

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
13 July 2006 (13.07.2006)

PCT

(10) International Publication Number
WO 2006/073496 A3

(51) International Patent Classification:
C12N 15/864 (2006.01) *A61P 31/00* (2006.01)
A61K 39/21 (2006.01) *A61P 37/00* (2006.01)

(74) Agents: ZHOU, Jie et al.; Morrison & Foerster LLP, 755
Page Mill Road, Palo Alto, California 94304-1018 (US).

(21) International Application Number:
PCT/US2005/027091

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 29 July 2005 (29.07.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/592,889 30 July 2004 (30.07.2004) US

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT,
RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicants (for all designated States except US): TAR-
GETED GENETICS CORPORATION [US/US]; 1100
Olive Way, Suite 100, Seattle, Washington 98101 (US).
CHILDREN'S HOSPITAL, INC. [US/US]; 700 Chil-
dren's Drive, Columbus, Ohio 43205 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): PELUSO, Richard
[US/US]; 454 Northern Parkway, Ridgewood, New
Jersey 07450 (US). ARNOLD, Susan [US/US]; 8100
Frankford Avenue, Philadelphia, Pennsylvania 19136
(US). WUSTNER, Jason [US/US]; 12 Sunset Drive,
Paoli, Pennsylvania 19301 (US). JOHNSON, Philip, R.
[US/US]; 206 Indian Creek Road, Winwood, Pennsylvania
19096 (US). SCHULTZ, Alan, M. [US/US]; 9431 Quill
Place, Gaithersburg, Maryland 20886 (US). STEPAN,
Anthony, M. [US/US]; 3211 41st Avenue, S.W., Seattle,
Washington 98110 (US).

Published:

— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
3 May 2007

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: RECOMBINANT AAV BASED VACCINE METHODS

(57) Abstract: The present invention relates to recombinant adeno-associated virus (rAAV) based materials and methods for eliciting an immune response to a pathogen. The present invention provides vector sets comprising a priming vector and a boosting vector, wherein at least one of the vectors in the vector set is a rAAV vector, and methods for eliciting a prophylactic immune response in a mammalian subject susceptible to infection by a pathogen, such as for example, an RNA virus, including HIV-1, and methods for eliciting a therapeutic immune response in a mammalian subject infected by a pathogen that has progressed to a disease state associated with the pathogen, such as for example, an RNA virus, including HIV-1. In particular, the present invention provides methods for eliciting an enhanced boost immune response in a mammalian subject susceptible to infection by or infected by a pathogen.

WO 2006/073496 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/027091A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/864 A61K39/21 A61P31/00 A61P37/00

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)
C12N A61K A61P

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, BIOSIS, EMBASE, MEDLINE, SCISEARCH, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	XIN KE-QIN ET AL: "A novel recombinant adeno-associated virus vaccine induces a long-term humoral immune response to human immunodeficiency virus" HUMAN GENE THERAPY, vol. 12, no. 9, 10 June 2001 (2001-06-10), pages 1047-1061, XP002395739 ISSN: 1043-0342 the whole document ----- -/--	1-34

 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

11 January 2007

Date of mailing of the international search report

14/03/2007

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Domingues, Helena

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/027091

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>PEDEN CARMEN S ET AL: "Circulating anti-wild-type adeno-associated virus type 2 (AAV2) antibodies inhibit recombinant AAV2 (rAAV2)-mediated, but not rAAV5-mediated, gene transfer in the brain"</p> <p>JOURNAL OF VIROLOGY, vol. 78, no. 12, June 2004 (2004-06), pages 6344-6359, XP002395740 ISSN: 0022-538X the whole document</p>	1-34
Y	<p>HALBERT C L ET AL: "Repeat transduction in the mouse lung by using adeno-associated virus vectors with different serotypes"</p> <p>JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 74, no. 3, February 2000 (2000-02), pages 1524-1532, XP002242061 ISSN: 0022-538X the whole document</p>	1-34
Y	<p>WO 03/042397 A (THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA; GAO, GUANGPING; WILSON) 22 May 2003 (2003-05-22) pages 45-46 examples 1-10</p>	1-34
Y	<p>WO 01/68888 A (NEUROLOGIX, INC) 20 September 2001 (2001-09-20) example 1</p>	1-34
Y	<p>JOHNSON PHILIP R ET AL: "Pre-clinical evaluation of a novel HIV vaccine based on an adeno-associated virus vector."</p> <p>PEDIATRIC RESEARCH, vol. 53, no. 4 Part 2, April 2003 (2003-04), page 334A, XP009071316 & ANNUAL MEETING OF THE PEDIATRIC ACADEMIC SOCIETIES'; SEATTLE, WA, USA; MAY 03-06, 2003 ISSN: 0031-3998 the whole document</p>	1-34
	----- -/--	

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/027091

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>CLARK K REED ET AL: "A single dose, adeno-associated virus vector SIV vaccine elicits long-lived immune responses in macaques" JOURNAL OF MEDICAL PRIMATOLOGY, vol. 29, no. 3-4, August 2000 (2000-08), pages 290-291, XP009071318 & 17TH ANNUAL SYMPOSIUM ON NONHUMAN PRIMATE MODELS FOR AIDS; NEW ORLEANS, LOUISIANA, USA; OCTOBER 06-09, 1999 ISSN: 0047-2565 the whole document</p>	1-34
Y	<p>SHIVER J W ET AL: "RECENT ADVANCES IN THE DEVELOPMENT OF HIV-1 VACCINES USING REPLICATION-INCOMPETENT ADENOVIRUS VECTORS" ANNUAL REVIEW OF MEDICINE : SELECTED TOPICS IN THE CLINICAL SCIENCES, ANNUAL REVIEWS INC., PALO ALTO, CA, US, vol. 55, 10 December 2003 (2003-12-10), pages 355-372, XP009058216 ISSN: 0066-4219 the whole document</p>	1-34
Y	<p>NEWMAN M J: "HETEROLOGOUS PRIME-BOOST VACCINATION STRATEGIES FOR HIV-1: AUGMENTING CELLULAR IMMUNE RESPONSES" CURRENT OPINION IN INVESTIGATIONAL DRUGS, PHARMAPRESS, US, vol. 3, no. 3, March 2002 (2002-03), pages 374-378, XP009037697 ISSN: 1472-4472 the whole document</p>	1-34
Y	<p>RAMA RAO AMARA ET AL: "CONTROL OF A MUCOSAL CHALLENGE AND PREVENTION OF AIDS BY A MULTIPROTEIN DNA/MVA VACCINE" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 292, no. 5514, 6 April 2001 (2001-04-06), pages 69-74, XP000986110 ISSN: 0036-8075 the whole document</p>	1-34
Y	<p>WO 99/43843 A (UNIV JOHNS HOPKINS MED [US]; HE TONG CHUAN [US]; VOGELSTEIN BERT [US];) 2 September 1999 (1999-09-02) page 3, lines 15-26 page 7, lines 18-27 page 9, lines 27-30 page 12, lines 3-13 page 14, lines 17-31</p>	35-125

-/--

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/027091

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>LICHTENSTEIN D L ET AL: "FUNCTIONS AND MECHANISMS OF ACTION OF THE ADENOVIRUS E3 PROTEINS" INTERNATIONAL REVIEWS OF IMMUNOLOGY, HARWOOD ACADEMIC PUBLISHERS, US, vol. 23, no. 1/2, January 2004 (2004-01), pages 75-111, XP009071853 ISSN: 0883-0185 page 100, paragraph 2</p>	35-125
Y	<p>TOLLEFSON ANN E ET AL: "The Ed3-11.6-kDa adenovirus death protein (ADP) is required for efficient cell death: Characterization of cells infected with adp mutants" VIROLOGY, ACADEMIC PRESS, ORLANDO, US, vol. 220, no. 1, 1996, pages 152-162, XP002162708 ISSN: 0042-6822 pages 154-155 figures 2,3</p>	35-125
Y	<p>DORONIN K ET AL: "Tumor-specific, replication-competent adenovirus vectors overexpressing the adenovirus death protein" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 74, no. 13, July 2000 (2000-07), pages 6147-6155, XP002162706 ISSN: 0022-538X page 6151</p>	35-125
Y	<p>DORONIN KONSTANTIN ET AL: "Overexpression of the ADP (E3-11.6K) protein increases cell lysis and spread of adenovirus." VIROLOGY, vol. 305, no. 2, 20 January 2003 (2003-01-20), pages 378-387, XP002414301 ISSN: 0042-6822 page 381</p>	35-125
E	<p>WO 2006/078279 A (THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA; WILSON, JAMES, M) 27 July 2006 (2006-07-27) example 2</p> <p style="text-align: center;">----- -/--</p>	1-34

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/027091

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	JOHNSON PHILIP R ET AL: "Novel adeno-associated virus vector vaccine restricts replication of simian immunodeficiency virus in macaques" JOURNAL OF VIROLOGY, vol. 79, no. 2, January 2005 (2005-01), pages 955-965, XP002395741 ISSN: 0022-538X the whole document	1-34
X,P	----- GALLEZ-HAWKINS G ET AL: "DNA and low titer, helper-free, recombinant AAV prime-boost vaccination for cytomegalovirus induces an immune response to CMV-pp65 and CMV-IE1 in transgenic HLA A*0201 mice" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 23, no. 6, 21 December 2004 (2004-12-21), pages 819-826, XP004637089 ISSN: 0264-410X the whole document -----	1-34

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/027091

Box 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:
Although claims 1-17 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 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 fee, this Authority did not invite payment of any additional fee.
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.
- 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: 1-34

Concern aspects related to a method for eliciting a boost immune response to a pathogen in a mammalian subject susceptible to infection by or infected by the pathogen comprising the administration of a boost dose of an antigen of a pathogen, particularly of an RNA viral pathogen, by a recombinant vector to a mammalian subject having previously received a prime dose of said antigen by a recombinant vector; wherein at least the prime dose or the boost dose are administered by a recombinant adeno-associated virus (rAAV) vector, with the proviso that when both the prime and boost dose are administered by rAAV, they are not both administered by AAV2.

2. claims: 35-125

Concern aspects related to methods for generating a recombinant adenoviral vector or particle using a linear DNA molecule and a supercoiled adenoviral vector comprising an adenoviral genome with one or more deletions, particularly an E3 deletion, but encoding a functional E3 adenoviral death protein; and to kits comprising two plasmids that can be used to obtain recombinant adenoviral vectors.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2005/027091

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03042397	A	22-05-2003	AT 317916 T	15-03-2006
			BR 0214119 A	28-06-2005
			CA 2406745 A1	13-05-2003
			CA 2465868 A1	22-05-2003
			DE 60209193 T2	28-09-2006
			DK 1310571 T3	19-06-2006
			EP 1310571 A2	14-05-2003
			EP 1456419 A2	15-09-2004
			ES 2258601 T3	01-09-2006
			HK 1056198 A1	16-06-2006
			JP 2003235562 A	26-08-2003
			JP 2005525086 T	25-08-2005
			KR 20050058234 A	16-06-2005
			MX PA04004600 A	13-08-2004
WO 0168888	A	20-09-2001	AU 4565401 A	24-09-2001
			CA 2373110 A1	20-09-2001
			EP 1228234 A2	07-08-2002
			JP 2003526377 T	09-09-2003
WO 9943843	A	02-09-1999	AU 747847 B2	23-05-2002
			AU 2787599 A	15-09-1999
			CA 2322066 A1	02-09-1999
			EP 1056881 A1	06-12-2000
			US 5922576 A	13-07-1999
WO 2006078279	A	27-07-2006	CA 2563538 A1	27-07-2006