



- (51) International Patent Classification:
A61K 35/12 (2015.01)
- (21) International Application Number:
PCT/IB2014/002164
- (22) International Filing Date:
13 June 2014 (13.06.2014)
- (25) Filing Language:
English
- (26) Publication Language:
English
- (30) Priority Data:
61/834,759 13 June 2013 (13.06.2013) US
61/834,767 13 June 2013 (13.06.2013) US
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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, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, 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.

- (84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, 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))*

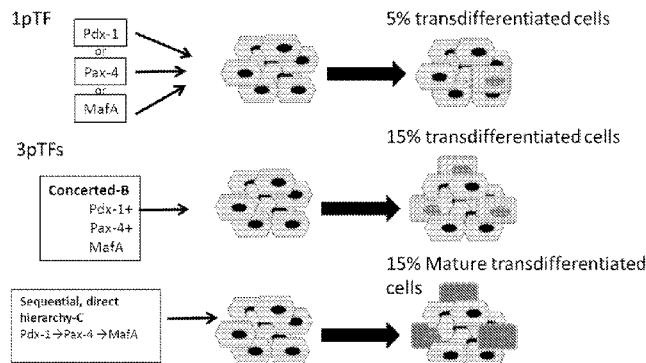
Published:

— *with international search report (Art. 21(3))*

- (88) Date of publication of the international search report:
11 September 2015

(54) Title: CELL POPULATIONS, METHODS OF TRANSDIFFERENTIATION AND METHODS OF USE THEREOF

Figure 9



(57) Abstract: The present invention provides methods for the sequential and temporally-regulated administration of pancreatic transcription factors to induce non-pancreatic cells to transdifferentiate and mature along the pancreatic β -cell lineage. The present invention also provides methods for identifying, isolating and enriching transdifferentiation predisposed cells and methods for treating a degenerative pancreatic disorder such as diabetes.

WO 2014/207578 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2014/002164

<p>A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 35/12 (2015.01) CPC - A61K 35/12 (2015.04) According to International Patent Classification (IPC) or to both national classification and IPC</p>																							
<p>B. FIELDS SEARCHED</p> <p>Minimum documentation searched (classification system followed by classification symbols) IPC(8) - A61K 35/12, 38/18; C12N 5/08, 5/12, 15/12, 15/63, 15/85 (2015.01) CPC - A61K 35/12, 38/18; C12N 15/12, 15/63, 15/85 (2015.04)</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched CPC - A61K 35/12, 38/18; C12N 5/12, 15/12, 15/63, 15/85 (2015.04) (keyword delimited) USPC - 435/370; 514/12</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Orbit, Google Patents, Google Scholar, Google, PubMed Search terms used: inducing, pancreatic beta cells, PDX1, Pax-4, neuroD1, MafA, Sox9, liver cell transdifferentiation, glutamine synthetase response element</p>																							
<p>C. DOCUMENTS CONSIDERED TO BE RELEVANT</p> <table border="1" style="width:100%; border-collapse: collapse;"> <thead> <tr> <th style="width:10%;">Category*</th> <th style="width:70%;">Citation of document, with indication, where appropriate, of the relevant passages</th> <th style="width:20%;">Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>WO 2010/022395 A2 (PRESIDENT AND FELLOWS OF HARVARD COLLEGE) 25 February 2010 (25.02.2010) entire document</td> <td>1-9, 15-22, 27, 28</td> </tr> <tr> <td>Y</td> <td></td> <td>37-40, 42, 57-61</td> </tr> <tr> <td>Y</td> <td>BHANDARI et al. "Cloning, nucleotide sequence, and potential regulatory elements of the glutamine synthetase gene from murine 3T3-L1 adipocytes" Proc. Natl. Acad. Sci. August 1988, Vol. 85, Pgs. 5789-5793. entire document</td> <td>29-31, 37-40, 42, 57-61</td> </tr> <tr> <td>Y</td> <td>US 2006/0122104 A1 (PRESNELL et al) 08 June 2006 (08.06.2006) entire document</td> <td>29-31</td> </tr> <tr> <td>A</td> <td>WO 2011/159726 A2 (THE SCRIPPS RESEARCH INSTITUTE) 22 December 2011 (22.12.2011) entire document</td> <td>1-9, 15-22, 27-31, 37-40, 42, 57-61</td> </tr> <tr> <td>A</td> <td>WO 2013/021389 A2 (YEDA RESEARCH AND DEVELOPMENT CO LTD) 14 February 2013 (14.02.2013) entire document</td> <td>1-9, 15-22, 27-31, 37-40, 42, 57-61</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	WO 2010/022395 A2 (PRESIDENT AND FELLOWS OF HARVARD COLLEGE) 25 February 2010 (25.02.2010) entire document	1-9, 15-22, 27, 28	Y		37-40, 42, 57-61	Y	BHANDARI et al. "Cloning, nucleotide sequence, and potential regulatory elements of the glutamine synthetase gene from murine 3T3-L1 adipocytes" Proc. Natl. Acad. Sci. August 1988, Vol. 85, Pgs. 5789-5793. entire document	29-31, 37-40, 42, 57-61	Y	US 2006/0122104 A1 (PRESNELL et al) 08 June 2006 (08.06.2006) entire document	29-31	A	WO 2011/159726 A2 (THE SCRIPPS RESEARCH INSTITUTE) 22 December 2011 (22.12.2011) entire document	1-9, 15-22, 27-31, 37-40, 42, 57-61	A	WO 2013/021389 A2 (YEDA RESEARCH AND DEVELOPMENT CO LTD) 14 February 2013 (14.02.2013) entire document	1-9, 15-22, 27-31, 37-40, 42, 57-61
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/></p>																							
<p>* Special categories of cited documents:</p> <table style="width:100%;"> <tr> <td style="width:50%;"> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </td> <td style="width:50%;"> <p>"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</p> <p>"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</p> <p>"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</p> <p>"&" document member of the same patent family</p> </td> </tr> </table>			<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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</p> <p>"&" document member of the same patent family</p>																			
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<p>Date of the actual completion of the international search</p> <p>21 April 2015</p>		<p>Date of mailing of the international search report</p> <p align="center">27 MAY 2015</p>																					
<p>Name and mailing address of the ISA/US</p> <p>Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300</p>		<p>Authorized officer:</p> <p align="center">Blaine R. Copenheaver</p> <p>PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774</p>																					

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2014/002164

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.: 10-14, 23-26, 32-36, 41, 43-56, 62, 63
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.