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(54) Title: *IN VITRO* PLATFORM FOR SCREENING AGENTS INDUCING ISLET CELL NEOGENESIS

(57) Abstract: The present invention relates to an *in vitro* method for screening agents inducing islet cell neogenesis or duct-to-islet cell transdifferentiation, which comprises the steps of: a) expanding *in vitro* cells of a duct-like structure obtained by inducing cystic formation in cells in or associated with post-natal islets of Langerhans; b) treating said expanded cells of said duct-like structure with an agent screened; and c) determining potency of said agent of inducing islet cell differentiation of said duct-like structure in becoming insulin-producing cells.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/CA2004/000788

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 G01N33/50 C12N5/06 C12Q1/68		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N G01N		
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, BIOSIS, WPI Data, PAJ, EMBASE		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KORSGREN O ET AL: "IN VITRO SCREENING OF PUTATIVE COMPOUNDS INDUCING FETAL PROCINE PANCREATIC BETA-CELL DIFFERENTIATION: IMPLICATIONS FOR CELL TRANSPLANTATION IN INSULIN-DEPENDENT DIABETES MELLITUS" UPSALA JOURNAL OF MEDICAL SCIENCES, UPSALA MEDICAL SOCIETY, SE, vol. 98, no. 1, 1993, pages 39-52, XP000978995 ISSN: 0300-9734 see the whole document ----- -/--	1-4
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.		
<input checked="" type="checkbox"/> 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  <p style="text-align: center; font-size: 1.2em;">17 September 2004</p>	Date of mailing of the international search report  <p style="text-align: center; font-size: 1.2em;">11.02.05</p>	
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  <p style="text-align: center; font-size: 1.2em;">Grosskopf, R</p>	

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA2004/000788

C/(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BONNER-WEIR ET AL: "In vitro cultivation of human islets from expanded ductal tissue" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 97, no. 14, 5 July 2000 (2000-07-05), pages 7999-8004, XP002144480 ISSN: 0027-8424 see abstract -----	1-4
Y	OBERG-WELSH C ET AL: "Effects of certain growth factors on in vitro maturation of rat fetal *islet*-like structures" PANCREAS, RAVEN PRESS, NEW YORK, NY, US, vol. 12, no. 4, 1 May 1996 (1996-05-01), pages 334-339, XP002090017 ISSN: 0885-3177 see para. bridging page 334 and 335 -----	1-4
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A	US 2003/082155 A1 (ZULEWSKI HENRYK ET AL) 1 May 2003 (2003-05-01) -----	
A	US 5 587 309 A (BEATTIE GILLIAN M ET AL) 24 December 1996 (1996-12-24) see col. 4, lines 14 to 51 -----	
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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA2004/000788

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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA2004/000788

## Box 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 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 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.:

1-4

### 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: 1-4

An in vitro method for screening agents inducing islet cell neogenesis or duct-to-islet cell transdifferentiation, which comprises the steps of

- (a) expanding in vitro cells of a duct-like structure obtained by inducing cystic formation in cells in or associated with post-natal islets of Langerhans;
- (b) treating said expanded cells of said duct-like structure with an agent being screened; and
- (c) determining potency of said agent of inducing islet cell differentiation of said duct-like structure in becoming insulin-producing cells

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2. claims: 5-7

A kit comprising

- (a) a solid matrix for 3-D culture cells;
- (b) a culture medium supplemented

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3. claims: 8-12

An islet cell culture, which comprises insulin-producing islet cells in a suitable culture medium, wherein said islet cells are characterised and a method for evaluating biological effects of agents on said cells

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