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EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID,
IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK,
LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW,
MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT,
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(54) Title: METHODS AND TOOLS FOR PROGNOSIS OF CANCER IN HER2+ PATIENTS

(57) Abstract: The present invention is related to a gene or protein set comprising or consisting of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, and possibly 40, 45, 50, 55, 60, 65 genes or proteins or the entire set selected from the table 12 and/or the table 13, antibodies or hypervariable portion thereof directed against the proteins encoded by these genes.



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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2008/061827

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE GENBANK [Online] NCBI; 3 June 2007 (2007-06-03), XP002517884 retrieved from NCBI Database accession no. NM_018351.3 the whole document ----- -/--	1-10



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

"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

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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2008/061827

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	YOU FANGLEI ET AL: "Validating predictive profiles in HER2 positive early stage breast cancer using RNA microarray." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 46, April 2005 (2005-04), pages 442-443, XP002517883 & 96TH ANNUAL MEETING OF THE AMERICAN-ASSOCIATION-FOR-CANCER-RESEARCH; ANAHEIM, CA, USA; APRIL 16 -20, 2005 ISSN: 0197-016X the whole document	1-10,12
A	FAN CHENG ET AL: "Concordance among gene-expression-based predictors for breast cancer" NEW ENGLAND JOURNAL OF MEDICINE, vol. 355, no. 6, August 2006 (2006-08), pages 560-569, XP009076969 ISSN: 0028-4793 the whole document	1-10,12
A	HELLAND A ET AL: "Molecular subtypes among HER2 positive tumors defined by expression profiling." BREAST CANCER RESEARCH AND TREATMENT, vol. 88, no. Suppl. 1, 2004, page S215, XP008103143 & 27TH ANNUAL CHARLES A COLTMAN SAN ANTONIO BREAST CANCER SYMPOSIUM; SAN ANTONIO, TX, USA; DECEMBER 08 -11, 2004 ISSN: 0167-6806 the whole document	1-10,12
A	TOVEY S M ET AL: "Low expression of HER2 protein in breast cancer is biologically significant" JOURNAL OF PATHOLOGY, vol. 210, no. 3, November 2006 (2006-11), pages 358-362, XP008103153 ISSN: 0022-3417 the whole document	1-10,12
A	YU KUN ET AL: "A molecular signature of the Nottingham prognostic index in breast cancer" CANCER RESEARCH, vol. 64, no. 9, 1 May 2004 (2004-05-01), pages 2962-2968, XP002319405 ISSN: 0008-5472 the whole document	1-10,12

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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2008/061827

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KUN YU ET AL: "Classifying the estrogen receptor status of breast cancers by expression profiles reveals a poor prognosis subpopulation exhibiting high expression of the ERBB2 receptor." HUMAN MOLECULAR GENETICS 15 DEC 2003, vol. 12, no. 24, 15 December 2003 (2003-12-15), pages 3245-3258, XP002319404 ISSN: 0964-6906 the whole document -----	1-10,12
A	WO 2005/021788 A (IPSOGEN [FR]; INST NAT SANTE RECH MED [FR]; INST PAOLI CALMETTES [FR];) 10 March 2005 (2005-03-10) the whole document -----	1-10,12
A	WO 2005/033699 A (NCC TECHNOLOGY VENTURES PTE LT [SG]; YU KUN [SG]; TAN PATRICK [SG]; FO) 14 April 2005 (2005-04-14) the whole document -----	1-10,12
A	WO 2006/119593 A (UNIV BRUXELLES [BE]; SOTIRIOU CHRISTOS [BE]; DELORENZI MAURO [CH]; PIC) 16 November 2006 (2006-11-16) the whole document -----	1-10,12

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2008/061827

Box No. 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 No. 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 allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers 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.:

see annex

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ 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: 1-10,12 (partially)

Invention Number 1:

FGD6 (the first gene listed in table 12 on page 72), antibodies or hypervariable portions thereof directed against the proteins encoded by this gene, diagnostic kit or device comprising said gene / protein, and a method using said gene for a prognosis of cancer in a mammal subject;

2. claims: 1-10,12 (partially)

Idem for Invention Number 2 - 45

starting with PLAC9 (Invention Number 2 / second gene listed in table 12 on page 72) and ending with COL10A1 (Invention Number 45, the last gene listed in Table 12 on page 72);

3. claims: 1-12 (partially)

Invention Number 46:

PLAU (the first gene listed in table 13 on page 72), antibodies or hypervariable portions thereof directed against the proteins encoded by this gene, diagnostic kit or device comprising said gene / protein, and a method for a prognosis of cancer in a mammal subject;

4. claims: 1-12 (partially)

IDEM for Invention Numbers 47 - 114

starting with BMP1 (Invention Number 47) and ending with JPH2 (Invention Number 114, for list of genes c.f. table 13 on page 72);

5. claims: 11,12 (partially)

Invention Number 115:

ACP5 (listed as first entry in Table 11 on page 71), and the use of said gene / protein in a method for prognosis of cancer in a mammal subject;

6. claims: 11,12 (partially)

Idem for Invention Number 116 - 213

starting with ADAMDEC1 (Invention Number 116) and ending with ZC3HAV1 (Invention Number 213); (for the gene listing c.f. table 11 on page 71 of the description);

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2008/061827

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2005021788	A	10-03-2005	AT 403755 T	15-08-2008
			EP 1668152 A1	14-06-2006
			EP 1980629 A2	15-10-2008
			ES 2311852 T3	16-02-2009
			US 2009092983 A1	09-04-2009
			US 2005089899 A1	28-04-2005
WO 2005033699	A	14-04-2005	CN 101194166 A	04-06-2008
			EP 1668357 A2	14-06-2006
			JP 2007508812 T	12-04-2007
			US 2007059706 A1	15-03-2007
WO 2006119593	A	16-11-2006	AU 2006246241 A1	16-11-2006
			CA 2608643 A1	16-11-2006
			JP 2008539737 T	20-11-2008
			KR 20080064725 A	09-07-2008