



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12Q 1/68, A61K 49/00, 31/70, 48/00, A01K 67/027, A61K 38/17, 35/39 // C07K 14/47	A3	(11) International Publication Number: WO 98/29565 (43) International Publication Date: 9 July 1998 (09.07.98)
(21) International Application Number: PCT/EP97/07320 (22) International Filing Date: 30 December 1997 (30.12.97) (30) Priority Data: 08/778,394 31 December 1996 (31.12.96) US (71) Applicant (for all designated States except US): MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG DER WISSENSCHAFTEN E.V. [DE/DE]; Berlin (DE). (72) Inventors; and (75) Inventors/Applicants (for US only): GRUSS, Peter [DE/DE]; Herzberger Landstrasse 1, D-37085 Göttingen (DE). ST-ONGE, Luc [CA/DE]; Rautenbreite 5, D-37077 Göttingen (DE). (74) Agent: VOSSIUS & PARTNER GBR; Postfach 86 07 67, D-81634 München (DE).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 17 September 1998 (17.09.98)
(54) Title: NOVEL METHOD FOR TESTING THE DIFFERENTIATION STATUS IN PANCREATIC CELLS OF A MAMMAL		
(57) Abstract The present invention relates to a novel method for testing the developmental status in pancreatic cells of a mammal. The present invention further relates to applications in the medical field that directly arise from the method of the invention. Additionally, the present invention relates to transgenic mammals comprising at least one inactivated Pax6 allele and optionally at least one inactivated Pax4 allele.		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon	KR	Republic of Korea	PL	Poland		
CN	China	KZ	Kazakstan	PT	Portugal		
CU	Cuba	LC	Saint Lucia	RO	Romania		
CZ	Czech Republic	LI	Liechtenstein	RU	Russian Federation		
DE	Germany	LK	Sri Lanka	SD	Sudan		
DK	Denmark	LR	Liberia	SE	Sweden		
EE	Estonia			SG	Singapore		

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 97/07320

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12Q1/68 A61K49/00 A61K31/70 A61K48/00 A01K67/027
A61K38/17 A61K35/39 //C07K14/47

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 6 C12Q A61K C07K 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 40872 A (ONTOGENY INC) 19 December 1996	1,11
A	see page 17, paragraph 5; claims 55-61 see page 27, paragraph 2; table 1 ---	27-31
A	DE 42 25 569 A (MAX-PLANCK GESELLSCHAFT ZUR FÖRDERUNG DER WISSENSCHAFT EV) 10 February 1994 see table 1 ---	1,11
A	MANSOURI A ET AL: "Pax genes in development" JOURNAL OF CELL SCIENCE, vol. 18, 1994, pages 35-42, XP002067720 see page 37, paragraph 3 - page 40 --- -/--	13,15, 20-22



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

17 June 1998

Date of mailing of the international search report

15. 07. 1998

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

Osborne, H

INTERNATIONAL SEARCH REPORT

Internat Application No

PCT/EP 97/07320

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	STOYKOVA A ET AL: "Roles of Pax-genes in developing and adult brain as suggested by expression patterns" THE JOURNAL OF NEUROSCIENCE, vol. 14, no. 303-94, pages 1395-1412, XP002067721 cited in the application see the whole document ---	1,11
A	TURQUE N ET AL: "Pax-QNR/Pax-6, a paired box- and homeobox-containing gene expressed in neurons, is also expressed in pancreatic endocrine cells" MOLECULAR ENDOCRINOLOGY, vol. 8, no. 7, 1994, pages 929-38, XP002067722 see the whole document ---	1,13,15
A	SOND D-L ET AL: "Two pax binding sites are required for early embryonic brain expression of engrailed - transgene" DEVELOPMENT, vol. 122, no. 2, 1996, pages 627-35, XP002067723 ---	
A	WALTER C ET AL: "Pax-6, a murine paired box, is expressed in the developing CNS" DEVELOPMENT, vol. 113, 1991, pages 1435-49, XP002067905 ---	
P,X	ST-ONGE L ET AL: "Pax6 is required for differentiation of glucagon-producing alpha cells in mouse pancreas" NATURE, vol. 387, May 1997, pages 406-9, XP002067724 see the whole document ---	1-31
P,X	SOSA-PINEDA B ET AL: "The Pax4 gene is essential for differentiation of insulin producing beta cells in the mammalian pancreas" NATURE, vol. 386, 27 March 1997, pages 399-402, XP002067725 see the whole document -----	1-31

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 97/07320

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:

Although claims 1-5 (partially); 6; 7-11 (partially); 12-19; 27-31 are directed to diagnostic/treatment methods practised on the human/animal body the search has been carried out and based on the alleged effects of the compound/composition.
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:

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 97/07320

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9640872 A	19-12-1996	AU 6264496 A EP 0832194 A	30-12-1996 01-04-1998
DE 4225569 A	10-02-1994	AT 162721 T CA 2141678 A DE 59308082 D WO 9403196 A EP 0655926 A ES 2114615 T JP 7509477 T US 5747250 A	15-02-1998 17-02-1994 05-03-1998 17-02-1994 07-06-1995 01-06-1998 19-10-1995 05-05-1998