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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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18 March 2010

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(54) Title: MESENCHYMAL STEM CELLS, COMPOSITIONS, AND METHODS FOR TREATMENT OF CARDIAC TISSUE DAMAGE

(57) Abstract: The present invention provides compositions comprising mesenchymal stem cells (MSCs), and methods for their novel use in the repair of cardiac damage and treatment of inflammatory diseases. The invention also provides methods for using TSG-6 protein that is secreted by MSCs under certain conditions, for repair of cardiac damage and inflammatory disease. The compositions of the invention may be particularly useful in restoring cardiac function following cardiac damage, including, but not limited to, myocardial infarction, as well as in reducing symptoms of inflammatory disease.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 09/03657

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C07K 14/525 (2010.01)
USPC - 530/350, 351; 435/41, 70.1
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 - 530/350, 351; 435/41, 70.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 435/325, 70.3, 366

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST (PGPB, USPT, EPAB, JPAB); Google: PubMed

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,386,013 A (Lee et al.) 31 January 1995 (31 January 1995) Especially abstract; col 23, ln 55-60; col 31, ln 54-62.	1-6, 11-21
Y	US 2007/0128719 A1 (Tseng et al.) 07 June 2007 (07.06.2007) Especially para [0076], [0100].	1-6, 11-21
Y	US 2007/0213255 A1 (Hastings et al.) 13 September 2007 (13.09.2007) Especially para [0625], [0729].	11-21
Y	US 2004/0115199 A1 (Halkier et al.) 17 June 2004 (17.06.2004) Especially [0128].	15-21

☐ 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	Date of mailing of the international search report
29 December 2009 (29.12.2009)	27 JAN 2010
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 09/03657

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:

Group I, claims 1-6 and 11-21, directed to mesenchymal stem cells (MSC's) which produce TSG-6 protein.

Group II, claim 7 and 8, directed to methods for purifying self-renewing MSC's.

Group III, claims 9, 10 and 22, directed to methods for reducing symptoms of cardiac muscle cell necrosis, comprising, inter alia, administering TSG-6 protein to a subject.

Group IV, claims 23 and 24, directed to methods of diagnosing sterile inflammation as a function of the serum level of two or more of plasmin activity, macrophage chemoattractant protein -1 (MCP-I), macrophage inflammatory protein-I alpha (MIP-Ialpha), beta thromboglobulin, soluble ST2 receptor, C-reactive protein (CRP), and natriuretic peptide.

Continued on 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.:
1-6, 11-21

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/US 09/03657

Box No. III Observations where unity of invention is lacking - continued:

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:

The special technical feature of Group I, claims 1-6 and 11-21, is the population of MSC's which produce TSG-6 protein. This specific type of cell is not required by any of Groups II-IV.

The special technical features of Group II, claims 7 and 8, are the methods for purifying self-renewing MSC's. Purification is not required by any of Groups I, III or IV.

The special technical feature of Group III, claims 9, 10 and 22, is the administration of TSG-6 protein to a subject. This group does not require that the TSG-6 come from MSC's (required by Group I), the particular methods of purification required by Group II, or the methods of detecting sterile inflammation required by Group IV.

The special technical feature of Group IV, claims 23 and 24, is the method of detecting sterile inflammation by measuring serum levels of a number of factors not including TSG-6 protein. This group does not require the presence of TSG-6 protein (required by Group I), methods of purifying MSC's (required by Group II) or administering the TSG-6 protein to a patient (required by Group III).

Accordingly, there is no unity of invention.