

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
1 July 2004 (01.07.2004)

PCT

(10) International Publication Number  
**WO 2004/054512 A3**

- (51) International Patent Classification<sup>7</sup>: **A01N 63/00**, C07H 21/04, C12N 15/00
- (21) International Application Number: PCT/US2003/039526
- (22) International Filing Date: 11 December 2003 (11.12.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/433,321 13 December 2002 (13.12.2002) US  
60/475,822 4 June 2003 (04.06.2003) US  
60/513,312 21 October 2003 (21.10.2003) US
- (71) Applicants: **GENETIX PHARMACEUTICALS, INC.** [US/US]; 840 Memorial Drive, Cambridge, MA 02139 (US). **MASSACHUSETTS INSTITUTE OF TECHNOLOGY** [US/US]; Five Cambridge Center, Kendall Square, Cambridge, MA 02142-1493 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **LEBOULCH, Philippe** [US/US]; 197 Eighth Street, Unit 729, Charlestown, MA 02129 (US). **PAWLIUK, Robert** [US/US]; 62 Hume Avenue, Medford, MA 02155 (US). **WESTERMAN, Karen** [US/US]; 17 Avon Street, Reading, MA 01867 (US).
- (74) Agents: **REMILLARD, Jane, E.** et al.; Lahive & Cockfield, L.L.P., 28 State Street, Boston, MA 02109 (US).
- (81) Designated States (national): 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, 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.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, 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, 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:  
6 January 2005
- 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.



WO 2004/054512 A3

(54) Title: THERAPEUTIC RETROVIRAL VECTORS FOR GENE THERAPY

(57) Abstract: Retroviral gene therapy vectors that are optimized for erythroid specific expression and treatment of hemoglobinopathic conditions are disclosed.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US03/39526

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
IPC(7) : A01N 63/00; C07H 21/04; C12N 15/00		
US CL : 435/320.1; 424/93.2; 536/23.5, 24.1		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/320.1; 424/93.2; 536/23.5, 24.1		
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 practicable, search terms used) WEST, STN, MEDLINE, CAPLUS, BIOSIS, SCISEARCH		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	IMREN et al., Correction of Anemia in Beta-Thalassemia Mice Transplanted with Syngeneic Marrow Transduced with antiviral Vector Encoding Human Beta-Globin Gene, Blood, November 2001, Vol. 98, No. 11, Part 1, pp 692a.	1-4
---		-----
Y		64-73
X	PAWLIUK et al., Correction of Sickle Cell Disease in Transgenic Mouse Models by Hematopoietic Stem Cell Gene Therapy, Blood, 16 November 2001, Vol. 98, No. 11, Part 1, pp. 781a.	1-4
Y		64-73
	WO 94/23046 A1 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA) 13 October 1994 (12.10.1994), especially abstract, page 7.	
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> 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	"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 application or patent 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 25 May 2004 (25.05.2004)		Date of mailing of the international search report <b>19 OCT 2004</b>
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer Shin-Lin Chen <i>Janice Fred</i> Telephone No. 703-308-0196 <i>for</i>

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/39526

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim 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.  Claim Nos.: 5-24, 38-43, 57-63, 74-82, 89-104  
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:  
Please See Continuation 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.: 1-4, 64-73
- Remark on Protest**
- |                          |                                                                         |
|--------------------------|-------------------------------------------------------------------------|
| <input type="checkbox"/> | The additional search fees were accompanied by the applicant's protest. |
| <input type="checkbox"/> | No protest accompanied the payment of additional search fees.           |

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-4 and 64-73, drawn to a retroviral vector comprising a left retroviral LTR, a cPPT/FLAP, a retroviral export element, such as lentiviral reverse response element (RRE), a promoter and a locus control region (LCR) operably linked to a gene of interest, and a right retroviral LTR.

Group II, claim(s) 25-37, drawn to a method of achieving erythroid-specific expression of a gene of interest by introducing the retroviral vector of group I into erythrocyte or precursor thereof.

Group III, claim(s) 44-56 and 83-88, drawn to a method of treating a hemoglobinopathic condition by using the retroviral vector of group I.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the "special technical feature" shared by groups I-III is the retroviral vector as discussed in group I. Imren et al., 2001 (Blood, Vol. 98, No. 11, Part 1, pp. 692a) teaches a lentiviral vector containing the central polypurine tract (cPPT) and the rev/rre RNA export element of HIV, and a wild type human beta-globin gene linked in cis to a promoter region (815 bp) and a large 2.7 kb fragment encompassing hypersensitive sites (HS) 2, 3 and 4 of LCR in order to improve virus titer. Therefore, no special technical feature has been contributed by the present invention over the prior art. Thus, Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1.