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(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*

Published:

— *with international search report*

(88) Date of publication of the international search report:
15 July 2004

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 DIAGNOSING PANCREATIC CANCER

(57) Abstract: Objective methods for detecting and diagnosing pancreatic cancer (PNC) are described herein. In one embodiment, the diagnostic method involves determining the expression level of PNC-associated gene that discriminates between PNC cells and normal cells. The present invention further provides methods of screening for therapeutic agents useful in the treatment of pancreatic cancer, methods of treating pancreatic cancer and method of vaccinating a subject against pancreatic cancer.

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International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68

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 C12Q C12N C07K

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, EMBASE, Sequence Search, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GRESS TM ET AL: "A PANCREATIC CANCER-SPECIFIC EXPRESSION PROFILE" ONCOGENE, BASINGSTOKE, HANTS, GB, vol. 13, 1996, pages 1819-1830, XP002916550 ISSN: 0950-9232 the whole document Table 3, xs403	1-3, 6-11, 15-19, 21,29,30
X	WO 01/094629 A (AVALON PHARMACEUTICALS) 13 December 2001 (2001-12-13) abstract; claim 38 SEQ ID NO: 8131, 794-1573 bp	1-3, 6-11, 15-19, 21,29,30

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[X] Further documents are listed in the continuation of box C.

[X] 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	Date of mailing of the international search report
19 January 2004	27 04 2004

Name and mailing address of the ISA	Authorized officer
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	Aguilera, M

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Form PCT/ISA/210 (second sheet) (January 2004)

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/55350 A (HUMAN GENOME SCIENCES INC ;ROSEN CRAIG A (US); RUBEN STEVEN M (US)) 21 September 2000 (2000-09-21) abstract claim 1 SEQ ID NO: 594, 867-1646 bp -----	1-3, 6-11, 15-19, 21,29,30
X	WO 02/29103 A (ALVARES CHRISTOPHER ;HORNE DARCI (US); GENE LOGIC INC (US); PERES) 11 April 2002 (2002-04-11) abstract claim 1 SEQ ID NO: 3668, 794-1573 bp -----	1-3, 6-11, 15-19, 21,29,30
X	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1990, SILVERMAN J A ET AL: "EXPRESSION OF C-MYC C-RAF-1 AND C-KI-RAS IN AZASERINE-INDUCED PANCREATIC CARCINOMAS AND GROWING PANCREAS IN RATS" XP002267298 Database accession no. PREV199191074872 abstract & MOLECULAR CARCINOGENESIS, vol. 3, no. 6, 1990, pages 379-386, ISSN: 0899-1987 -----	1-3, 6-11, 15-19, 21,29,30
X	CRNOGORAC-JURCEVIC TATJANA ET AL: "Expression profiling of microdissected pancreatic adenocarcinomas" ONCOGENE, vol. 21, no. 29, 4 July 2002 (2002-07-04), pages 4587-4594, XP002267283 ISSN: 0950-9232	1
Y	the whole document -----	2,3, 6-11, 15-19, 21,29,30
X	CRNOGORAC-JURCEVIC TATJANA ET AL: "Gene expression profiles of pancreatic cancer and stromal desmoplasia" ONCOGENE, vol. 20, no. 50, 1 November 2001 (2001-11-01), pages 7437-7446, XP002267284 ISSN: 0950-9232	1
Y	the whole document -----	2,3, 6-11, 15-19, 21,29,30

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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 6 429 302 B1 (KENNEDY GIULIA) 6 August 2002 (2002-08-06)	1
Y	column 3, line 45 - column 4, line 50 column 6, line 50 - column 7, line 14 column 25, line 34 - column 35, line 36 table 1	2,3, 6-11, 15-19, 21,29,30

X	WO 99/67386 A (CHIRON CORP) 29 December 1999 (1999-12-29)	1
Y	example 1	2,3, 6-11, 15-19, 21,29,30

X	WO 98/53319 A (KINZLER KENNETH W ;VOGELSTEIN BERT (US); UNIV JOHNS HOPKINS (US)) 26 November 1998 (1998-11-26)	1
Y	table 4	2,3, 6-11, 15-19, 21,29,30

X	WO 99/31274 A (ABBOTT LAB) 24 June 1999 (1999-06-24)	1
Y	abstract	2,3, 6-11, 15-19, 21,29,30

X	LACOBUZIO-DONAHUE C A ET AL: "DISCOVERY OF NOVEL TUMOR MARKERS OF PANCREATIC CANCER USING GLOBAL GENE EXPRESSION TECHNOLOGY" AMERICAN JOURNAL OF PATHOLOGY, PHILADELPHIA, PA, US, vol. 160, no. 4, April 2002 (2002-04), pages 1239-1249, XP008003747 ISSN: 0002-9440	1
Y	the whole document	2,3, 6-11, 15-19, 21,29,30

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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HAN HAIYONG ET AL: "Identification of differentially expressed genes in pancreatic cancer cells using cDNA microarray" CANCER RESEARCH, vol. 62, no. 10, 15 May 2002 (2002-05-15), pages 2890-2896, XP002267297 ISSN: 0008-5472	1
Y	the whole document	2,3, 6-11, 15-19, 21,29,30

X	ZHANG L ET AL: "Gene expression profiles in normal and cancer cells" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 276, 23 May 1997 (1997-05-23), pages 1268-1272, XP002083785 ISSN: 0036-8075	1
Y	the whole document	2,3, 6-11, 15-19, 21,29,30

X	RYU BYUNGWOO ET AL: "Relationships and differentially expressed genes among pancreatic cancers examined by large-scale serial analysis of gene expression" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 62, no. 3, 1 February 2002 (2002-02-01), pages 819-826, XP002251739 ISSN: 0008-5472	1
Y	the whole document	2,3, 6-11, 15-19, 21,29,30

X	JORDAN M A ET AL: "MICROTUBULES AND ACTIN FILAMENTS: DYNAMIC TARGETS FOR CANCER CHEMOTHERAPY" CURRENT OPINION IN CELL BIOLOGY, CURRENT SCIENCE, LONDON, GB, vol. 10, no. 1, 1998, pages 123-130, XP000939151 ISSN: 0955-0674	15-18
	the whole document	

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INTERNATIONAL SEARCH REPORT

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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. [X] Claims Nos.: 12-14, 22-28
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [X] Claims Nos.: 20, 31
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:

see FURTHER INFORMATION sheet PCT/ISA/210

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. [X] 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.:

1-3, 6-11, 15-19, 21, 29, 30; all partially

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

Continuation of Box I.1

Claims Nos.: 12-14, 22-28

Claims 12-14 are directed to "expression profiles", which are considered mere presentations of information in the sense of Rule 39 (v), PCT. According to Article 17(2)(a)(i) PCT, claims 12-14 are not subject of this International Search Report.

Although claims 22-28 are directed to methods of treatment of the human body in the sense of Rule 39 (iv) PCT, the search has been carried out and based on the alleged effects of the compounds/compositions.

Continuation of Box I.2

Claims Nos.: 20, 31

Present claim 20 refers to a "detection reagent" defined by reference to a desirable characteristic or property, namely "a reagent which binds to two or more nucleic acid sequences selected from the group consisting of PNC 1-605 or polypeptides encoded thereby". The claims cover all products having this characteristic or property, whereas the application provides support within the meaning of PCT Article 6 and disclosure within the meaning of PCT Article 5 for only a very limited number of such products, i.e. nucleic acids complementary to said sequences and antibodies or antibody fragments directed to said polypeptides. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole scope of claims 20 is impossible.

Present claim 31 relates to a product defined by reference to a desirable characteristic or property, namely "a compound selected by the [screening] method...". The claims cover all products having this characteristic or property, whereas the application provides no support within the meaning of PCT Article 6 nor disclosure within the meaning of PCT Article 5 for any of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search of claim 31 impossible.

Independent of the above reasoning, claims 20 and 31 also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, and which relate to Invention 1 (see Invitation to pay additional fees), namely:

Methods of diagnosing pancreatic cancer comprising detecting altered level of expression of ACTB gene (PNC 1, GenBank AccNr: V00478). Methods of screening for compounds for treating pancreatic cancer comprising the use of nucleic acids, regulatory regions, or polypeptide products of said gene. Kits comprising nucleic acids, antibodies and antibody fragments binding the products of said gene. Arrays comprising nucleic acids of said gene. Compositions comprising antisense polynucleotides, siRNAs or antibodies directed against products of said gene.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ JP 03/11817

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-3, 6-11, 15-19, 21, 29, 30; all partially

Inventions 1-259:

Methods of diagnosing pancreatic cancer comprising detecting altered level of expression of ACTB gene (PNC 1, GenBank AccNr: V00478). Pancreatic cancer expression profiles comprising patterns of expression of said gene. Methods of screening for compounds for treating pancreatic cancer comprising the use of nucleic acids, regulatory regions, or polypeptide products of said gene. Kits comprising reagents which bind nucleic acids or polypeptide products of said gene. Arrays comprising nucleic acids of said gene. Methods of treating pancreatic cancer comprising administering to a patient compounds that modulate the expression or activity of said gene. Compositions comprising antisense polynucleotides, siRNAs or antibodies directed against products of said gene. Compositions comprising compounds selected by the above mentioned screening methods.
1-3, 6-11, 15-19, 21, 29, 30; all partially

[idem for each one of the genes listed in Table 3]

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2. claims: 1, 4-11, 15-19, 21, 29, 30; all partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Inventions 260-605:

Methods of diagnosing pancreatic cancer comprising detecting altered level of expression of ACAA2 gene (PNC 260, GenBank AccNr: D16294). Pancreatic cancer expression profiles comprising patterns of expression of said gene. Methods of screening for compounds for treating pancreatic cancer comprising the use of nucleic acids, regulatory regions, or polypeptide products of said gene. Kits comprising reagents which bind nucleic acids or polypeptide products of said gene. Arrays comprising nucleic acids of said gene. Methods of treating pancreatic cancer comprising administering to a patient compounds that modulate the expression or activity of said gene. Compositions comprising antisense polynucleotides, siRNAs or antibodies directed against products of said gene. Compositions comprising compounds selected by the above mentioned screening methods.
1-3, 6-11, 15-19, 21, 29, 30; all partially

[idem for each one of the genes listed in Table 4]

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3. claims: 32-46, all partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Inventions 606-849:

Methods of screening for compounds for treating malignant pancreatic cancer comprising the use of nucleic acids, regulatory regions, or polypeptide products of HADHA gene (PNC 606, GenBank AccNr: D16480). Methods of treating malignant pancreatic cancer comprising administering to a patient compounds that modulate the expression or activity of said gene. Compositions comprising antisense polynucleotides, siRNAs or antibodies directed against products of said gene. Compositions comprising compounds selected by the above mentioned screening methods.
32-46, all partially

[idem for each one of the genes listed in Tables 6 and 7]

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4. claims: 47-67, all partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Inventions 850-933:

Methods of screening for compounds for preventing recurrence of pancreatic cancer comprising the use of nucleic acids, regulatory regions, or polypeptide products of ARGBP2 (PNC 850, GenBank AccNr: AF049884). Methods of treating recurrence of pancreatic cancer comprising administering to a patient compounds that modulate the expression or activity of said gene. Compositions comprising antisense polynucleotides, siRNAs or antibodies directed against products of said gene. Compositions comprising compounds selected by the above mentioned screening methods. Methods of predicting recurrence of pancreatic cancer comprising the detection of altered expression levels of said gene. Pancreatic cancer expression profiles comprising patterns of expression of said gene. Kits comprising reagents which bind nucleic acids or polypeptide products of said gene. Arrays comprising nucleic acids of said gene.
47-67, all partially

[idem for each one of the genes listed in Table 8]

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/JP 03/11817

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