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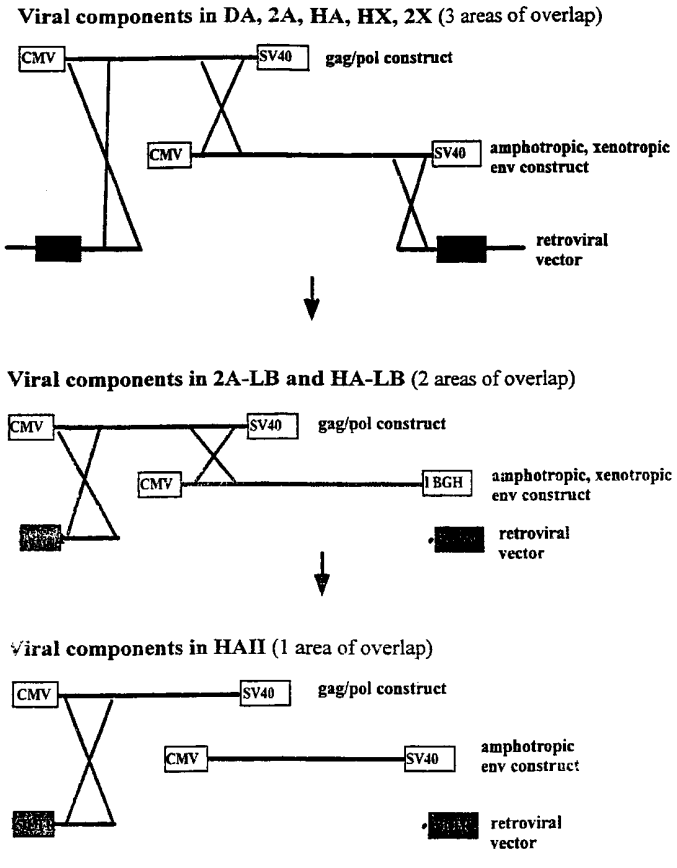
[Continued on next page]

(54) Title: RETROVIRUS PRODUCTING CELLS UTILIZING A HIGH MULTIPLICITY OF TRANSDUCTION



(57) Abstract: Retroviral vector particle producing cells are provided, wherein the cell (a) has greater than 5 stably integrated copies of a retroviral vector construct; (b) produces greater than 10 infectious recombinant retroviral vector particles per cell per day; and (c) produces replication incompetent retroviral vector particles.

WO 00/55343 A3

(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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INTERNATIONAL SEARCH REPORT

In ial Application No
PCT/US 00/07041

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/86 C12N5/10 C07K14/15 C07K14/145

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PERSONS DA, MEHAFFEY MG, KALEKO M, NIENHUIS AW, VANIN EF : "An improved method for generating retroviral producer clones for vectors lacking a selectable marker gene" BLOOD CELLS, MOLECULES AND DISEASES, vol. 24, no. 9, 15 May 1998 (1998-05-15), pages 167-182, XP000949384	1-3,5-7, 9-11
Y	the whole document	1-8, 12-16
X	WO 92 05266 A (VIAGENE INC) 2 April 1992 (1992-04-02) cited in the application	1-7,9-14
Y	page 15, line 19 - line 25; claims 3,11-22,24-31 page 34, line 4 - line 33	1-8, 12-16
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[X] Further documents are listed in the continuation of box C. [X] 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	Date of mailing of the international search report
25 September 2000	10/10/2000

Name and mailing address of the ISA	Authorized officer
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	Chambonnet, F

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 07225 A (CELL GENESYS INC) 27 February 1997 (1997-02-27) page 4, line 34 - line 36 page 7, line 5 - line 20 page 10, line 21 -page 12, line 15 page 19, line 26 - line 37	1,5-8, 11-13
Y	page 31, line 27 -page 33, line 36; table 1 page 43, line 8 -page 48, line 10; claims; examples VI,VII; tables 4,5,14	1-8
Y	YEE J - K ET AL: "GENERATION OF HIGH-TiteR PSEUDOTYPED RETROVIRAL VECTORS WITH VERY BROAD HOST RANGE" METHODS IN CELL BIOLOGY,GB,LONDON, vol. 43, 1994, pages 99-112, XP000570503 cited in the application page 111, line 4 - line 8	1,8
A	KOTANI H, NEWTON PB 3RD, ZHANG S, CHIANG YL, OTTO E, WEAVER L, BLAESE RM, ANDERSON WF, MCGARRITY GJ.: "Improved methods of retroviral vector transduction and production for gene therapy." HUM GENE THER. 1994 JAN;5(1):19-28., XP000653182 page 22, column 2, paragraph 2 -page 23, column 2, paragraph 2; figure 3	1
Y	page 24, column 2, paragraph 2 -page 25, column 1, paragraph 3 page 27, column 1, paragraph 3	15,16
T	SHERIDAN PL,: "Generation of retroviral packaging and producer cell lines for large-scale vector production and clinical application: improved safety and high titer" MOL THER 2000 SEP;2(3):262-75, vol. 2, no. 3, September 2000 (2000-09), pages 262-275, XP002148205 the whole document	1-16

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-14

A retroviral vector particle producing cell, wherein said cell(a) has greater than 5 stably integrated copies of a retroviral vector construct; (b) produces greater than 10 infectious recombinant retroviral vector particles per cell per day; and (c) produces replication incompetent retroviral vector particles; method for producing said cell.

2. Claims: 15-16

A method for producing recombinant vector particle produing cells, comprising:
(a) generating VSV-G pseudotyped retroviral vector particles;
(b) concentrating said particles;
(c) introducing said vector particles into a packaging cell line, such that recombinant vetor particle producing cells are produced

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-14

Present claims 1 to 14 relate to a product - a retroviral vector particle producing cell- defined by reference to a desirable characteristic , namely (a) having greater than 5 stably integrated copies of a retroviral vector construct, and desirable properties namely (b) producing greater than 10 infectious recombinant retroviral vector particles per cell per day and (c) producing replication incompetent retroviral vector particles.

The claims cover all products having these characteristic and properties, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the cell lines prepared in examples 8 and 9.

Present claims 1, 2,10 also relate to a product defined (inter alia) by reference to the following parameter:
P1 : the number of stably integrated copies of a retroviral vector construct,

Present claims 1, 3,10 also relate to a product defined (inter alia) by reference to the following parameter:
P2 : the number of infectious recombinant retroviral vector particles per cell per day.

Present claim 9 also relates to a product defined (inter alia) by reference to the following parameter:

P3 : the number of transductions of recombinant retroviral vector particles per cell

The use of these parameters in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is difficult or impossible to compare the parameters the applicant has chosen to employ with what is set out in the prior art. The lack of clarity is such as to render a meaningful complete search impossible. Consequently, the search has been restricted to the cell lines prepared in examples 8 and 9.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int onal Application No
PCT/US 00/07041

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