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(71) Applicant: **THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY** [US/US]; Office of the General Counsel, Building 170, 3rd Floor, Main Quad, P.O. Box 20386, Stanford, California 94305-2038 (US).

(72) Inventors: **MEYER, Everett Hurteau**; 3308 Adelaide Way, Belmont, California 94002 (US). **NEGRIN, Robert S.**; 269 West Campus Drive, BMT Division - CCSR Building, Room 2205, Stanford, California 94305-5170 (US).

(74) Agent: **SHERWOOD, Pamela J.**; BOZICEVIC, FIELD & FRANCIS LLP, 201 Redwood Shores Parkway, Suite 200, Redwood City, California 94065 (US).

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30 April 2020 (30.04.2020)

(54) Title: METHODS FOR ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

(57) Abstract: The disclosure provides methods for improved hematopoietic stem cell transplantations, including methods to enhance protection from graft versus host disease while maintaining effective immune responses such as graft versus tumor immune responses. The disclosure provides methods for administering, for example, hematopoietic stem and progenitor cells, regulatory T cells, and conventional T cells, wherein the conventional T cells are administered after the hematopoietic stem and progenitor cells and regulatory T cells. The disclosure also provides methods for administering, for example, hematopoietic stem and progenitor cells, regulatory T cells, and conventional T cells, wherein the regulatory T cells have not been cryopreserved prior to administration.

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INTERNATIONAL SEARCH REPORT

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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.: 4-52, 56-104, 108-155
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:

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.:

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/US2019/017017

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 35/12; A61K 35/15; A61K 35/17; A61K 35/28; A61P 37/06; C12N 5/02 (2019.01)

CPC - A61K 35/15; A61K 35/17; A61K 35/28; A61K 2035/122; A61K 2035/124; A61K 2300/00; A61P 37/06; C12N 5/0647 (2019.02)

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)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 424/489; 424/85.2; 424/93.21; 424/93.71; 435/325; 435/372; 435/375; 435/1.1; 435/372.3; 514/885 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2014/0294793 A1 (LITTMAN et al) 02 October 2014 (02.10.2014) entire document	1-3, 53-55, 105-107
Y	TANG et al. "CD4+Foxp3+ Regulatory T Cell Therapy in Transplantation," Journal of Molecular Cell Biology, 14 December 2011 (14.12.2011), Vol. 4, Pgs. 11-21. entire document	1-3, 53-55, 105-107
Y	US 2005/0163760 A1 (CARTIER-LACAVE et al) 28 July 2005 (28.07.2005) entire document	2, 54, 106
Y	LU et al. "Characterization of Protective Human CD4+CD25+FOXP3+ Regulatory T Cells Generated with IL-2, TGF-b and Retinoic Acid," PLoS One, 17 December 2010 (17.12.2010), Vol. 5, Iss. 12, e15150, Pgs. 1-12. entire document	53-55
A	MEHROTRA et al. "Amelioration of a Mouse Model of Osteogenesis Imperfecta with Hematopoietic Stem Cell Transplantation: Micro-Computed Tomography Studies," Exp Hematol, 24 April 2010 (24.04.2010), Vol. 38, No. 7, Pgs. 593-602. entire document	1-3, 53-55, 105-107
A	US 2012/0121539 A1 (SANDS et al) 17 May 2012 (17.05.2012) entire document	1-3, 53-55, 105-107
A	US 2017/0073406 A1 (SCHOLAR ROCK, INC.) 16 March 2017 (16.03.2017) entire document	1-3, 53-55, 105-107
A	US 2015/0110738 A1 (UNIVERSITY OF SOUTHERN CALIFORNIA) 23 April 2015 (23.04.2015) entire document	1-3, 53-55, 105-107

☐ 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

Date of the actual completion of the international search

26 March 2019

Date of mailing of the international search report

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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, VA 22313-1450
Facsimile No. 571-273-8300

Authorized officer

Blaine R. Copenheaver

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774