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(54) Title: LYMPHOCYTE BIOMARKERS FOR DETERMINING THE CLINICAL RESPONSE TO THERAPY WITH MESCENCHYMAL STROMAL CELLS(MSC)

(57) Abstract: The present invention provides a method for determining the clinical prognosis of a human subject to the administration of a pharmaceutical composition comprising of stem cells (preferably mesenchymal stem cells), stromal cells, regulatory T-cells, fibroblasts and combinations thereof.



INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2014/055282

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:

see additional 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 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.:

4-6, 12-14, 16-18(completely); 1-3, 8-11(partially)

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/EP2014/055282

A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N33/569 A61K35/14
ADD. A61P37/06

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)

G01N A61K

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)

EPO-Internal, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	OLGA DELAROSA ET AL: "Mesenchymal stem cells as therapeutic agents of inflammatory and autoimmune diseases", CURRENT OPINION IN BIOTECHNOLOGY, vol. 23, no. 6, 1 December 2012 (2012-12-01), pages 978-983, XP055096416, ISSN: 0958-1669, DOI: 10.1016/j.copbio.2012.05.005 p. 979 Box 1 ----- -/--	1-6, 8-14, 16-18



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 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

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Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/055282

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Clinical & Investigative Sciences Group (clinical And Laboratory Haematology) ET AL: "Conditioning Protocols - allogeneic transplantation", 23 September 2012 (2012-09-23), XP055137189, Retrieved from the Internet: URL: http://www.imperial.nhs.uk/prdcons/groups/public/@clinical/@cancer/documents/doc/hhnt_005219.pdf [retrieved on 2014-08-28] the whole document	1-6, 8-14, 16-18
Y	----- KRAMPERA MAURO ET AL: "Role for interferon-gamma in the immunomodulatory activity of human bone marrow mesenchymal stem cells", STEM CELLS, ALPHAMED PRESS, DAYTON, OH, US, vol. 24, no. 2, 1 February 2006 (2006-02-01), pages 386-398, XP002422937, ISSN: 1066-5099 p. 396	1-6, 8-14, 16-18
Y	----- M KRAMPERA: "Mesenchymal stromal cell 'licensing': a multistep process", LEUKEMIA, vol. 25, no. 9, 1 September 2011 (2011-09-01), pages 1408-1414, XP055137780, ISSN: 0887-6924, DOI: 10.1038/leu.2011.108 p. 1911	1-6, 8-14, 16-18
X,P	----- DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; October 2013 (2013-10), WANG DANDAN ET AL: "A CD8 T Cell-IFN-gamma-IDO Axis Is Required For Mesenchymal Stem Cell Suppression Of Human SLE", XP002729197, Database accession no. PREV201300782514 abstract & ARTHRITIS & RHEUMATISM, vol. 65, no. Suppl. 10, Sp. Iss. SI, October 2013 (2013-10), pages S674-S675, 77TH ANNUAL MEETING OF THE AMERICAN-COLLEGE-OF-RHEUMATOLOGY / 48TH ANNUAL MEETING OF THE ASSOCIATION; SAN DIEGO, CA, USA; OCTOBER 25 -30, 2013 ISSN: 0004-3591(print) ----- -/--	1-6, 8-14, 16-18

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/055282

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DELAROSA OLGA ET AL: "Requirement of IFN-gamma-mediated indoleamine 2,3-dioxygenase expression in the modulation of lymphocyte proliferation by human adipose-derived stem cells", TISSUE ENGINEERING, LARCHMONT, NY, US, vol. 15, no. 10, 7 October 2009 (2009-10-07), pages 2795-2806, XP002563369, ISSN: 1076-3279, DOI: 10.1089/TEN.TEA.2008.0630 [retrieved on 2009-04-03] the whole document -----	1-6, 8-14, 16-18

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 4-6, 12-14, 16-18(completely); 1-3, 8-11(partially)

Method for predicting clinical response to the administration of MSC and treatment of a patient with MSC suffering from an inflammatory and/or an immune disorder by evaluating levels of CD8+ and/or CD4+ lymphocyte levels.

2. claims: 7, 15, 19(completely); 1-3, 8-11(partially)

Method for predicting clinical response to the administration of MSC and treatment of a patient with MSC suffering from an inflammatory and/or an immune disorder by evaluating levels of HLA-II.
