

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
13 September 2007 (13.09.2007)

PCT

(10) International Publication Number
WO 2007/102162 A3

- (51) International Patent Classification:
C12N 5/06 (2006.01)
- (21) International Application Number:
PCT/IL2007/000308
- (22) International Filing Date: 8 March 2007 (08.03.2007)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/780,781 8 March 2006 (08.03.2006) US
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- (81) Designated States (unless otherwise indicated, for every kind of national protection available): 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, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (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:
23 April 2009



WO 2007/102162 A3

(54) Title: REGULATING STEM CELLS

(57) Abstract: A composition of matter is provided, comprising a population of cultured cells that comprises a sub-population of cells that both stain as CD31Bright and demonstrate uptake of Ac-LDL+, and secrete IL-8. A method is also provided, comprising stimulating in vitro an initiating cell population (ICP) of at least 5 million cells that have a density of less than 1.072 g/ml, wherein at least 1% of the cells of the ICP is CD34+CD45-/Dim, and at least 25% of the cells of the ICP are CD31Bright, to differentiate into a progenitor/precursor cell population (PCP). Other embodiments are also described.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL 07/00308

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12N 5/06 (2008.04)

USPC - 435/377, 435/405

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)

USPC: 435/377, 435/405

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

USPC: 435/377, 375, 325, 405, 404 (text search)

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

Electronic Data Bases: (PGPB, USPT, JPAB, EPAB); Google Scholar

Search Terms: CD31, CD34, EPC, endothelial, progenitor, stem, IL-8, Ac-LDL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HUR et al. Characterization of two types of endothelial progenitor cells and their different contributions to neovasculogenesis. IN: Arterioscler Thromb Vasc Biol. Feb 2004 Vol 24 No 2 Pg:288-93. Especially abstract, pg 289 fig 1 and right col para 4, pg 290 fig 2 and fig 3, pg 292 fig 6.	1-12, 15-25
Y		13, 14
Y	WO 2005/120090 A2 (FULGA et al.) 15 December 2005 (15.12.2005). Especially pg 3 ln 30-31	13
Y	KOCHER et al. Myocardial homing and neovascularization by human bone marrow angioblasts is regulated by IL-8/Gro CXC chemokines. IN: J Mol Cell Cardiol. Epub 24 January 2006 Vol 40 No 4 Pg:455-64. Abstract only.	14

Further documents are listed in the continuation of Box C.

* 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 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

3 December 2008 (03.12.2008)

Date of mailing of the international search report

18 DEC 2008

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL 07/00308

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:

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:
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 Claims 1-25 are directed to a population of cultured cells that comprises a sub-population of cells that both stain as CD31Bright and demonstrate uptake of Ac-LDL+.

Group II Claims 26-60, 66-72, and 104-147 and 156-157 are directed to a method of stimulating in vitro an initiating cell population (ICP) to differentiate into a progenitor/precursor cell population (PCP).

Group III Claims 26-28 and 61- 65, and 73-103 are directed to identifying the PCP as being suitable for therapeutic implantation.

Group IV Claims 26-28, and 148-155 and 158-159 are directed to systemically administering the PCP to a patient.

-----continued in Supplemental Box-----

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 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 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.:
Group 1: Claims 1-25

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/IL 07/00308

continuation of BOX III:

The inventions listed as Groups I - IV 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:

Groups I-IV share the technical feature of cultured cells with a density of less than 1.072, have a population of CD31 Bright and (CD34+)/(CD45-/Dim) and demonstrate uptake of Ac-LDL. However, this is not an improvement over the prior art of WO 2005/120090 to Fulga et al. (15.12.2005) that teaches cultured cells with a density of less than 1.072, a population of CD31 Bright and (CD34+)/(CD45-/Dim) and demonstrate uptake of Ac-LDL (pg 16 ln 21-24, pg 58 example 3).