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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Declaration under Rule 4.17:
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:
— *with international search report*
— *with sequence listing part of description published separately in electronic form and available upon request from the International Bureau*

(88) Date of publication of the international search report:
25 October 2007

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 AND TREATING RENAL CELL CARCINOMA

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

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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. 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)
C12Q

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, EMBASE, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/024603 A (UNIV TEXAS [US]) 17 March 2005 (2005-03-17) page 8, last paragraph; claim 1; table 3 -----	1-3, 6-13, 15-21, 29,30, 38-54
X	WO 2005/030250 A2 (GANYMED PHARMACEUTICALS AG [DE]; TUERECI OEZLEM [DE]; SAHIN UGUR [DE];) 7 April 2005 (2005-04-07) claim 1; figures 16,17; example 8; sequence 21 ----- -/--	1-3, 6-13, 15-21, 29,30, 38-54

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

[X] 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

"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
24 November 2006	20 -03- 2007

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	MOLINA GALAN, E

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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	WO 03/101400 A2 (AVALON PHARMACEUTICALS INC [US]; SHEA MARTIN [US]; EBNER REINHARD [US]) 11 December 2003 (2003-12-11) claims; sequences 1, 3-5, 6, 7, 14, 16, 18-20, 27, 29-33	1-3, 6-13, 15-21, 29,30, 38-54
X	WO 2004/000997 A (CURAGEN CORP [US]; ANDERSON DAVID W [US]; BOLDOG FERENC L [US]; BURGES) 31 December 2003 (2003-12-31) page 311 - page 320; sequences 5, 17, 21	1-3, 6-13, 15-21, 29,30, 38-54
X	WO 02/074237 A2 (CORIXA CORP [US]; ALGATE PAUL A [US]; MANNION JANE [US]; GAIGER ALEXAN) 26 September 2002 (2002-09-26) claims; example 6; sequences 1852-1855	1-3, 6-13, 15-21, 29,30, 38-54
X	WO 2004/074506 A2 (MERGEN LTD [US]; HU QIANJIN [US]; PENG ALLAN [US]; LIU BIN [CN]; LOVE) 2 September 2004 (2004-09-02) paragraph [0089]; claims; sequence 53	1-3, 6-13, 15-21, 29,30, 38-54
X	WO 2005/019475 A2 (ONCOTHERAPY SCIENCE INC [JP]; UNIV TOKYO [JP]; NAKAMURA YUSUKE [JP]; K) 3 March 2005 (2005-03-03) the whole document	1,3,6-11
X	TOGASHI AKIRA ET AL: "Hypoxia-inducible protein 2 (HIG2), a novel diagnostic marker for renal cell carcinoma and potential target for molecular therapy" CANCER RESEARCH, vol. 65, no. 11, June 2005 (2005-06), pages 4817-4826, XP002408861 ISSN: 0008-5472 the whole document	1,3,6-11
A	TAMAGNONE LUCA ET AL: "To move or not to move? Semaphorin signalling in cell migration." EMBO REPORTS. APR 2004, vol. 5, no. 4, April 2004 (2004-04), pages 356-361, XP002408863 ISSN: 1469-221X cited in the application	

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INTERNATIONAL SEARCH REPORT

International application No
PCT/JP2006/314946

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LORKOWSKI STEFAN ET AL: "Genomic sequence and structure of the human ABCG1 (ABC8) gene" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 280, no. 1, 12 January 2001 (2001-01-12), pages 121-131, XP002408864 ISSN: 0006-291X	
A	WO 99/32619 A (CARNEGIE INST OF WASHINGTON [US]; UNIV MASSACHUSETTS [US]; FIRE ANDREW) 1 July 1999 (1999-07-01) cited in the application	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/JP2006/314946

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005024603 A	17-03-2005	NONE	
WO 2005030250 A2	07-04-2005	AU 2004275500 A1	07-04-2005
		CA 2539837 A1	07-04-2005
		DE 10344799 A1	14-04-2005
		EP 1664113 A2	07-06-2006
WO 03101400 A2	11-12-2003	AU 2003239969 A1	19-12-2003
		CA 2488284 A1	11-12-2003
		EP 1575492 A2	21-09-2005
		US 2005220798 A1	06-10-2005
WO 2004000997 A	31-12-2003	AU 2003272200 A1	06-01-2004
		EP 1572948 A2	14-09-2005
WO 02074237 A2	26-09-2002	NONE	
WO 2004074506 A2	02-09-2004	NONE	
WO 2005019475 A2	03-03-2005	EP 1660677 A2	31-05-2006
WO 9932619 A	01-07-1999	AU 743798 B2	07-02-2002
		AU 1938099 A	12-07-1999
		CA 2311999 A1	01-07-1999
		EP 1042462 A1	11-10-2000
		JP 2002516062 T	04-06-2002
		US 6506559 B1	14-01-2003
		US 2003056235 A1	20-03-2003
		US 2003051263 A1	13-03-2003
		US 2003055020 A1	20-03-2003

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2006/314946

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. [X] Claims Nos.: 22-28, 31-37
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy (22-28, 32-37)

2. [X] Claims Nos.: 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 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. [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, 6-13, 15-21, 29, 30, 38-54 (partially)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

Continuation of Box II.1

Claims Nos.: 22-28, 31-37

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy (22-28, 32-37)

Continuation of Box II.2

Claims Nos.: 31

The present claim 31 encompasses compounds defined only by their desired function, contrary to the requirements of clarity of Article 6 PCT, because the result-to-be-achieved type of definition does not allow the scope of the claim to be ascertained. The fact that any compound could be screened does not overcome this objection, as the skilled person would not have knowledge beforehand as to whether it would fall within the scope claimed. Undue experimentation would be required to screen compounds randomly. This non-compliance with the substantive provisions is to such an extent, that no search could be performed for claim 31.

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.

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

1. claims: 1-3, 6-13, 15-21, 29, 30, 38-54 (partially)

Invention 1:
Method for diagnosing (a predisposition to) RCC by comparative determination of the expression level of the gene ABCG1 (RCC 1 in table 4), expression profiles comprising ABCG1 and at least another gene of table 4, methods for screening for compounds involving ABCG1 or its products, kits arrays and compositions containing them or molecules binding to them.

1.1. claims: 1-3, 6-13, 15-21, 29, 30, 38-54 (partially)

Invention 81:
Method for diagnosing (a predisposition to) RCC by comparative determination of the expression level of the gene SEMA5B (RCC 81 in table 4), expression profiles comprising it and at least another gene of table 4, methods for screening for compounds involving said gene or its products, kits arrays and compositions containing them or molecules binding to them, double stranded molecules inhibiting its expression and vectors containing the same.

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2. claims: 1-3, 6-13, 15-21, 29, 30

Inventions 2-80, 82-125, 127-172 and 174-251:
Method for diagnosing (a predisposition to) RCC by comparative determination of the expression level of the gene defined by its respective assignment (RCC) number in table 4, expression profiles comprising it and at least another gene of table 4, methods for screening for compounds involving said gene or its products, kits, arrays and compositions containing them or molecules binding to them.

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3. claims: 1-3, 6-13, 15-21, 29, 30, 38-54 (partially)

Invention 126:
Method for diagnosing (a predisposition to) RCC by comparative determination of the expression level of the gene PFKFB4 (RCC 126 in table 4), expression profiles comprising it and at least another gene of table 4, methods for screening for compounds involving said gene or its products, kits arrays and compositions containing them or molecules binding to them, double stranded molecules inhibiting its expression and vectors containing the same.

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4. claims: 1-3, 6-13, 15-21, 29, 30, 38-54 (partially)

Invention 173:
Method for diagnosing (a predisposition to) RCC by comparative determination of the expression level of the gene FBXL16 (RCC 173 in table 4), expression profiles comprising it and at least another gene of table 4, methods for screening for compounds involving said gene or its products, kits arrays and compositions containing them or molecules binding to them, double stranded molecules inhibiting its expression and vectors containing the same.

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5. claims: 1, 4-12, 14-21

Inventions 252-972:
Method for diagnosing (a predisposition to) RCC by comparative determination of the expression level of the gene defined by its respective assignment (RCC) number in table 4, expression profiles comprising it and at least another gene of table 4, methods for screening for compounds involving said gene or its products, kits, arrays and compositions containing them or molecules binding to them.
