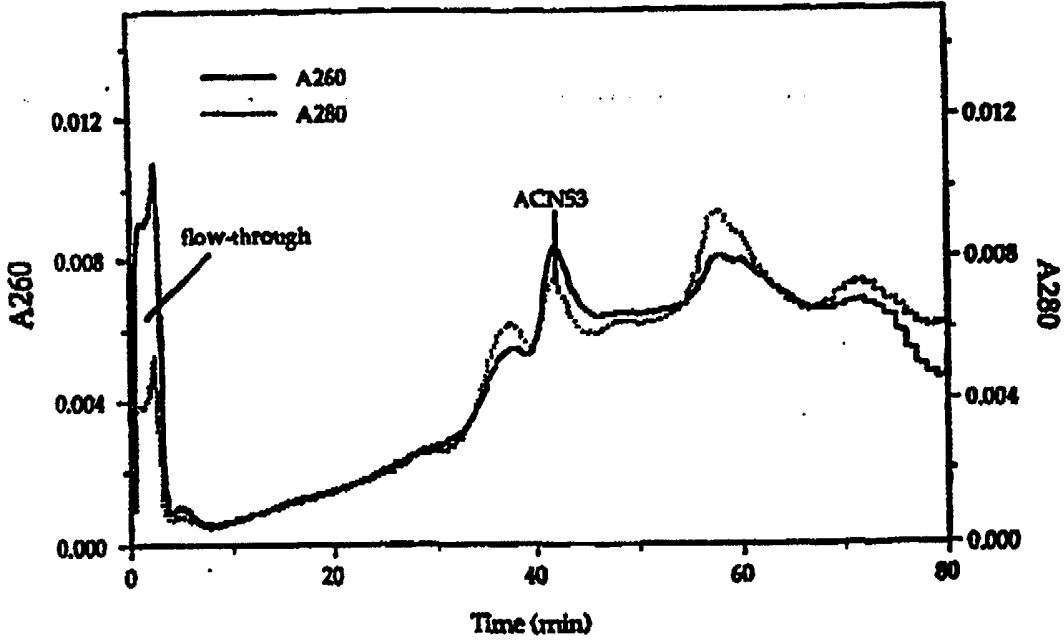




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁶ : C12N 15/86, 7/02, C12Q 1/00</p>	<p>A3</p>	<p>(11) International Publication Number: WO 96/27677 (43) International Publication Date: 12 September 1996 (12.09.96)</p>
<p>(21) International Application Number: PCT/US96/03369 (22) International Filing Date: 6 March 1996 (06.03.96) (30) Priority Data: 08/400,793 7 March 1995 (07.03.95) US (71) Applicant: CANJI, INC. [US/US]; Suite 302, 3030 Science Park Road, San Diego, CA 92121 (US). (72) Inventors: SHABRAM, Paul, W.; 165 Rancho Santa Fe Road, Olivenhain, CA 92024 (US). HUYGHE, Bernard, G.; 5215 Fiore Terrace #A313, San Diego, CA 92122 (US). LIU, Xiaodong; Apt. 23C, 501 West 121st Avenue, New York, NY 10027 (US). SHEPARD, H. Michael; P.O. Box 8333, Rancho Santa Fe, CA 92067 (US). (74) Agent: FITTS, Renee, A.; Townsend and Townsend and Crew L.L.P., Two Embarcadero Center, 8th floor, San Francisco, CA 94111 (US).</p>	<p>(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 16 January 1997 (16.01.97)</p>	

(54) Title: METHOD OF PURIFICATION OF RECOMBINANT VIRAL VECTORS CONTAINING A THERAPEUTIC GENE



(57) Abstract

The invention provides a method for purifying viral vectors containing therapeutic genes for use in gene therapy. The invention comprises a method of purification from a cell lysate of a recombinant viral vector containing a therapeutic gene, which comprises: a) treating said lysate with an enzymatic agent that selectively degrades both unencapsulated DNA and RNA; b) chromatographing the treated lysate from step a) on a first resin; and c) chromatographing the eluant from step b) on a second resin; wherein one resin is an anion exchange resin and the other is an immobilized metal ion chromatography (IMAC) resin.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/03369

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/86 C12N7/02 C12Q1/00

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 6 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	HUM. GENE THER. (1995), 6(11), 1403-16 CODEN: HGTHE3;ISSN: 1043-0342, November 1995, XP000601674 HUYGHE, BERNARD G. ET AL: "Purification of a type 5 recombinant adenovirus encoding human p53 by column chromatography" see the whole document ---	1-24
A	VIROLOGY, vol. 13, 1961, pages 264-267, XP000601693 I. HARUNA ET AL: "Separation of Adenovirus by chromatography on DEAE-cellulose" cited in the application see the whole document ---	1,2,11, 12,20,21
	-/--	

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	"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
"E" earlier document but published on or after the international filing date	"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
"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)	"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.
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 9 September 1996	Date of mailing of the international search report 03. 12. 96
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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 VAN DER SCHAAL C.A.
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/03369

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BIOTECHNOLOGY, vol. 11, 1993, pages 173-178, XP000195205 P. O'NEIL AND E. BALKOVIC: "Virus harvesting and affinity-based liquid chromatography" see the whole document ---	
A	WO 95 02688 A (VIAGENE INC) 26 January 1995 see the whole document ---	
A	JOURNAL OF GENERAL MICROBIOLOGY, vol. 19, 1958, pages 451-455, XP002012869 J. TAVERNE ET AL: "The purification and concentration of viruses and virus soluble antigens on calcium phosphate" see the whole document ---	
A	WO 84 04696 A (BAXTER TRAVENOL LAB) 6 December 1984 see the whole document -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 96/ 03369

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

- 1. claims 1-24: Method for purification of a recombinant viral vector
- 2. claims 25-26: Method of determining the number of intact viral particles

- 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.:

1-24

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

Information on patent family members

International Application No

PCT/US 96/03369

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9502688	26-01-95	US-A- 5447859	05-09-95
		AU-A- 7359694	13-02-95
		CA-A- 2167392	26-01-95
		EP-A- 0707636	24-04-96

WO-A-8404696	06-12-84	EP-A- 0151108	14-08-85
