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(54) Title: MULTI-STEP METHOD FOR THE DIFFERENTIATION OF INSULIN POSITIVE, GLUCOSE

(57) Abstract: The present invention provides improved methods of differentiating insulin+, glucose responsive islet-like structures from insulin- cells. The invention further provides methods for using insulin+, glucose responsive islet-like structures, as well as the insulin+, glucose responsive cells which comprise said islet-like clusters.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/23852

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 5/00, 08, 16
US CL : 435/370, 373, 375, 377

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)
U.S. : 435/370, 373, 375, 377

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)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	US 6,6448,045 B1 (LEVINE et al) 10 September 2002 (10.09.2002), abstract, columns 1 - 5	1-14, 48-53, 75,76
X.P	US 2003/0138951 A1 (YIN) 24 July 2003 (24.07.2003), abstract, pages 1, 4 - 6	1-14, 48-53, 75-76
A	US 6,242,666 B1 (SARVETNICK et al) 5 June 2001 (05.06.2001), entire document	1-81

☐ 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	"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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

10 March 2004 (10.03.2004)

Date of mailing of the international search report

04 MAY 2004

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/23852

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim 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. ☐ Claim 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:
Please See Continuation 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.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1 - 14, drawn to a method for culturing insulin negative cells.

Group II, claims 15 - 40, drawn to a method for culturing insulin negative cells.

Group III, claims 41 - 47, drawn to a method for differentiating insulin negative cells.

Group IV, claims 48 - 51 and 75 - 76, drawn to a composition of cells.

Group V, claims 52 - 53, drawn to a method for treating a patient.

Group VI, claims 54 - 68, drawn to a method for increasing numbers of cells.

Group VI, claims 69 - 74, drawn to a method for dissociating cells.

Group VII, claims 77 - 81, drawn to a method for treating diabetes.

The inventions listed as Groups I - IVV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The methods are all independent with separate and/or distinct functions, steps and/or effects. There is not a special technical feature which links the groups together, as composition of cells that are responsive to insulin are known in the art.

Continuation of B. FIELDS SEARCHED Item 3:

WEST, STN CAS

search terms: insulin, islet, diabetes, differentiation, culture, glucose