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(54) **Title:** UNIVERSAL INFLUENZA A VACCINES

(57) **Abstract:** Universal flu vaccines are disclosed. The vaccines induce broad and sustained protection against a wide range of influenza A viruses, reduce the need for annual vaccination campaigns with vaccines based upon viral strains predicted to be the predominant circulating strains, and ameliorate the threat of future pandemics that can potentially kill millions.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 11/47900

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - C07K 14/00; A61K 39/00 (2012.01) USPC - 530/300, 350 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) IPC(8) - C07K 14/00; A61K 39/00 (2012.01) USPC - 530/300, 350 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 424/184.1, 192.1, 206.1 Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PubWest (PGPB,USPT,USOC,EPAB,JPAB); PubMed (MEDLINE) M2e, H1N1, H5N1, H7N2, NP		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2009/0196915 A1 (VAN NEST et al.) 06 August 2009 (06.08.2009) (para [0016], [0038]-[0040], [0076], [0089]; Example 3; Fig 1).	1, 4-9
A	US 2010/0184832 A1 (PUGACHEV et al.) 22 July 2010 (22.07.2010)	1, 4-9
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* 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 application or patent 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 22 February 2012 (22.02.2012)		Date of mailing of the international search report 16 MAR 2012
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201		Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 11/47900

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.: 10 - 20
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:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: claims 1 and 4-9, directed to a fusion protein comprising four components: a) a first matrix protein ectodomain (M2e) from a first strain of influenza A virus (strain 1); b) a second (M2e) from a second strain of influenza A virus (strain 2); c) a third (M2e) from a third strain of influenza A virus (strain 3); and d) a nucleoprotein (NP) from a fourth strain of influenza A virus (strain 4); wherein at least two of the strains are different strains.

- Please see extra sheet for continuation -

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 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.:
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.:
1 and 4-9

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.

INTERNATIONAL SEARCH REPORT

International application No.

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Continuation of Box III: Lack of Unity of Invention

Group II: claims 2, 3, 5, and 6, directed to a fusion polypeptide comprising a first M2e from a first strain of influenza A virus and a nucleoprotein (NP) from a different strain of influenza A virus.

The inventions listed as Groups I - II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of the Group I claims is a fusion polypeptide comprising three matrix protein 2 ectodomains and a nucleoprotein from at least two different strains of influenza A virus - not required by the claims of Group II. The special technical feature of the Group II claims is a fusion polypeptide comprising a first M2e from a first strain of influenza A virus and a nucleoprotein (NP) from a different strain of influenza A virus - not specifically required by the claims of Group I. Neither of these special technical features is common to the other group, nor do they correspond to a special technical feature in the other group.

The common technical elements shared by the above groups is that they are related to fusion polypeptides comprising at least one M2e domain and at least one NP domain. The polypeptides also comprise at least two domains from different strains of influenza A viruses. These common technical elements do not represent an improvement over the prior art of US 2010/0184832 A1 to Pugachev et al., which teaches chimeric flavivirus vectors (abstract), comprising M2e (para [0024]-[0026] and [0092]) and, optionally one or more other epitopes, including nucleoprotein (NP) from influenza A (para [0092]), wherein said vector encodes for said polypeptides as a fusion protein (polytope in which different epitopes can be separated by a flexible linker; para [0091]), and wherein said epitopes may be from different viral strains (The different epitopes can be derived from a single species of pathogen, or can be derived from different species and/or different genuses; para [0091]). Therefore, the inventions of Group I and Group II lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.