(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 January 2009 (15.01.2009)

PCT

(10) International Publication Number
WO 2009/009752 A3

(51) International Patent Classification:
C12Q 1/68 (2006.01) *G06F 19/00* (2006.01)

(21) International Application Number:
PCT/US2008/069834

(22) International Filing Date: 11 July 2008 (11.07.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/949,172 11 July 2007 (11.07.2007) US
60/951,110 20 July 2007 (20.07.2007) 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, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),

[Continued on next page]

(54) Title: GENETIC MODELS FOR STRATIFICATION OF CANCER RISK

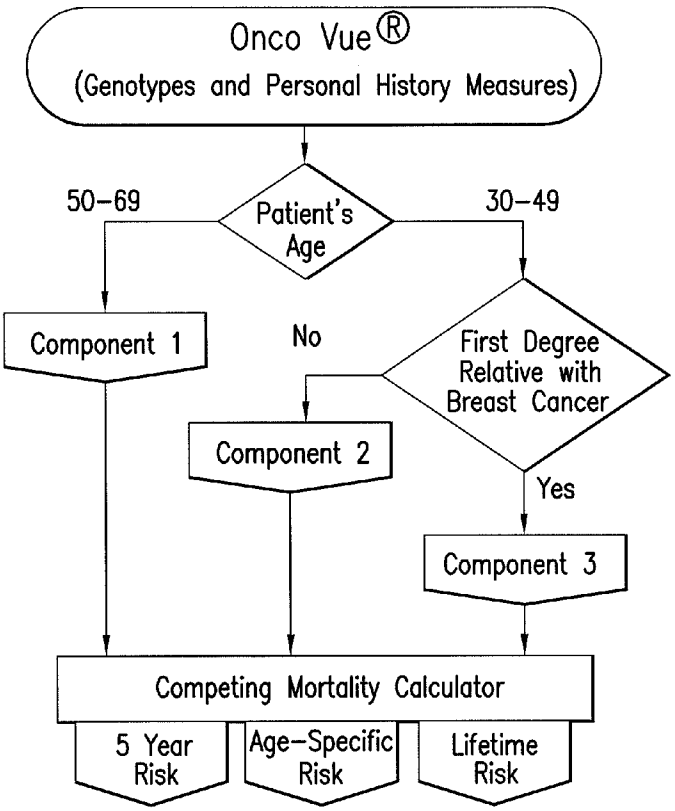

FIG. 1

(57) Abstract: The present invention provides new methods for the assessment of cancer risk in the general population. These methods utilize particular alleles of in multiple selected genes to identify individuals with increased or decreased risk of breast cancer. In addition, personal history measures such as age and family history are used to further refine the analysis. Using such methods, it is possible to reallocate healthcare costs in cancer screening to patient subpopulations at increased cancer risk. It also permits identification of candidates for cancer prophylactic treatment.

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European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

(88) Date of publication of the international search report:
26 February 2009

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/069834

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12Q1/68 G06F19/00

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SINILNIKOVA OLGA M ET AL: "Haplotype-based analysis of common variation in the acetyl-CoA carboxyiase alpha gene and breast cancer risk: A case-control study nested within the European prospective investigation into cancer and nutrition" CANCER EPIDEMIOLOGY, BIOMARKERS AND PREVENTION, PHILADELPHIA, PA, vol. 16, no. 3, 1 March 2007 (2007-03-01), pages 409-415, XP002460681 ISSN: 1055-9965 the whole document	1,5-9, 13-16, 19,20
Y		2-4

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[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
19 September 2008	11/12/2008

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, Fax: (+31-70) 340-3016	Pinta, Violaine

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/069834

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 03/025141 A (INTERGENETICS INC [US]; OKLAHOMA MED RES FOUND [US]; RALPH DAVID [US];) 27 March 2003 (2003-03-27) cited in the application the whole document claims 19,20	2-4,17, 18
Y	ASTON C.E. ET AL: "Oligogenic combinations associated with breast cancer risk in women under 53 years of age" HUMAN GENETICS, SPRINGER, BERLIN, DE, vol. 116, no. 3, 1 February 2005 (2005-02-01), pages 208-221, XP019346055 ISSN: 1432-1203 cited in the application the whole document	2-4,17, 18
Y	ASTON C ET AL: "Multigene combinations to estimate individual risk for breast cancer" AMERICAN JOURNAL OF HUMAN GENETICS, AMERICAN SOCIETY OF HUMAN GENETICS, CHICAGO, IL, US, vol. 73, no. 5, 1 November 2003 (2003-11-01), page 248, XP009092956 ISSN: 0002-9297 abstract	2-4,17, 18
Y	RALPH DAVID ET AL: "Predicting breast cancer risk with combinations of genetic polymorphisms" PROCEEDINGS OF THE ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, NEW YORK, NY, vol. 43, 1 March 2002 (2002-03-01), page 854, XP001537680 ISSN: 0197-016X abstract	2-4,17, 18
A	RALPH D A ET AL: "Genetics-based risk assesment models for sporadic breast cancer" BREAST CANCER RESEARCH AND TREATMENT, SPRINGER, NEW YORK, NY, vol. 88, no. Suppl.1, 1 January 2004 (2004-01-01), pages S162-S163, XP009092958 ISSN: 0167-6806 abstract	

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/069834

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ASTON CHRISTOPHER E ET AL: "Functional common genetic polymorohisms interact to predict breast cancer risk" PROCEEDINGS OF THE ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, NEW YORK, NY, vol. 45, 1 March 2004 (2004-03-01), page 1037, XP001537676 ISSN: 0197-016X abstract	
A	SINILNIKOVA OLGA M ET AL: "Acetyl-CoA carboxylase alpha gene and breast cancer susceptibility" CARCINOGENESIS, IRL PRESS, LONDON, GB, vol. 25, no. 12, 1 December 2004 (2004-12-01), pages 2417-2424, XP002460680 ISSN: 0143-3334 the whole document figure 1; table III	
A	WO 02/100896 A (CENTRE NAT RECH SCIENT [FR]; UNIV CLAUDE BERNARD LYON [FR]; DALLA VENE) 19 December 2002 (2002-12-19) the whole document	
P,A	WO 2007/150044 A (INTERGENETICS INC [US]; OKLAHOMA MED RES FOUND [US]; RALPH DAVID [US];) 27 December 2007 (2007-12-27) the whole document	
P,A	JUPE E R ET AL: "The OncoVue (R) model for predicting breast cancer risk." BREAST CANCER RESEARCH AND TREATMENT, vol. 106, no. Suppl. 1, December 2007 (2007-12), page S179, XP002496510 & 30TH ANNUAL SAN ANTONIO BREAST CANCER SYMPOSIUM; SAN ANTONIO, TX, USA; DECEMBER 13 -16, 2007 ISSN: 0167-6806 abstract	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/069834

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.:

1 - 16, 19 - 20 (partially), 17 - 18 (completely)

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:

Invention 1: claims 1-16, 19-20 (partially), 17-18 (completely)

Method for assessing a risk of developing breast cancer, method for determining the need for routine diagnostic testing for breast cancer and method for determining the need for prophylactic anti-breast cancer therapy in which the allelic profiles of more than one SNP selected from the group of SNPs of claim 1 are determined and wherein said more than one SNP comprise at least one of ACACA (IVS17) T>C, ACACA (5'UTR) T>C or ACACA (PIII) T>G, and microarray according to claims 17-18.

Inventions 2-14: claims 1-16, 19-20 (partially), 17-18 (completely)

Method for assessing a risk of developing breast cancer, method for determining the need for routine diagnostic testing for breast cancer and method for determining the need for prophylactic anti-breast cancer therapy in which the allelic profiles of more than one SNP selected from the group of SNPs of claim 1 are determined and wherein said more than one SNP comprise:
- for invention 2: COMT (rs4680) A>G,
- for invention 3: CYP19 (rs10046) T>C,
- for invention 4: CYPA1 (rs4646903) T>C,
- for invention 5: CYP1B1 (rs1800440) A>G,
- for invention 6: EPHX (rs1051740) T>C,
- for invention 7: TNFSF6 (rs763110) C>T,
- for invention 8: IGF2 (rs2000993) G>A,
- for invention 9: INS (rs3842752) C>T,
- for invention 10: KLK10 (rs3745535) G>T,
- for invention 11: MSH6 (rs3136229) G>A,
- for invention 12: RAD51L3 (rs4796033) G>A,
- for invention 13: XPC (rs2228000) C>T,
- for invention 14: XRCC2 (rs3218536) G>A,

and microarray according to claims 17-18.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/069834

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03025141 A	27-03-2003	CA 2460721 A1	27-03-2003
		EP 1436423 A2	14-07-2004
		JP 2005532780 T	04-11-2005
WO 02100896 A	19-12-2002	AU 2002327870 A1	23-12-2002
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