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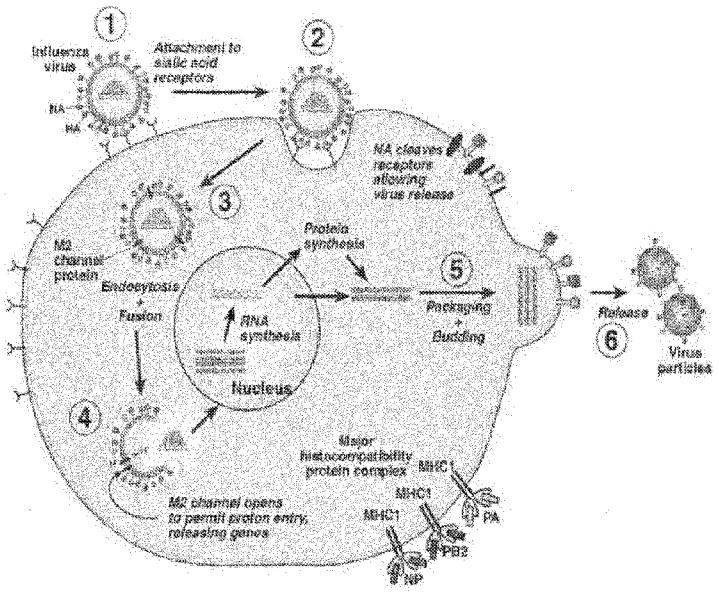
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*[Continued on next page]*

(54) Title: INFLUENZA VIRUS VECTORS AND USES THEREFOR

(57) Abstract: Disclosed herein are compositions and methods related to mutant viruses, and in particular, mutant influenza viruses. The mutant viruses disclosed herein include a mutant M2 sequence, and are useful in immunogenic compositions, e.g., as vaccines. The mutant viruses disclosed herein including a mutant M2 sequence are also useful to deliver antigens to a subject, e.g., to induce an immune response to the antigen. Also disclosed herein are methods, compositions and cells for propagating the viral mutants, and methods, devices and compositions related to vaccination.

FIGURE 1




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DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Declarations under Rule 4.17**:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

**Published**:

— *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))*

**(88) Date of publication of the international search report**:
12 November 2015

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 15/20580

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12N 7/00, C12N 7/01, C12N 7/04, C12N 15/00, A01N 63/00, A61K 48/00, A61K 39/145 (2015.01)
CPC - C12N 7/00, C07K 14/005, C12N 15/86, A61K 39/00, A61K 48/00, A61K 2039/5254, A61K 38/00
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)
CPC- C12N 7/00, C07K 14/005, C12N 15/86, A61K 39/00, A61K 48/00, A61K 2039/5254, A61K 38/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC- C07K 2319/00, A01N 63/00, C12N 2710/10343, A61K 39/145, C12N 2760/16134, C12N 2760/16122
USPC- 435/235.1, 424/184.1, 424/209.1, 424/93.2; 424/93.6, 435/236, 435/320.1, 536/23.72

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST(PGPB,USPT,USOC,EPAB,JPAB); PatBase, Google/Scholar: influenza viral vector, M2SRTMDEL, M2 ectodomain, M1fusion, deletion, TM, cytoplasmic tail/domain, C-terminus, carboxy-terminus, eM2-M1 fusion, live attenuated, VLP, nanoparticle...
GenCore 6.4.1: SEQ ID NO: 35, 36, 1

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| A | US 8,475,806 B2 (Kawaoka) 02 July 2013 (02.07.2013) Abstract, SEQ ID NO:5 | 1-39, 43-48, 65-67 |

☐ Further documents are listed in the continuation of Box C. ☐

* 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 | Date of mailing of the international search report |
|---|---|
| 20 August 2015 (20.08.2015) | 08 SEP 2015 |

| Name and mailing address of the ISA/US | Authorized officer: |
|---|---|
| Mail Stop PCT, Attn: ISA/US, Commissioner for Patents<br>P.O. Box 1450, Alexandria, Virginia 22313-1450<br>Facsimile No. 571-273-8300 | Lee W. Young<br>PCT Helpdesk: 571-272-4300<br>PCT OSP: 571-272-7774 |

Form PCT/ISA/210 (second sheet) (January 2015)

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 15/20580

**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.: 40-42
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.

Group I: claims 1-39, 43-48, 65-67, drawn to a nucleic acid sequence of SEQ ID NO:35.

Group II: claims 49-64, 68, 69, drawn to a composition comprising an influenza viral vector and a method of using the composition.

The inventions listed as Groups I and 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:

..... See Supplemental Sheet to continue .....

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.:
1-39, 43-48, 65-67

**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.

Supplemental Sheet

In Continuation of Box III. Observations where unity of invention is lacking:

Special Technical Features
The inventions of Group I do not include the shared or common technical feature of a composition comprising an influenza viral vector and a method of using the composition, as required by Group II.

The inventions of Group II do not include the shared or common technical feature of a nucleic acid sequence of SEQ ID NO:35, as required by Group I.

Common Technical Features
The inventions of Groups I and II share the technical feature of a nucleic acid sequence encoding an influenza viral protein, wherein the nucleic acid further encoding one or more foreign antigens, and a method of using thereof. However, this shared technical feature does not represent a contribution over prior art as being anticipated by a paper titled "Influenza virus NS vectors expressing the mycobacterium tuberculosis ESAT-6 protein induce CD4+ Th1 immune response and protect animals against tuberculosis challenge" by Sereinig, et al. (Clin Vaccine Immunol. 2006 Aug;13(8):898-904) (hereinafter "Sereinig").

Sereinig discloses a nucleic acid sequence encoding an influenza viral protein, wherein the nucleic acid further encoding one or more foreign antigens (pg 900, FIG. 1 and its legend, "Expression of the ESAT-6 antigen in Vero cells infected with the recombinant influenza virus vectors. (a) Diagram of the recombinant NS1 protein expressed by influenza A vectors."), and a method of using thereof (Abstract, "We generated several subtypes of attenuated recombinant influenza A viruses expressing the 6-kDa early secretory antigenic target protein (ESAT-6) of M. tuberculosis from the NS1 reading frame. We were able to demonstrate the potency of influenza virus NS vectors to induce an M. tuberculosisspecific Th1 immune response in mice. Moreover, intranasal immunization of mice and guinea pigs with such vectors induced protection against mycobacterial challenge, similar to that induced by BCG vaccination"). As said technical feature was known in the art at the time of the invention, this cannot be considered special technical feature that would otherwise unify the groups.

Groups I and II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.