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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,
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SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
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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
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amendments (Rule 48.2(h))

— with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:
3 March 2016

(54) Title: METHOD FOR REPROGRAMMING CELLS

(57) Abstract: A method of generating an induced trophoblast stem cell (iTSC) from a cell is provided. Accordingly there is provided a method comprising expressing within the cell at least one exogenous transcription factor selected from the group consisting of Gata3, Eomes and Tfap2c, under conditions which allow generation of an iTSC from the cell, thereby generating the iTSC from the cell, with the proviso that the method does not consist of expressing within the cell Eomes, Cdx2, Elf5, cMyc and Klf4. Also provided are nucleic acid constructs, isolated cells and iTSCs.



INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2015/050715

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N5/073
ADD.

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

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

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

EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEN YING ET AL: "Roles of CDX2 and EOMES in human induced trophoblast progenitor cells", BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 431, no. 2, 8 January 2013 (2013-01-08), pages 197-202, XP028970948, ISSN: 0006-291X, DOI: 10.1016/J.BBRC.2012.12.135	3-24, 26-37, 42,43
Y	cited in the application the whole document ----- -/--	38,40,41



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

15 December 2015

Date of mailing of the international search report

21/01/2016

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2015/050715

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	P. KUCKENBERG ET AL: "The Transcription Factor TCFAP2C/AP-2 Cooperates with CDX2 To Maintain Trophoctoderm Formation", MOLECULAR AND CELLULAR BIOLOGY, vol. 30, no. 13, 1 July 2010 (2010-07-01), pages 3310-3320, XP055215974, ISSN: 0270-7306, DOI: 10.1128/MCB.01215-09 cited in the application	1,9,10, 16-23, 28-36, 39,42,43
Y	the whole document	38,40,41
X	KUBACZKA CAROLINE ET AL: "Derivation and maintenance of murine trophoblast stem cells under defined conditions.", STEM CELL REPORTS 11 FEB 2014, vol. 2, no. 2, 11 February 2014 (2014-02-11), pages 232-242, XP055216132, ISSN: 2213-6711 cited in the application	16-23, 28-37, 39,42,43
Y	the whole document	38,40,41
A	A. RALSTON ET AL: "Gata3 regulates trophoblast development downstream of Tead4 and in parallel to Cdx2", DEVELOPMENT, vol. 137, no. 3, 1 February 2010 (2010-02-01), pages 395-403, XP055216021, ISSN: 0950-1991, DOI: 10.1242/dev.038828 cited in the application	1-43
Y	the whole document	38,40,41
Y	JAMES J L ET AL: "Can we fix it? Evaluating the potential of placental stem cells for the treatment of pregnancy disorders", PLACENTA, vol. 35, no. 2, 2 February 2014 (2014-02-02), pages 77-84, XP028608339, ISSN: 0143-4004, DOI: 10.1016/J.PLACENTA.2013.12.010 cited in the application	38,40,41
	the whole document	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL2015/050715

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
- a. ☒ forming part of the international application as filed:
- ☒ in the form of an Annex C/ST.25 text file.
- ☐ on paper or in the form of an image file.
- b. ☐ furnished together with the international application under PCT Rule 13~~ter~~.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
- c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
- ☐ in the form of an Annex C/ST.25 text file (Rule 13~~ter~~.1(a)).
- ☐ on paper or in the form of an image file (Rule 13~~ter~~.1(b) and Administrative Instructions, Section 713).
2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2015/050715

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.:
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:

see additional 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 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.:

1-43

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-43

A method of generating an induced trophoblast stem cell (iTSC) from a cell comprising expressing within the cell at least one exogenous transcription factor selected from the group consisting of Gata3, Eomes and Tfap2c, a nucleic acid construct or system comprising at least one polynucleotide comprising a nucleic acid sequence encoding at least two transcription factors selected from the group consisting of Gata3, Eomes and Tfap2c, an isolated cell expressing at least two exogenous transcription factor selected from the group consisting of Gata3, Eomes and Tfap2c, an isolated iTSC, a cell culture comprising said iTSC, a pharmaceutical composition comprising said iTSC, an isolated placenta or blastocyst comprising said iTSC, the methods using said iTSCs

2. claim: 44

A method of discovering a gene which can generate an iTSC

3. claims: 45-48

A nucleic acid construct or system comprising a polynucleotide comprising three reporters and three regulatory elements under the control of, respectively a first early predictive marker of iTSC and/or iPSC, a second early predictive marker of an iTSC and/or and iPSC and a late predictive marker of an iTSC and/or iPSC, a cell comprising said construct, a transgenic animal comprising said construct and method using said cell or transgenic animal
