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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))

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28 January 2010

(54) Title: ENGINEERING AND DELIVERY OF THERAPEUTIC COMPOSITIONS OF FRESHLY ISOLATED CELLS

(57) Abstract: The present invention relates to the transient modification of cells. In particular embodiments, the cells are immune systems, such as PBMC, PBL, T (CD3+ and/or CD8+) and Natural Killer (NK) cells. The modified cells provide a population of cells that express a genetically engineered chimeric receptor which can be administered to a patient therapeutically. The present invention further relates to methods that deliver mRNA coding for the chimeric receptor to unstimulated resting PBMC, PBL, T (CD3+ and/or CD8+) and NK cells and which delivers the mRNA efficiently to the transfected cells and promotes significant target cell killing.



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A. CLASSIFICATION OF SUBJECT MATTER*C12N 15/87(2006.01)i, C12N 5/08(2006.01)i, A61K 48/00(2006.01)i, A61P 35/02(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)

IPC 8 C12N 15/87, A61K 48/00

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

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

eKOMPASS (KIPO internal), WPI, USPTO, PAJ, NCBI, INSPECT "chimeric receptor, mRNA, CD19, leukemia, PBMC, isolating NK cell, surface, etc."

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	PX: WO 2008/097926 A2 (Yale Univ. US) 14 Aug 2008 - page 19, line 19 ~ page 21, line 15; and page 30, line 6 ~ page 36, line 19	1-7, 22-24
Y	Blood Cells Mol Dis. Vol.33(1):83-89. (Cooper, L.J., et al. US) Jul-Aug 2004 "Development and application of CD19-specific T cells for adoptive immunotherapy of B cell malignancies." - see abstract; Fig. 1; pages 83-85	1-7, 22-24
X	Hum Gene Ther. Vol.17(10):1027-1035 (Rabinovich, P.M., et al., US) Oct 2006 "Synthetic messenger RNA as a tool for gene therapy." - see the whole document; cited in the application	1-7, 22-24
Y	Blood. Vol.107(7): 2643-2652 (Serrano, L.M., et al., US) 1 April 2006 "Differentiation of naive cord-blood T cells into CD19-specific cytolytic effectors for posttransplantation adoptive immunotherapy" - abstract; pages 2643-2644; Fig. 1; page 2648, the 2nd paragraph of the left column	1-7, 22-24

 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

"&" document member of the same patent family

Date of the actual completion of the international search

01 DECEMBER 2009 (01.12.2009)

Date of mailing of the international search report

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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

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Box No. 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.: 8-21
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 8-21 are directed to a method of treating cancer in a subject, for which ISA is not required to search an international application because the subject matter falls into the category of methods for treatment of the human body by therapy under Article 17(2)(a)(i) & Rule 39.1(iv) PCT.
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 No. 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:

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.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2009/040040

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Cancer Immunol Immunotherapy. Vol.53(10):893-903 (Baxevanix, C., et al., GR) Oct 2004 "Targeting of tumor cells by lymphocytes engineered to express chimeric receptor genes" - abstract; pages 894-895; Fig. 2; and Table 1	1-7, 22-24
A	WO 1996/024671 A1 (CELL GENESYS, INC., US) 15 Aug 1996 - see abstract; page 28, line 11 ~ page 29, line 14; page 31, line 25 ~ page 33, line 5; and claims	1-7, 22-24
A	US 2003-0026790 A1 (Hwu, P., et al., US) 06 Feb 2003 - see abstract; [0057]; [0060] ~ [0062]; and Example 11	1-7, 22-24

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2009/040040

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2008-097926 A2	14.08.2008	US 2008-260706 A1 WO 2008-097926 A3	23.10.2008 23.10.2008
WO 1996-024671 A1	15.08.1996	AU 4776196 A EP 0871726 A1 EP 0871726 A4 US 06103521 A	27.08.1996 21.10.1998 04.10.2000 15.08.2000
US 2003-0026790 A1	06.02.2003	AT 403734 T EP 1379670 A4 EP 1379670 A1 EP 1379670 B1 WO 2002-072850 A1	15.08.2008 15.12.2004 14.01.2004 06.08.2008 19.09.2002