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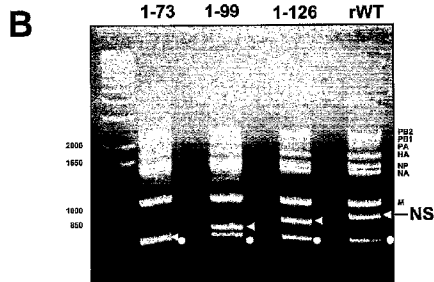
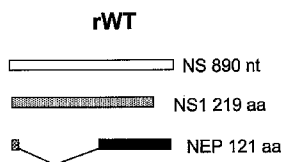
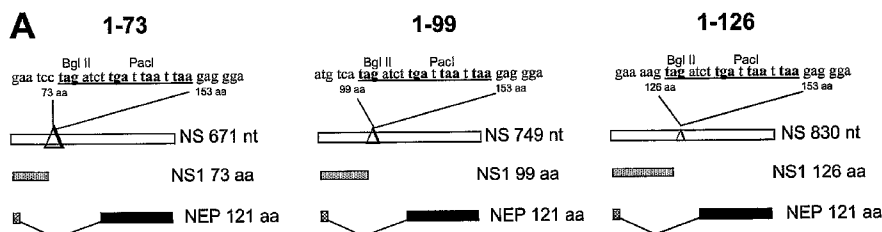
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(54) Title: GENETICALLY ENGINEERED SWINE INFLUENZA VIRUS AND USES THEREOF



(57) Abstract: The present invention relates, in general, to attenuated swine influenza viruses having an impaired ability to antagonize the cellular interferon (IFN) response, and the use of such attenuated viruses in vaccine and pharmaceutical formulations. In particular, the invention relates to attenuated swine influenza viruses having modifications to a swine NS1 gene that diminish or eliminate the ability of the NS1 gene product to antagonize the cellular IFN response. These viruses replicate *in vivo*, but demonstrate decreased replication, virulence and increased attenuation, and therefore are well suited for use in live virus vaccines, and pharmaceutical formulations.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/19382

A. CLASSIFICATION OF SUBJECT MATTER
 IPC: A61K 39/00(2006.01),39/295(2006.01),39/12(2006.01),39/145(2006.01);C12N 15/64(2006.01),5/00(2006.01)
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 USPC: 424/184.1,202.1,205.1,206.1,209.1;435/91.4,325
 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)
 U.S. : 424/184.1,202.1,205.1,206.1,209.1;435/91.4,325
 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 practicable, search terms used)
 EAST, Pubmed

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|--|
| Y | US 6,300,090 A (STEINMAN et al.) 09 October 2001 (09.10.2001), columns 3, 4, 7-10. | 2-6, 22-24, 28-30, 62-64 and 73-75 |
| Y | LANDOLT et al. Comparison of the Pathogenesis of Two Genetically Different H3N2 Influenza A Viruses in Pigs. Journal of Clinical Microbiology. 2003, Vol. 41, No. 5, pages 1936-1941, especially pages 1936, 1937 and 1940. | 1, 3, 7, 14, 19, 20, 25, 26, 31-34, 36-39, 51-54 and 76 |
| Y | TALON et al. Influenza A and B viruses expressing altered NS1 proteins: A vaccine approach. PNAS. 11 April 2000, Vol. 97, No. 8, pages 4309-4314, especially pages 4309, 4311, 4312 and 4314. | 1-3, 8-11, 13, 15-21, 25-27, 31-34, 36-39, 41, 42, 44, 47, 48, 50, 55-59 and 70-72 |
| Y | WANG et al. Functional Replacement of the Carboxy-Terminal Two-Thirds of the Influenza A Virus NS1 Protein with Short Heterologous Dimerization Domains. Journal of Virology. December 2002, Vol. 76, No. 24, pages 12951-12962, especially pages 12954, 12958, 12959 and 12961. | 1-3, 8, 9, 11, 12, 13, 19-21, 25-27, 31-34, 36-39, 41, 42, 44, 47, 48, 50, 55-59 and 70- |

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 | "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 |
| "E" | earlier application or patent published on or after the international filing date | "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 |
| "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) | "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 |
| "O" | document referring to an oral disclosure, use, exhibition or other means | "&" | document member of the same patent family |
| "P" | document published prior to the international filing date but later than the priority date claimed | | |

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| Date of the actual completion of the international search 28 September 2006 (28.09.2006) | Date of mailing of the international search report 25 OCT 2006 |
| 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 <i>Benjamin P. Blumel</i> Benjamin P. Blumel Telephone No. 5712724960 |

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/19382

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.: 60, 61 and 65-69
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:

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 any 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.:
- 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.
PCT/US05/19382

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|---|
| Y | US 5,786,199 A (PALESE et al.) 28 July 1998 (28.07.1998), columns 3, 4, 23 and 24. | 1-4, 5, 21-23, 27-29, 58, 62, 63, 73 and 74 |