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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: IMPROVED AAV VECTOR FOR GENE THERAPY

(57) Abstract: Described are recombinant AAV vectors characterized in that they carry capsid protein modification(s) resulting in a reduced or eliminated heparin binding function. The AAV vectors of the present invention are particularly suitable for gene therapy by systemic application, since (a) transduction of the liver is eliminated or at least drastically reduced and (b) the transduction efficiency of non-hepatic tissues is increased.



WO 2004/111248 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/006222

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/86

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

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, MEDLINE, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GAO GUANGPING ET AL: "Adeno-associated viruses undergo substantial evolution in primates during natural infections." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 100, no. 10, 13 May 2003 (2003-05-13), pages 6081-6086, XP002255703 May 13 2003 2003 ISSN: 0027-8424 page 6083, left-hand column, last paragraph - right-hand column, paragraph 1; figure 2A -/--	1-3,7

☒ 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

13 December 2004

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/006222

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	& DATABASE SWALL EMBL; 1 June 2003 (2003-06-01), GAO ET AL.: "Adeno-associated viruses undergo substantial evolution in primates during natural infections" XP002255706 Database accession no. Q808Y0 the whole document -----	1-3,7
X	WO 02/053703 A (CHILDRENS HOSPITAL INC) 11 July 2002 (2002-07-11) "AAV vectors and methods" page 20; example 3; table 4 claims 4,6,7 -----	1,6-10
A	CALDWELL ELIZABETH E O ET AL: "Importance of specific amino acids in protein binding sites for heparin and heparan sulfate." INTERNATIONAL JOURNAL OF BIOCHEMISTRY & CELL BIOLOGY, vol. 28, no. 2, 1996, pages 203-216, XP002255704 ISSN: 1357-2725 abstract page 206, left-hand column, paragraph 2 - right-hand column, paragraph 1 -----	1-10
P,X	KERN A ET AL: "Identification of a heparin-binding motif on adeno-associated virus type 2 capsids." JOURNAL OF VIROLOGY, vol. 77, no. 20, October 2003 (2003-10), pages 11072-11081, XP002310361 ISSN: 0022-538X the whole document -----	1-10
P,X	WO 03/054197 A (BUENING HILDEGARD ;HUTTNER NADJA (DE); MEDIGENE AG (DE); PERABO LU) 3 July 2003 (2003-07-03) "A library of modified structural genes or capsid modified particles useful for the identification of viral clones with desired cell tropism" page 35; example 5 claims 13,41,42; table 1 ----- -/--	1,6-10

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP2004/006222

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	OPIE SHAUN 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, no. 12, 20 June 2003 (2003-06-20), pages 6995-7006, XP009018010 ISSN: 0022-538X the whole document -----	1-10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/006222

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:
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.:

1-10

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: 1-10

Mutant R475A, a pharmaceutical composition containing said mutant and its use for gene therapy

2. claims: 1-10

Mutant R484A, supra

3. claims: 1-10

Mutant R484E, supra

4. claims: 1-10

Mutant R487A, supra

5. claims: 1-10

Mutant R487E, supra

6. claims: 1-10

Mutant K527A, supra

7. claims: 1-10

Mutant K532A, supra

8. claims: 1-10

Mutant R585E, supra

9. claims: 1-10

Mutant R588E, supra

10. claims: 1-10

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Due to the large number of combinatorial possibilities, the total number of inventions has not been determined. However, it is considered that each modification at a certain position and each combination of modifications at more than one position may constitute a separate invention.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/006222

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02053703	A	11-07-2002	WO 02053703 A2	11-07-2002
			US 2002192823 A1	19-12-2002

WO 03054197	A	03-07-2003	AU 2002352261 A1	09-07-2003
			CA 2468882 A1	03-07-2003
			WO 03054197 A2	03-07-2003
			EP 1456383 A2	15-09-2004
