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Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

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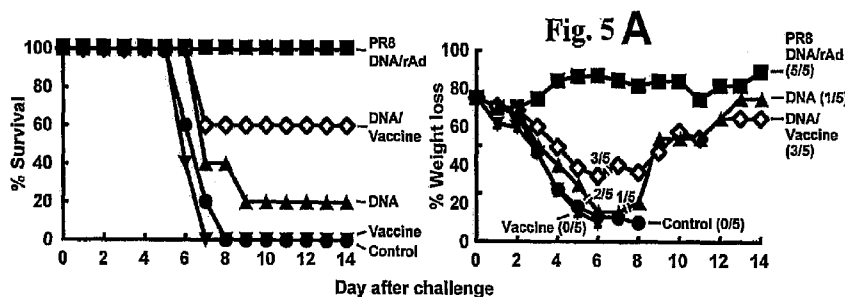
— with international search report (Art. 21(3))

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

— with sequence listing part of description (Rule 5.2(a))

(88) **Date of publication of the international search report:**
10 September 2010

(54) **Title:** DNA VACCINE AGAINST INFLUENZA VIRUS AND PRIME BOOST METHOD



(57) **Abstract:** The present invention relates to a combination of a priming composition and a boosting composition to prime and boost an immune response in a subject whereby the immune response resulting from administration of the priming composition to the subject is capable of being boosted. The priming composition comprises a DNA plasmid that comprises a nucleic acid molecule encoding an influenza virus hemagglutinin (HA) or an epitope-bearing domain thereof. The boosting composition comprises an influenza vaccine. The present invention also relates to a method to use such a combination to vaccinate a subject and to enhance an immune response to an influenza vaccine administered alone. Such a combination can elicit an immune response not only against at least one influenza virus strain from which the priming composition or boosting composition is derived but also to at least one heterologous influenza virus strain.

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/058464

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/145 C07K14/11
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/092792 A2 (GLOBEIMMUNE INC [US]; DUKE RICHARD C [US]; FRANZUSOFF ALEX [US]; HALLE) 16 August 2007 (2007-08-16) the whole document	1,2,4,5, 13-20, 22, 27-31, 35-43
X	GAO WENTAO ET AL: "Protection of mice and poultry from lethal H5N1 avian influenza virus through adenovirus-based immunization" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 80, no. 4, 1 February 2006 (2006-02-01), pages 1959-1964, XP002400987 ISSN: 0022-538X the whole document	1,2,4,5, 13-20, 22, 27-31, 35-43



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

9 July 2010

Date of mailing of the international search report

26/07/2010

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/058464

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>HOELSCHER M A ET AL: "Development of adenoviral-vector-based pandemic influenza vaccine against antigenically distinct human H5N1 strains in mice" LANCET THE, LANCET LIMITED. LONDON, GB, vol. 367, no. 9509, 11 February 2006 (2006-02-11), pages 475-481, XP025093947 ISSN: 0140-6736 [retrieved on 2006-02-11] the whole document</p>	<p>1,2,4, 13-20, 27-30, 35,38-43</p>
X	<p>WANG S ET AL: "Heterologous HA DNA vaccine prime-inactivated influenza vaccine boost is more effective than using DNA or inactivated vaccine alone in eliciting antibody responses against H1 or H3 serotype influenza viruses" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 26, no. 29-30, 4 July 2008 (2008-07-04), pages 3626-3633, XP022735980 ISSN: 0264-410X [retrieved on 2008-06-17] the whole document</p>	<p>1,2,4,6, 11, 13-20, 23, 27-30, 32,35, 38-43</p>
X	<p>PARKER CHRISTOPHER: "Comparison of Codon Optimized and Non-Optimized Influenza HA DNA Vaccines" Worcester Polytechnic Institute, E-project-010406-095229 URL: http://www.wpi.edu/Pubs/E-project/Available/E-project-010406-095229/unrestricted/ChrisParkerMQP.pdf XP002584763 the whole document</p>	<p>1,2,4,6, 11, 13-20, 23, 27-30, 32,35, 38-43</p>
X	<p>WO 2007/100584 A2 (GOVERNMENT OF THE UNITED STATES [US]; GOVERNMENT OF THE UNITED STATES [U] 7 September 2007 (2007-09-07) the whole document</p>	<p>1,2,4,6, 11, 13-20, 23, 27-30, 32,35, 38-43</p>

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2009/058464

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>"Grippeimpfung" Wikipedia 21 September 2008 (2008-09-21), XP002584764 Retrieved from the Internet: URL: http://de.wikipedia.org/w/index.php?title=Grippeimpfung&oldid=50999352&printable=yes [retrieved on 2010-05-28] the whole document</p> <p style="text-align: center;">-----</p>	11

INTERNATIONAL SEARCH REPORT

International application No.
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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
5, 6, 11, 22, 23, 31, 32(completely); 1-4, 13-21, 27-30, 35-43(partially)

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 5, 22, 31(completely); 1, 2, 4, 13-20, 27-30, 35-43(partially)

A priming composition comprising a DNA plasmid encoding an influenza virus hemagglutinin or an epitope-bearing domain thereof;
 a combination containing such a priming composition and a boosting composition comprising an influenza vaccine;
 a method of enhancing an immune response comprising administering the priming composition and subsequently the boosting composition;
 wherein the hemagglutinin encoded by the first composition is A/Vietnam/1203/2004 HA.

- 2-11. claims: 6-8, 23-25, 32-34(completely); 1-4, 13-21, 27-30, 35-43(partially)

As invention 1,
 wherein the priming composition is selected from
 A/New Caledonia/20/1999 HA;
 A/Wisconsin/67/2005 HA;
 A/Brisbane/59/2007 HA;
 A/Solomon Islands/3/2006 HA;
 SEQ ID NO. 11;
 SEQ ID NO. 15;
 SEQ ID NO. 19;
 SEQ ID NO. 31;
 SEQ ID NO. 39; and
 SEQ ID NO. 43.

12. claims: 9, 26(completely); 1, 13-19, 27-29, 38-43(partially)

As Invention 1,
 wherein the DNA plasmid is a "CMV/R" plasmid.

- 13-17. claims: 10-12(completely); 1-4, 13-21, 27-30, 35-43(partially)

As invention 1,
 wherein the boosting composition is selected from
 monovalent influenza subvirion vaccine
 rgA/Vietnam/1203/2004;
 2006-2007 seasonal influenza vaccine;
 a seasonal influenza vaccine comprising an influenza A group 1 strain, an influenza A group 2 strain and an influenza B strain;
 a 2007-2008 seasonal influenza vaccine; and
 a 2008-2009 seasonal influenza vaccine

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2009/058464

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007092792 A2	16-08-2007	AU 2007212076 A1	16-08-2007
		CA 2638815 A1	16-08-2007
		CN 101405026 A	08-04-2009
		EP 1988919 A2	12-11-2008
		JP 2009528987 T	13-08-2009
		KR 20080089671 A	07-10-2008
		US 2008003239 A1	03-01-2008
WO 2007100584 A2	07-09-2007	CA 2642644 A1	07-09-2007
		CN 101484466 A	15-07-2009
		EP 1991571 A2	19-11-2008
		KR 20090034297 A	07-04-2009
		US 2009208531 A1	20-08-2009