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- Published:**
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- (88) Date of publication of the international search report:
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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: METHOD FOR GENERATING INSULIN-SECRETING CELLS SUITABLE FOR TRANSPLANTATION

(57) Abstract: The invention relates to methods for generating insulin secreting cells from precursor stem cells or from adult pancreatic exocrine cells by exposing them to a nucleic acid molecule encoding neurogenin3 (ngn3) or NeuroD/ $\beta 2$. The methods of the invention are useful, for example, for generation of glucose sensitive insulin-secreting β -cells suitable for transplantation, as well as for in situ development of insulin-secreting cells in a patient in need thereof. Further, the method of the invention relates to methods for preventing premature differentiation of precursor stem cells into insulin-secreting β -cells. Still further, the invention relates to assay methods for identification of compounds that prevent or activate β -cell differentiation.



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK 02/00130

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/00 C12N5/12

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)

IPC 7 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 practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 59936 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 12 October 2000 (2000-10-12) page 3, line 1 - line 26 page 15, line 7 -page 18, line 32 page 21, line 10 - line 22 page 33, line 18 -page 36, line 19 abstract	1-6, 10-20, 25-30, 32-34, 36,37
A	--- -/--	7-9, 21-24, 31,35, 38-41

Further documents are listed in the continuation of box C.

Patent family members are listed in 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 document 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

22 January 2003

Date of mailing of the international search report

13. 02 2003

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/DK 02/00130

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 695 995 A (WEINTRAUB DECEASED HAROLD M ET AL) 9 December 1997 (1997-12-09) column 1, line 19 - line 59 column 5, line 11 - line 26 column 10, line 1 - line 9 column 10, line 32 - line 63	7-12, 21-28, 31,32, 35,36, 38-40
A		1-6, 13-20, 29,30, 33,34, 37,41
X	--- GRAPIN-BOTTON, A. ET AL: "KEY EVENTS OF PANCREAS FORMATION ARE TRIGGERED IN GUT ENDOTERM BY ECTOPIC EXPRESSION OF PANCREATIC REGULARORY GENES." GENES & DEVELOPMENT, vol. 15, 2001, pages 444-454, XP002902732 page 448, column 2, last paragraph -page 449, line 1 abstract	1-3, 13-16, 29,33
A		4-12, 17-28, 30-32, 34-41
A	--- JENSEN J ET AL: "INDEPENDENT DEVELOPMENT OF PANCREATIC ALPHA- AND BETA-CELLS FROM NEUROGENIN3-EXPRESSING PRECURSORS A ROLE FOR THE NOTCH PATHWAY IN REPRESSION OF PREMATURE DIFFERENTIATION" DIABETES, NEW YORK, NY, US, vol. 49, no. 2, February 2000 (2000-02), pages 163-176, XP001078766 ISSN: 0012-1797 page 175	10-12, 25-28, 32,36, 38-41
A	--- WO 99 35245 A (BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM) 15 July 1999 (1999-07-15) page 55 -page 58 page 62, line 15 - line 29 page 124, line 21 - line 29; table 2 -----	41

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 02/00130

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.:
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 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:

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 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. Claims: 1-6, 13-20, 29-30, 33-34 and 37:

Claims 1-6, 13-20, 29-30, 33-34 and 37 relating to the use of neurogenin 3 for the generation of insulin-secreting cells.

2. Claims: 7-12, 21-28, 31-32, 35-36 and 38-40

Claims 7-12, 21-28, 31-32, 35-36 and 38-40 relating to the use of NeuroD/B2 for the generation of insulin-secreting cells.

3. Claim : 41

Claim 41 relating to an isolated insulin-secreting cell characterised by the absence and presence of certain RNA transcripts non-related to neurogenin 3 or NeuroD/B2.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/DK 02/00130

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