



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: PCT/IL99/00398</p> <p>(22) International Filing Date: 20 July 1999 (20.07.99)</p> <p>(30) Priority Data: 125532 27 July 1998 (27.07.98) IL</p> <p>(71) Applicant (for all designated States except US): YEDA RESEARCH AND DEVELOPMENT CO. LTD. [IL/IL]; Weizmann Institute of Science, P.O. Box 95, 76100 Rehovot (IL).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): LAPIDOT, Tsvee [IL/IL]; Boxer Street 6, 74046 Nes-Ziona (IL). PELED, Amnon [IL/IL]; Balfour Street 33b, 65211 Tel-Aviv (IL).</p> <p>(74) Agent: BEN-AMI, Paulina; Yeda Research and Development Co. Ltd., Weizmann Institute of Science, P.O. Box 95, 76100 Rehovot (IL).</p>	<p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, 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, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 16 March 2000 (16.03.00)</p>	
<p>(54) Title: HEMATOPOIETIC CELL COMPOSITION FOR USE IN TRANSPLANTATION</p>		
<p>(57) Abstract</p> <p>Cell compositions consisting essentially of mammalian hematopoietic CXCR4⁺ stem and progenitor cells capable to migrate in response to stromal-derived factor 1 (SDF-1) and/or capable to adhere to stromal cells in response to an adhesion-inducing agent, are provided for clinical transplantation. Hematopoietic CXCR4^{-low} stem and progenitor cells can be converted into CXCR4⁺ cells by stimulation with a suitable agent. The composition consists preferably of human CD38^{-low} CXCR4⁺ cells.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL 99/00398

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>US 5 541 103 A (KANZ LOTHAR ET AL) 30 July 1996 (1996-07-30)</p> <p>the whole document</p>	<p>1-3, 7-10, 13-27, 33-49</p>
Y	<p>MOHLE R ET AL.: "The chemokine receptor CXCR-4 is expressed on CD34+ hematopoietic progenitors and leukemic cells and mediates transendothelial migration induced by stromal cell-derived factor-1." BLOOD, vol. 91, no. 12, 15 June 1998 (1998-06-15), pages 4523-4530, XP002127667 the whole document</p>	<p>1-3, 7-11, 25-27, 29,30, 35-38, 41-52</p>
A	<p>AIUTI A ET AL.: "The chemokine SDF-1 is a chemoattractant for human CD34+ hematopoietic progenitor cells and provides a new mechanism to explain the mobilization of CD34+ progenitors to peripheral blood." J. EXP. MED., vol. 185, no. 1, 6 January 1997 (1997-01-06), pages 111-120, XP000866066 cited in the application page 116, column 2, line 29 -page 118</p>	<p>1-3, 6-27, 35-38, 41-52</p>
X	<p>LAROCHELLE ET AL.: "Identification of primitive human hematopoietic cells capable of repopulating NOD/SCID mouse bone marrow: Implications for gene therapy." NATURE MEDICINE, vol. 2, no. 12, December 1996 (1996-12), pages 1329-1337, XP002127668 cited in the application page 1329, column 1, line 22 -column 2, line 3 page 1335, column 1, line 9 - line 10 page 1335, column 2, line 13 - line 26</p>	<p>28,31, 32,34</p>
Y A	<p>the whole document</p>	<p>29,30 1-3, 7-10,13, 14,19, 20,23, 24, 35-38, 41-52</p>
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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ZANJANI E ET AL.: "Human bone marrow CD34- cells engraft in vivo and undergo multilineage expression that includes giving rise to CD34+ cells." EXPERIMENTAL HEMATOLOGY, vol. 26, no. 4, April 1998 (1998-04), pages 353-360, XP000866082 cited in the application page 353, column 2, line 15 - line 20	4, 30, 39
A	CIVIN C ET AL.: "Sustained, retransplantable, multilineage engraftment of highly purified adult human bone marrow stem cells in vivo." BLOOD, vol. 88, no. 11, 1 December 1996 (1996-12-01), pages 4102-4109, XP000866291 cited in the application page 4108, column 1, line 10 - line 20	5, 40
P, X	LAPIDOT T ET AL.: "Ex-vivo expansion of migrating human CXCR4+ SCID repopulating cells by upregulation of surface CXCR4 expression in response to stimulation with SCF or IL-6" BLOOD, vol. 90, no. 10 Supplement 1, 15 November 1998 (1998-11-15), page 717a XP000866556 the whole document	1-52
P, X	LAPIDOT T ET AL.: "The chemokine SDF-1 and the cytokine SCF mediate CXCR4 dependant homing of human CD34+ CD38- stem cells to the bone marrow of NOD/SCID mice." BLOOD, vol. 92, no. 10 Supplement 1, 15 November 1998 (1998-11-15), page 504a XP000866555 the whole document	1-52
P, X	VIARDOT A ET AL.: "The human immunodeficiency virus (HIV)-type 1 coreceptor CXCR4 (fusin) is preferentially expressed on the more immature CD34+ hematopoietic stem cells." ANNALS OF HEMATOLOGY, vol. 77, no. 5, 5 November 1998 (1998-11-05), pages 193-197, XP000866301 the whole document	1-3, 5, 7-11, 25-27, 33

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL 99/ 00398

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: X
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 35-47 and 52 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.
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 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:

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IL 99/00398

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9615813 A	30-05-1996	US 5665350 A AU 4378996 A	09-09-1997 17-06-1996
US 5541103 A	30-07-1996	DE 4240635 A US 5472867 A	09-06-1994 05-12-1995