

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
21 August 2003 (21.08.2003)

PCT

(10) International Publication Number  
**WO 2003/068937 A3**

- (51) International Patent Classification<sup>7</sup>: A01N 1/02, 31/70, C12N 5/02
- (21) International Application Number: PCT/US2003/004539
- (22) International Filing Date: 13 February 2003 (13.02.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
10/076,180 13 February 2002 (13.02.2002) US  
60/437,292 31 December 2002 (31.12.2002) US
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
22 April 2004

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

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(54) Title: EMBRYONIC-LIKE STEM CELLS DERIVED FROM POST-PARTUM MAMMALIAN PLACENTA AND USES AND METHODS OF TREATMENT USING SAID CELLS

(57) Abstract: The present invention provides compositions and methods of using embryonic-like stem cells that originate from a post-partum placenta with conventional cord blood compositions or other stem or progenitor cells. The embryonic-like stem cells can be used alone or in a mixture with other stem cell populations. In accordance with the present invention, the embryonic-like stem cells may be mixed with other stem cell populations, including but not limited to, umbilical cord blood, fetal and neonatal hematopoietic stem cells and progenitor cells, human stem cells and progenitor cells derived from bone marrow. The embryonic-like stem cells and the mixed populations of embryonic-like stem cells and stem cells have a multitude of uses and applications, including but not limited to, therapeutic uses for transplantation and treatment and prevention of disease, and diagnostic and research uses.



WO 2003/068937 A3

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US03/04539

<p><b>A. CLASSIFICATION OF SUBJECT MATTER</b>                  IPC(7) : A01N 1/02, 31/70; C12N 5/02                  US CL : 435/1.1, 1.2, 325; 424/93.1                  According to International Patent Classification (IPC) or to both national classification and IPC</p>																	
<p><b>B. FIELDS SEARCHED</b></p> <p>Minimum documentation searched (classification system followed by classification symbols)                  U.S. : 435/1.1, 1.2, 325; 424/93.1</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)                  EAST, BIOSIS, MEDLINE, CAPLUS, EMBASE</p>																	
<p><b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b></p> <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>WANG et al. Enhanced recovery of hematopoietic progenitor and stem cells from cultivated, postpartum human placenta. Blood. 2001 November 16, Vol. 98, page 183a, see entire document.</td> <td>1-4, 7-16, 19-25 ----- 5, 6, 26,</td> </tr> <tr> <td>X</td> <td>US 6,179,819 A (HASWELL) 30 January 2001, see entire document particularly abstract and claims.</td> <td>1-17, 19-26 ----- 27-39, 41-84, 86, 90-96</td> </tr> <tr> <td>Y</td> <td>US 6,146,888 A (SMITH et al.) 14 November 2000, col 5, lines 28-45.</td> <td>1, 2, 16, 17, 27, 38, 39, 45, 53, 54, 78, 83, 84</td> </tr> <tr> <td>Y</td> <td>US 5,861,315 A (NAKAHATA) 19 January 1999, see entire document, particularly figures.</td> <td>27, 43-45, 58-60, 78, 86-88</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	WANG et al. Enhanced recovery of hematopoietic progenitor and stem cells from cultivated, postpartum human placenta. Blood. 2001 November 16, Vol. 98, page 183a, see entire document.	1-4, 7-16, 19-25 ----- 5, 6, 26,	X	US 6,179,819 A (HASWELL) 30 January 2001, see entire document particularly abstract and claims.	1-17, 19-26 ----- 27-39, 41-84, 86, 90-96	Y	US 6,146,888 A (SMITH et al.) 14 November 2000, col 5, lines 28-45.	1, 2, 16, 17, 27, 38, 39, 45, 53, 54, 78, 83, 84	Y	US 5,861,315 A (NAKAHATA) 19 January 1999, see entire document, particularly figures.	27, 43-45, 58-60, 78, 86-88
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C.      <input type="checkbox"/> See patent family annex.</p>																	
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"E" earlier application or patent published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"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</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&amp;" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"E" earlier application or patent published on or after the international filing date	"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	"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)	"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	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed						
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<p>Date of the actual completion of the international search                  25 November 2003 (25.11.2003)</p>		<p>Date of mailing of the international search report                  24 FEB 2004</p>															
<p>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. (703)305-3230</p>		<p>Authorized officer  <i>J. Janice Li</i>                  Telephone No. 703-308-0196</p>															

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US03/04539

**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

- 1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
- 2.  Claim 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.  Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation 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 fee, this Authority did not invite payment of any additional fee.
- 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.:

- Remark on Protest**
- The additional search fees were accompanied by the applicant's protest.
  - No protest accompanied the payment of additional search fees.

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

- I. Types of stem or progenitor cells selected from the group consisting of umbilical cord blood and placenta, fetal or neonatal, adult peripheral blood, and bone marrow; or one type of nucleated cells (it is noted that except red blood cells and platelet, all cells are nucleated).
- II. Each set of markers expressed or lack of on the cell surface, such as CD 34+/CD38- or CD 34+/CD38+.
- III. Status of cells, selected from the group consisting of untreated, growth factor-treated for inducing differentiation, and various growth factor-treated for prevention differentiation. Moreover, when one of the later two are elected, further identifying a particular growth factor or a particular combination of growth factors is necessary.
- IV. Type of diseases to be treated.

Applicants are required to elect at least one combination from each of the listed elements. The following claim(s) are generic: 1, 3-9, 19-22, 26-31, 41, 42, 78-82, 90-93.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The species of the invention are drawn to different stem or progenitor cells hearing different combinations of cell surface markers. The special technical feature of each of the combination of surface markers as listed in claims is drawn to different nucleated cells, stem or progenitor cells from different sources, they bear mutually exclusive surface markers having different biological functions. The results from one type of cells cannot necessarily be assumed to be the same for all types of cells nor would it necessarily be obvious to that if one type of cell works in the claimed method that all cells would be as effective. Accordingly, they are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

Applicant is advised that a reply to this Invitation must include an identification of the species that is elected consonant with this requirement, and a list of all claims readable thereon.

If no additional fee is paid, the following claims drawn to a composition comprising untreated CD34+/CD38- umbilical cord blood stem or progenitor cells and embryonic-like stem cells, methods of making and using such for treating a vascular disease would be examined. Claims read on the species are claims 1-14, 19-36, 38-42, 45-51, 53-57, 62, 63, 74-85, 90-96.