

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
19 August 2010 (19.08.2010)

PCT

(10) International Publication Number  
**WO 2010/093784 A3**

(51) International Patent Classification:

C07K 14/075 (2006.01) A61P 9/00 (2006.01)  
C12N 15/861 (2006.01) A61P 3/00 (2006.01)  
A61P 21/00 (2006.01)

(21) International Application Number:

PCT/US2010/023885

(22) International Filing Date:

11 February 2010 (11.02.2010)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/151,736 11 February 2009 (11.02.2009) US

(71) Applicant (for all designated States except US): **THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL** [US/US]; 308 Bynum Hall, Campus Box 4105, Chapel Hill, North Carolina 27599-4105 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SAMULSKI, Richard, Jude** [US/US]; 102 Darlin Circle, Chapel Hill, North Carolina 27514 (US). **ASOKAN, Aravind** [IN/US]; 102-B Copperline Drive, Chapel Hill, North Carolina 27516 (US).

(74) Agent: **MYERS BIGEL SIBLEY & SAJOVEC, P.A.**; P.O. Box 37428, Raleigh, North Carolina 27627 (US).

(81) Designated States (unless otherwise indicated, for every

kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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

Published:

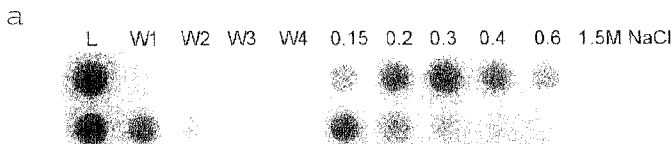
- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

16 December 2010

(54) Title: MODIFIED VIRUS VECTORS AND METHODS OF MAKING AND USING THE SAME

Figure 1



(57) Abstract: The present invention provides AAV capsid proteins (VP1, VP2 and/or VP3) comprising a modification in the amino acid sequence in the three-fold axis loop 4 and virus capsids and virus vectors comprising the modified AAV capsid protein. In particular embodiments, the modification comprises a substitution of one or more amino acids at amino acid positions 585 to 590 (inclusive) of the native AAV2 capsid protein sequence or the corresponding positions of other AAV capsid proteins. The invention also provides methods of administering the virus vectors and virus capsids of the invention to a cell or to a subject in vivo.



WO 2010/093784 A3

**A. CLASSIFICATION OF SUBJECT MATTER***C07K 14/075(2006.01)i, C12N 15/861(2006.01)i, A61P 21/00(2006.01)i, A61P 9/00(2006.01)i, A61P 3/00(2006.01)i*

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)

C07K 14/075; C12N; C12N 15/86; A61K 48/00; C12N 15/861

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models  
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal), Pubmed, Delphion

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	OPIE, S. R. et al. 'Identification of amino acid residues in the capsid proteins of adeno-associated virus type 2 that contribute to heparan sulfate proteoglycan binding' Journal of Virology. Vol. 77(12), pp. 6995-7006 (June 2003) See the abstract; Table 3; Fig.7 and legend.	1-27
A	WO 2004-111248 A2 (DEUTSCHES KREBSFORSCHUNGSZENTRUM STIFTUNG DES OFFENTLICHEN RECHTS et al.) 23 December 2004 See the abstract; Example 6.	1-27
A	US 2005-0287122 A1 (JEFFREY BARTLETT et al.) 29 December 2005 See the abstract.	1-27
A	WO 2005-005610 A2 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA et al.) 20 January 2005 See the abstract.	1-27
A	WU, P. et al. 'Mutational analysis of the adeno-associated virus type 2 (AAV2) capsid gene and construction of AAV2 vectors with altered tropism.' Journal of Virology. Vol. 74(18), pp. 8635-8647 (September 2000) See the abstract.	1-27

 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 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 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

"&amp;" document member of the same patent family

Date of the actual completion of the international search

15 OCTOBER 2010 (15.10.2010)

Date of mailing of the international search report

**15 OCTOBER 2010 (15.10.2010)**

Name and mailing address of the ISA/KR

Korean Intellectual Property Office  
Government Complex-Daejeon, 139 Seonsa-ro, Seo-gu, Daejeon 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

KIM, JI YUN

Telephone No. 82-42-481-8288



**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No.

**PCT/US2010/023885**

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004-111248 A2	23.12.2004	AT 409750 T	15.10.2008
		DE 602004016871 D1	13.11.2008
		EP 1486567 A1	15.12.2004
		EP 1664314 A2	07.06.2006
		EP 1664314 B1	01.10.2008
		US 2007-0036757 A1	15.02.2007
		US 7629322 B2	08.12.2009
		WO 2004-111248 A3	07.07.2005
		WO 2004-111248 A3	23.12.2004
		US 2005-0287122 A1	29.12.2005
US 2002-192823 A1	19.12.2002		
US 2005-287122 A1	29.12.2005		
US 6962815 B2	08.11.2005		
US 7749492 B2	06.07.2010		
WO 2005-005610 A2	20.01.2005		
		CA 2530029-A1	20.01.2005
		CN 1826414 A	30.08.2006
		CN 1826414 C0	30.08.2006
		EP 1660678 A2	31.05.2006
		EP 1660678 A4	04.10.2006
		JP 2007-527219 A	27.09.2007
		JP 2007-527219 T	27.09.2007
		WO 2005-005610 A2	20.01.2005
		WO 2005-005610 A3	20.01.2005
		WO 2005-005610 A3	15.12.2005