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(88) Date of publication of the international search report:  
4 March 2010

(54) Title: HOMING IN MESENCHYMAL STEM CELLS

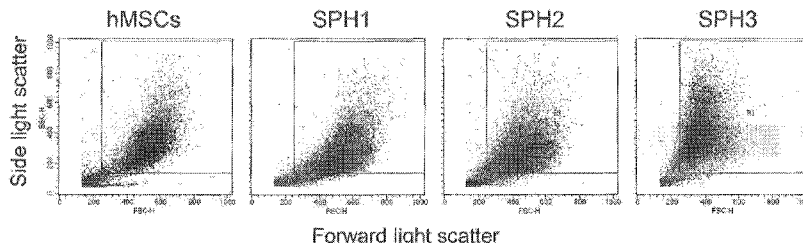


Fig. 1

(57) Abstract: The present invention relates to expression of CXCR4 in mesenchymal stem cells (MSCs) and homing of MSCs to sites of injury. In particular, the invention provides expanded cultures of MSCs which maintain cell surface expression of CXCR4. The MSCs are capable of homing to sites of injury and are suitable for treatment of ischemic disorders, including cardiac disorders, bone and cartilage disorders, liver disorders, inflammatory disorders, and stroke.



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**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US 09/36414

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC(8) - C12N 5/08 (2009.01)  
USPC - 435/372  
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)  
435/372

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
435/372, 375, 395; 424/93.7

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
PubWest, Google, Google Scholar;  
Search Terms used - Mesenchymal Stem Cells (MSCs), cell surface, expression, over-expression, CXCR4, fusin, inject, culture, hanging drop, adhesion, adhere, aggregate, spheroid, serum, dissociation, proportion, portion, %, hypoxia, ischemia,

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	US 2007/0258943 A1 (PENN, et al.) 08 November 2007 (08.11.2007) (abstract; para [0007], [0117]).	1 ----- 2-22,56-58
Y	US 2003/0119107 A1 (DANG, et al.) 26 June 2003 (26.06.2003) (abstract; para [0008], [0014], [0031], [0037], [0112], [0136], [0186]).	2,3,9,11-15,19-22,57,58
Y	AIUTI, et al. "Human CD34+ cells express CXCR4 and its ligand stromal cell-derived factor-1. Implications for infection by T-cell tropic human immunodeficiency virus" Blood, 1999, Volume 94, pgs 62-73; Entire document, esp: abstract; pg 65, col 1; pg 71, col 1.	4-6
Y	US 2005/0069527 A1 (LAUGHLIN, et al.) 31 March 2005 (31.03.2005) (abstract; para [0013], [0019], [0046], [0051], [0052], [0056], [0063], [0089], [0096], [0104], [0118], [0152], [0158], [0194], [0197]).	7,8,10,14-22,56-58

Further documents are listed in the continuation of Box C.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search 07 December 2009 (07.12.2009)	Date of mailing of the international search report <b>15 DEC 2009</b>
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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
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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/36414

**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.: 23-26 and 41  
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 1-22 and 56-58 are drawn to compositions of mesenchymal stem cells.

Group II: Claims 27-40 and 42-51 are drawn to methods of culturing mesenchymal stem cells.

Group III: Claims 52-55 are drawn to methods of treating diseases by administering mesenchymal stem cells.

Group IV: Claims 59-63 are drawn to compositions of conditioned medium.

The groups listed above 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 technical feature that links the listed groups is a mesenchymal stem cell culture, wherein a substantial proportion of the cell express cell surface CXCR4. However, this does not represent an improvement over the prior art of US 2007/0258943 to Penn et al. which teaches genetically modified mesenchymal stem cells which overexpress CXCR4 (para [0007]) to provide stable, long term expression of CXCR4 (para [0117]). Accordingly, unity of invention is lacking under PCT Rule 13.2 because the groups do not share a same or corresponding special technical feature providing a contribution over the prior art.

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.:  
Claims 1-22 and 56-58

**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.