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61/477,529 20 April 2011 (20.04.2011) US
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- (81) **Designated States (unless otherwise indicated, for every kind of national protection available):** AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, 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, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
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- Published:**
— with international search report (Art. 21(3))
- (88) **Date of publication of the international search report:**
1 August 2013

(54) **Title:** SPECIFIC COPY NUMBER ABERRATIONS AS PREDICTORS OF BREAST CANCER

(57) **Abstract:** Methods and compositions for the prognosis and classification of cancer, especially breast cancer, are provided. For example, in certain aspects methods for cancer prognosis using copy number analysis of selected biomarkers are described. In further aspects, copy number information may be used to predict metastasis risk and help treatment decision-making.



A. CLASSIFICATION OF SUBJECT MATTER*G01N 33/574(2006.01)i, C12Q 1/68(2006.01)i, C12N 15/11(2006.01)i*

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)

G01N 33/574; A61K 31/7088; C12Q 1/68

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal) & Keywords: breast, cancer, tumor, carcinoma, adenoma, neoplasm, copy number imbalance, cni, 22q11, CCT8L2, CECR8, XKR3, psiTPTE22, GAB4, CECR6, CECR7, IL17RA, CECR1, CECR4, CECR5, ATP6V1E1, CECR2, SLC25A18, RCT.21.13 RIT

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TARA L NAYLOR et al. High resolution genomic analysis of sporadic breast cancer using array-based comparative genomic hybridization. Breast Cancer Research. 2005, Vol. 7, No. 6, pp. 1186-1198 See the whole document, especially abstract, pp. 1, 2, 7, 10, table 1	1-10, 15
Y	LUKE HUGHES-DAVIES et al. EMSY Links the BRCA2 Pathway to Sporadic Breast and Ovarian Cancer. Cell. 2003, Vol. 115, No. 26, pp. 523-535	1-4, 6-10, 15
A	See the whole document, especially abstract	5
Y	YINFEI TAN et al. Upregulation of DLX5 Promotes Ovarian Cancer Cell Proliferation by Enhancing IRS-2-AKT Signaling. Molecular and Cellular Pathobiology. Cancer Research. 2010, Vol. 70, pp. 9197-9206	1, 2, 4, 6-10, 15
A	See the whole document, especially abstract, p. 9198	3, 5
Y	JA SEONG BAE et al. Genomic alterations of primary tumor and blood in invasive ductal carcinoma of breast. World Journal of Surgical Oncology. 2010, Vol. 8, p. 32(1-11)	3
A	See the whole document, especially abstract, pp. 1, 2, 5, tables 1, 3-5	1, 2, 4-10, 15



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 application or patent 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 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

29 April 2013 (29.04.2013)

Date of mailing of the international search report

30 April 2013 (30.04.2013)

Name and mailing address of the ISA/KR

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/034421

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	PETER O' CONNELL. Genetic and cytogenetic analyses of breast cancer yield different perspectives of a complex disease. Breast Cancer Research and Treatment. 2003, Vol. 78, pp. 347-357	3
A	See the whole document, especially abstract, table 1	1,2,4-10,15
Y	MADS THOMASSEN et al. Gene expression meta-analysis identifies chromosomal regions and candidate genes involved in breast cancer metastasis. Breast Cancer Research and Treatment. 2009, Vol. 113, pp. 239-249	5
A	See the whole document, especially abstract, pp. 8-10	1-4,6-10,15
A	AKIRA HIRANO et al. Allelic Losses of Loci at 3p25.1, 8p22, 13q12, 17p13.3, and 22q13 Correlate with Postoperative Recurrence in Breast Cancer. Clinical Cancer Research. 2001, Vol. 7, pp. 876-882 See the whole document	1-10,15
A	US 2009-0203051 A1 (GRAY JOE W. et al.) 13 August 2009 See the whole document	1-10,15

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/034421**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.: 11-14, 18, 20-23
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 11-14, 18, 20-22 pertain to diagnostic methods, claim 23 pertains to a method for treatment of the human body by surgery or therapy, and thus claims 11-14, 18, 20- 23 relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.
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 extra 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.:
1-10, 15(partial)
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 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.

(Continuation of Box No. III)

This application involves 63 inventions in total, based on the breast cancer biomarkers presented in claims 1-5, 11, 16-20.

The single general inventive concept linking 63 inventions together is assaying for a copy number imbalance(CNI) of one or more biomarkers in a breast cancer sample.

This common concept is, however, described in the following document, therefore, does not represent any contribution over the prior art.

- US 2009-0203051 A1 (GRAY JOE W. et al.) 19 March 2008

Hence the 63 inventions do not relate to a single general inventive concept under PCT Rule 13.1 because the above mentioned common concept fails to make a contribution over the prior art within the meaning of PCT Rule 13.2.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2012/034421Patent document
cited in search reportPublication
datePatent family
member(s)Publication
date

US 2009-0203051 A1

13.08.2009

WO 2007-143752 A2

13.12.2007

WO 2007-143752 A3

25.09.2008