

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
23 December 2004 (23.12.2004)

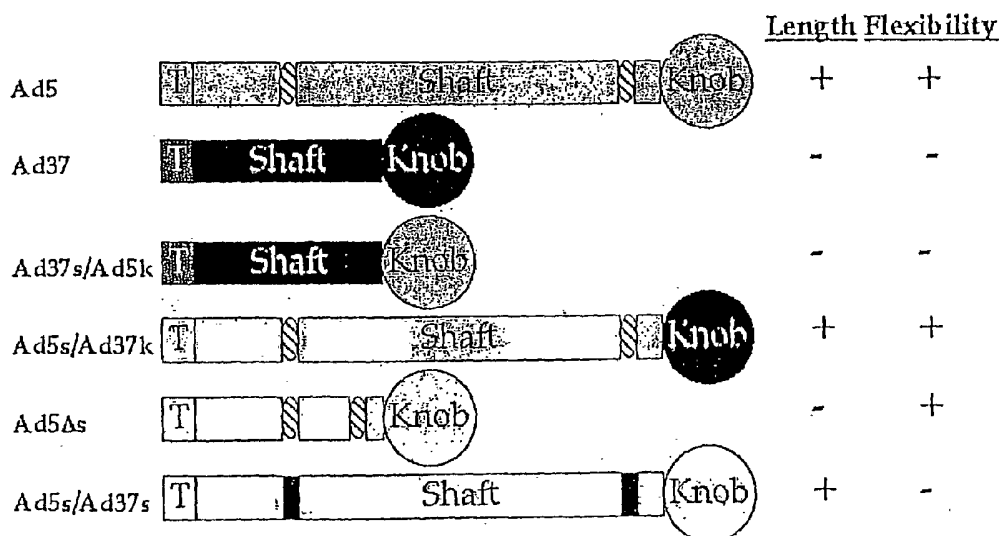
PCT

(10) International Publication Number
WO 2004/111251 A3

- (51) International Patent Classification⁷: C12N 15/861, C07K 14/075, C12N 15/34, A61K 48/00
- (74) Agents: SEIDMAN, Stephanie, L. et al.; Fish & Richardson P.C., 12390 El Camino Real, San Diego, CA 92130 (US).
- (21) International Application Number: PCT/US2004/018623
- (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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (22) International Filing Date: 10 June 2004 (10.06.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/478,008 11 June 2003 (11.06.2003) US
- (71) Applicants (for all designated States except US): THE SCRIPPS RESEARCH INSTITUTE [US/US]; 10550 North Torrey Pines Road, tpc-8, La Jolla, CA 92037 (US). THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US/US]; 1111 Franklin Street, 12th floor, Oakland, CA 94607-5200 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): NEMEROW, Glen, R. [US/US]; 462 Cerro Street, Encinitas, CA 92024 (US). WU, Eugene [US/US]; 4325 Cassanna Way, #616, Ocean-side, CA 92057 (US). STEWART, Phoebe [US/US]; 9442 Norwood Drive, Brentwood, TN 37027 (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, IT, LU, 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).
- Declaration under Rule 4.17:
— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW,

[Continued on next page]

(54) Title: MODIFIED FIBER PROTEINS FOR EFFICIENT RECEPTOR BINDING



(57) Abstract: Recombinant detargeted and retargeted adenovirus viral particles and vectors are provided. In particular, modified fibers from adenoviruses that bind to coxsackie-adenovirus receptor (CAR) *in vivo* that contain modifications in the fiber shaft are provided. Adenovirus (Ad) particles that express such fibers exhibit reduced binding to CAR. Hence detargeted Ad particles are provided; also provided are retargeted particles.

WO 2004/111251 A3



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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

Published:

— with international search report

(88) Date of publication of the international search report:
3 March 2005

(15) Information about Correction:**Previous Correction:**

see PCT Gazette No. 05/2005 of 3 February 2005, Section II

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

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/018623

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/861 C07K14/075 C12N15/34 A61K48/00

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)
IPC 7 C12N C07K A61K

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, WPI Data, PAJ, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 02/083902 A (UNIV IOWA RES FOUND ; LAW LANE K (US); DAVIDSON BEVERLY L (US)) 24 October 2002 (2002-10-24)</p> <p style="text-align: center;">figures 3,5a; examples 3,5 ----- -/--</p>	<p>1-10, 13-17, 19, 23-27, 31, 32, 34-36, 40, 42, 43, 46-79</p>

Further documents are listed in the continuation of box C.

Patent family members are listed in 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

29 October 2004

Date of mailing of the international search report

30/11/2004

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

Lonnoy, O

INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/US2004/018623

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HIDAKA CHISA ET AL: "CAR-dependent and CAR-independent pathways of adenovirus vector-mediated gene transfer and expression in human fibroblasts" JOURNAL OF CLINICAL INVESTIGATION, NEW YORK, NY, US, vol. 103, no. 4, February 1999 (1999-02), pages 579-587, XP002139783 ISSN: 0021-9738 see "AdF9sKBetaGal"	1-4,6-8, 13-20, 22, 24-26, 31,32, 34-36, 40,42, 43,46-79
X	VIGNE E ET AL: "GENETIC MANIPULATIONS OF ADENOVIRUS TYPE 5 FIBER RESULTING IN LIVER TROPISM ATTENUATION" GENE THERAPY, MACMILLAN PRESS LTD., BASINGSTOKE, GB, vol. 10, no. 2, January 2003 (2003-01), pages 153-162, XP001191248 ISSN: 0969-7128 see "BS1", "BS2" and "DB6" in figures 1, 3 and 5	1-10, 13-16, 19, 23-26, 31,32, 34-37, 40-44, 46-79
X	US 6 210 946 B1 (KRASNYKH VICTOR N ET AL) 3 April 2001 (2001-04-03) figure 1	1-9,21, 31,33, 35, 40-44, 46-79
A	VAN RAAIJ MARK J ET AL: "A triple beta-spiral in the adenovirus fibre shaft reveals a new structural motif for a fibrous protein" NATURE (LONDON), vol. 401, no. 6756, 28 October 1999 (1999-10-28), pages 935-938, XP002303348 ISSN: 0028-0836	
A	CHIU CHARLES Y ET AL: "Structural analysis of a fiber-pseudotyped adenovirus with ocular tropism suggests differential modes of cell receptor interactions" JOURNAL OF VIROLOGY, vol. 75, no. 11, June 2001 (2001-06), pages 5375-5380, XP002979963 ISSN: 0022-538X	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/018623

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 78 and 79 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:

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.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2004/018623

Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
- a. type of material
- a sequence listing
- table(s) related to the sequence listing
- b. format of material
- in written format
- in computer readable form
- c. time of filing/furnishing
- contained in the international application as filed
- filed together with the international application in computer readable form
- furnished subsequently to this Authority for the purpose of search
2. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No PCT/US2004/018623

Patent document cited in search report	A	Publication date	Patent family member(s)	Publication date
WO 02083902	A	24-10-2002	US 2002127721 A1	12-09-2002
			WO 02083902 A2	24-10-2002
			US 2004038924 A1	26-02-2004
			WO 03050238 A2	19-06-2003
			US 2003133912 A1	17-07-2003
US 6210946	B1	03-04-2001	AU 751542 B2	22-08-2002
			AU 3294099 A	30-08-1999
			BR 9908018 A	24-10-2000
			CA 2321135 A1	19-08-1999
			CN 1297479 T	30-05-2001
			EP 1070118 A1	24-01-2001
			JP 2002503459 T	05-02-2002
			NO 20004563 A	13-09-2000
			NZ 506451 A	30-06-2003
			WO 9941359 A1	19-08-1999
			ZA 200004208 A	21-11-2001