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(88) Date of publication of the international search report:
12 March 2009

(54) Title: CULTURE FOR EXPANDING STEM CELLS EX-VIVO

(57) Abstract: The present invention relates to a culture including a growth medium and a combination of cytokines consisting of i) interleukin-6 (IL6); ii) flt3-ligand (FLT3); iii) stem cell factor (SCF) and iv) thrombopoi- etin (TPO); the use of the culture for expanding.ex vivo stem cells and/or parental cells and cells differentiated therefrom, and the use of said cells obtainable from said expansion.

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2008/001798

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N5/06

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)
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, EMBASE, WPI Data, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ENCABO ARACELI ET AL: "Selective generation of different dendritic cell precursors from CD34+ cells by interleukin-6 and interleukin-3" STEM CELLS (MIAMISBURG), vol. 22, no. 5, 2004, pages 725-740, XP002510073 ISSN: 1066-5099 page 727, column 1, paragraph 2 ----- -/--	1-9,12, 15,16, 18,19

[X] Further documents are listed in the continuation of Box C.

[X] 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 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
14 January 2009	27/01/2009

Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MURRAY LESLEY J ET AL: "Thrombopoietin, flt3, and kit ligands together suppress apoptosis of human mobilized CD34+ cells and recruit primitive CD34+Thy-1+ cells into rapid division" EXPERIMENTAL HEMATOLOGY (CHARLOTTESVILLE), vol. 27, no. 6, June 1999 (1999-06), pages 1019-1028, XP002510074 ISSN: 0301-472X page 1019, column 2, paragraph 1 - page 1020, column 2, paragraph 1; figures 2-5; table 1	1-3,7,8, 15,16, 18,19, 21,22
X	WO 2005/007799 A (GAMIDA CELL LTD [IL]; HASSON ARIK [IL]; GRYNSPAN FRIDA [IL]) 27 January 2005 (2005-01-27) pages 6,96,97,, column 98; figures 3-6	1,2,4,5, 7,8,10, 11, 13-16, 18,19, 21,22
X	SANTONI DE SIO ET AL: "1038. Lentiviral Gene Transfer into HSC Is Enhanced by Early-Acting Cytokines without Impairing Stem Cell Properties and Involves Cellular Responses Distinct from Cell Cycle Control" MOLECULAR THERAPY, ACADEMIC PRESS, SAN DIEGO, CA, US, vol. 11, 15 August 2005 (2005-08-15), page 401, XP005016377 ISSN: 1525-0016 abstract	1,2,8, 15,16, 18,19, 21,22
X	PELED TONI ET AL: "Linear polyamine copper chelator tetraethylenepentamine augments long-term ex vivo expansion of cord blood-derived CD34+ cells and increases their engraftment potential in NOD/SCID mice" EXPERIMENTAL HEMATOLOGY (NEW YORK), vol. 32, no. 6, June 2004 (2004-06), pages 547-555, XP002510075 ISSN: 0301-472X page 548, column 1, paragraph 4	1,2,4,5, 8,10,11, 15,16, 18,19,22
X	BRUNO S ET AL: "Different growth factor requirements for the ex vivo amplification of transplantable human cord blood cells in a NOD/SCID mouse model" JOURNAL OF BIOLOGICAL REGULATORS AND HOMEOSTATIC AGENTS, vol. 15, no. 1, January 2001 (2001-01), pages 38-48, XP009110635 ISSN: 0393-974X figures 2,3; tables 1,2	1-6,8, 11-16, 18-20,22

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: -

The present claims 8-23 relate to an extremely large number of possible compounds/products/apparatus/methods. Support and disclosure in the sense of Article 6 and 5 PCT is to be found however for only a very small proportion of the compounds/products/apparatus/methods claimed, see pages 20-32. The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of claims 8-23 (PCT Guidelines 9.19 and 9.23).

The search of claims 8-23 was restricted to those claimed compounds/products/apparatus/methods which appear to be supported, namely the expansion of haematopoietic stem cells.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2)PCT declaration be overcome.

INTERNATIONAL SEARCH REPORT

International application No.
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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.:
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:

see FURTHER INFORMATION sheet PCT/ISA/210

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 allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers 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

Information on patent family members

International application No
PCT/IB2008/001798

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005007799 A	27-01-2005	EP 1649007 A2	26-04-2006
		US 2006205071 A1	14-09-2006