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(71) Applicant (for all designated States except US): **MED-IMMUNE VACCINES, INC.** [US/US]; One Medimmune Way, Gaithersburg, MD 20878 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **HOFFMANN, Erich** [US/US]; 1061 Natchez Point, Apartment 179, Memphis, TN 38103 (US). **JIN, Hong** [US/US]; 22385 Santa Paula Avenue, Cupertino, CA 95014 (US). **LU, Bin** [CN/US]; 74 Los Altos Square, Los Altos, CA 94022 (US). **DUKE, Gregory** [US/US]; 715 Upland Road, Redwood City, CA 94062 (US). **KEMBLE, George** [US/US]; 19585 Via Grande Drive, Saratoga, CA 95070 (US). **CHEN, Zhongying** [CN/US]; 10490 Davison Avenue, Cupertino, CA 95014 (US).

(74) Agent: **ALBAN, Patrick, Scott**; Medimmune, Inc., One Medimmune Way, Gaithersburg, MD 20878 (US).

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(54) Title: MULTI PLASMID SYSTEM FOR THE PRODUCTION OF INFLUENZA VIRUS

(57) Abstract: Vectors and methods for the production of influenza viruses suitable as recombinant influenza vaccines in cell culture are provided. Bi-directional expression vectors for use in a multi-plasmid influenza virus expression system are provided. Additionally, the invention provides methods of producing influenza viruses with enhanced ability to replicate in embryonated chicken eggs and/or cells (e.g., Vero and/or MDCK) and further provides influenza viruses with enhanced replication characteristics. A method of producing a cold adapted (ca) influenza virus that replicates efficiently at, e.g., 25°C (and immunogenic compositions comprising the same) is also provided.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/17734

A. CLASSIFICATION OF SUBJECT MATTER
 IPC: C12N 7/02(2006.01);C12P 19/34(2006.01);A61K 39/145(2006.01)
 USPC: 435/239,91,1,91.41,41;424/209,1,206.1
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B. FIELDS SEARCHED
 Minimum documentation searched (classification system followed by classification symbols)
 U.S. : 435/239,91,1,91.41,41; 424/209,1,206.1
 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)
 Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SUBBARAO et al Rescues of an Influenza A Virus Wild-Type PB2 Gene and a Mutant Derivative Bearing a Site-Specific Temperature-Sensitive and Attenuating Mutation Journal of Virology. December 1993, Vol. 67, No. 12, pages 7223-7228, especially the Abstract and page 7224.	1-2, 8-9 and 20-26

Further documents are listed in the continuation of Box C. See patent family annex.

Special categories of cited documents	Code	Description
"A" document defining the general state of the art which is not considered to be of particular relevance	"A"	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
"B" earlier application or patent published on or after the international filing date	"B"	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)	"L"	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	"O"	document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	"P"	

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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>Sharon Hurt</i> Sharon Hurt Telephone No. 571-272-1600

INTERNATIONAL SEARCH REPORT

International application No.
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Continuation of B. FIELDS SEARCHED Item 3:

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search terms: influenza, virus, cells, temperature, Arbor, encoding, sequence, vaccine, genome, surface, antigen