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C07K 14/705 (2006.01) A61L 27/36 (2006.01)

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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(54) Title: UNIVERSAL DONOR CELLS AND RELATED METHODS

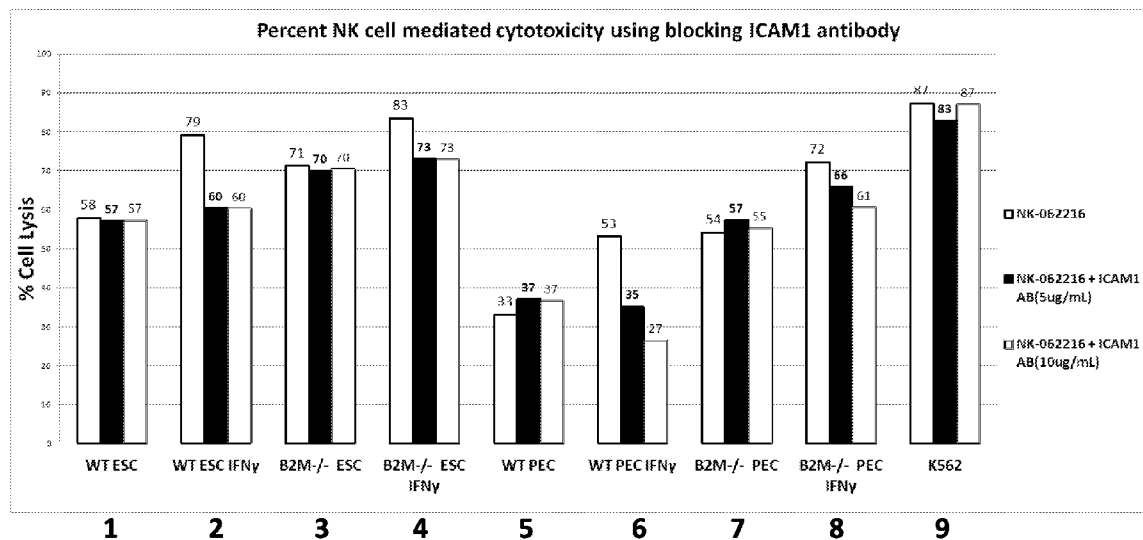


FIG. 15

(57) Abstract: Disclosed herein are universal donor stem cells and cells derived therefrom and related methods of their use and production. The universal donor stem cells disclosed herein are useful for overcoming allogeneic immune rejection in cell-based transplantation therapies. In certain embodiments, the universal donor cells disclosed herein are pancreatic endoderm cells that do not express one or more MHC-Class I cell-surface proteins and whose expression of at least one NK activating ligand is disrupted or inhibited.



EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *of inventorship (Rule 4.17(iv))*

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))*
- *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:

13 June 2019 (13.06.2019)

A. CLASSIFICATION OF SUBJECT MATTER

C12N 5/071(2010.01)i, C12N 15/85(2006.01)i, C07K 14/705(2006.01)i, A01K 67/027(2006.01)i, A61K 35/39(2006.01)i, A61L 27/36(2006.01)i

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)

C12N 5/071; A61K 35/00; A61K 35/23; A61K 35/28; A61K 39/00; C12N 15/85; C07K 14/705; A01K 67/027; A61K 35/39; A61L 27/36

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

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & Keywords: pancreatic lineage cell, donor, B2M, HLA-ABC, ICAM1, CD58, CD155, PVR, CEACAM1, CADM1, MICA, MICB

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 92-04033 A1 (THE GENERAL HOSPITAL CORPORATION) 19 March 1992 See abstract; claims 1-10, 18-20.	1-4
Y	WO 2016-183041 A2 (PRESIDENT AND FELLOWS OF HARVARD COLLEGE) 17 November 2016 See abstract; claims 1-7.	1-4
Y	KARABEKIAN, Z. et al., ' HLA Class I Depleted hESC as a Source of Hypoimmunogenic Cells for Tissue Engineering Applications ', Tissue Eng. Part A, 2015, Vol.21, No.19-20, pages 2559-2571 See abstract; pages 2560, 2562; figure 7.	1-4
Y	ZENG, Y. et al., ' INHIBITION OF TRANSPLANT REJECTION BY PRETREATMENT OF XENOGENEIC PANCREATIC ISLET CELLS WITH ANTI-ICAM-1 ANTIBODIES ', Transplantation, 27 September 1994, Vol.58, No.6, pages 681-689 See abstract; page 682-683; figure 1.	1-4
Y	US 2014-0134195 A1 (RUSSELL, DAVID W.) 15 May 2014 See abstract; claims 1-7.	1-4

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

07 May 2019 (07.05.2019)

Date of mailing of the international search report

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Name and mailing address of the ISA/KR

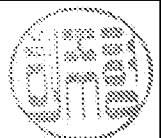
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2018/041648

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TEUNISSEN, M., ' Functional Role of Adhesion Molecules LFA-3 and ICAM-1 on Cultured Human Epidermal Langerhans Cells in Antigen-Specific T-Cell Activation ' . J. Invest. Dermatol., 1992, Vol.99, Pages 77S-79S See the whole document .	4

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.: 12,13
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 12, 13 pertain to a method for treatment of the human body by surgery, and thus relate to a subject matter which this International Searching Authority is not required, under PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv), to search.
2. Claims Nos.: 7,9,11
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:
Each of claims 7, 9, 11 refers to a claim which is not drafted in accordance with the third sentence of Rule 6.4(a).
3. Claims Nos.: 5,6,8,10,12,13
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 an additional fees, this Authority did not invite payment of any 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

Information on patent family members

International application No.

PCT/US2018/041648

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		JP 2018-174946 A	15/11/2018
		WO 2012-145384 A1	26/10/2012