Melnick et al.
5,691,189 A	11/1997	Kurtz et al.
5,843,446 A	12/1998	Ladd et al.
5,871,747 A	2/1999	Gengoux-Sedlik et al.
6,169,175 B1	1/2001	Frace et al.

FOREIGN PATENT DOCUMENTS

AU	49273/90	8/1990
WO	WO 92/22575	12/1992
WO	WO 94/06472	3/1994
WO	WO 98/23735	6/1998
WO	WO 99/07839	2/1999
WO	WO 01/49886	7/2001

OTHER PUBLICATIONS

Alford et al., Proc Soc Exp Biol Med. 122(3):800-804 (1966). Allen et al., "Influenza Virus RNA Segment 7 Has the Coding Capacity for Two Polypeptides", Virology, 107:548-551 (1980).

Arnon, et al., "Synthetic recombinant vaccines against viral agents" Int Arch Allergy Immunol 108(4):321-326 (1995).

Asanuma, et al., "Cross-protection against influenza virus infection in mice vaccinated by combined nasal/subcutaneous administration" Vaccine 1301:3-5 (1995).

Bachmayer, et al., "Potency of influenza vaccines: mouse protection experiments in correlation to field studies in man" Dev. Biol Stand 28:336-339 (1975).

Baez, et al., "Gene composition of high-yielding influenza vaccine strains obtained by recombination" J Infect Dis 141:362-365 (1980). Bastin, et al., "Use of synthetic peptides of influenza nucleoprotein to define epitopes recognized by class I-restricted cytotoxic T lymphocytes" J Exp. Med. 165:1508-1523 (1987)I.

Bednarek, et al., "The minimum peptide from the influenza-virus matrix protein. Extra and intracellular loading of HLA-A2" J Immunol 147:4047-4053 (1991).

Ben-Ahmeida, et al., "IgG subclass response and protection against challenge following immunisation of mice with various influenza A vaccines" J Med Microbiol 40(4):261-269 (1994).

Berendt, et al., "Evaluation of commercially prepared vaccines for experimentally induced type A/New Jersey/8/76 influenza virus infections in mice and squirrel monkeys" J. Infect Dis 136 Suppl:S712-717(1977)

Betakova, et al., "The NB protein is an integral component of the membrane of influenza B virus" J Gen Virol 77(Pt 11);2689-2694

Black, R.A. et al., "Antibody Response to the M2 Protein of Influenza A Virus Expressed in Insect Cells", Journal of General Virology

Bodmer, et al., "Enhanced Recognition of a Modified Peptide Antigen by Cytotoxic T Cells Specific for Influenza Nucleoprotein" Cell 52:253-258 (1988).

Borisova et at, "Recombinant Core Particles of Hepatitis B Virus Exposing Foreign Antigenic Determinants on Their Surface," FEBS Letters 259: 121-124 (1989).

Bottex, et al., "Comparative immunogenicity of live influenza viruses and their solubilized neuraminidases: results, of mouse protection experiments" Arch Virol 70(2):83-89 (1981).

Brassard, et al., "Influenza B virus NB glycoprotein is a component

of the virion" Virology 220(2): 350-360 (1996). Brett, et al., "Human T Cell Recognition of Influenza A Nucleoprotein. Specificity and Genetic Restriction Immunodominant T Helper Cell Epitopes" J Immunol 147:984-991

Brown et al., "Foreign Epitopes in Immunodominant Regions of Hepatitis B Core Particles are Highly Immunogenic and Conformationally Restricted," Vaccine 9:595-601 (1991).

Ceppelini, et al., "Binding of labelled influenza matrix peptide to HLA DR in living B lymphoid cells" Nature 339, 392-394 (1989). Cerundolo, et al., "CD8 independence and specificity of cytotoxic T-lymphocytes restricted by HLA Aw68.1" Proc Roy Soc Lond Series B Biol Sci 244:169-177 (1991).

Charbit et al., "Probing the Topology of a Bacterial Membrane Protein by Genetic Insertion of a Foreign Epitope; Expression at the Cell Surface," EMBO J. 5:3029-3037 (1986).

Charbit et al., "Presentation of Two Epitopes of the preS2 Region of Hepatitis B Virus on Live Recombinant Bacteria", J. Immunol., 139:1658-1664 (1987).

Chen, et al., "Protection against influenza B virus infection by immunization with DNA vaccines" Vaccine 19:1446-1455 (2001).

(Continued)

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(57)ABSTRACT

The present invention relates to an influenza antigen, comprising a fusion product of at least the extracellular part of a conserved influenza membrane protein or a functional fragment thereof and a presenting carrier, which may be a presenting (poly)peptide or a non-peptidic structure, such as glycans, peptide mimetics, synthetic polymers. The invention further relates to a vaccine against influenza, comprising at least an antigen of the invention, optionally in the presence of one or more excipients. The invention also relates to use of the antigen, a method for preparing the antigen and acceptor cells expressing the antigen.