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[Continued on next page]

(54) Title: PERSONALIZED TUMOR BIOMARKERS

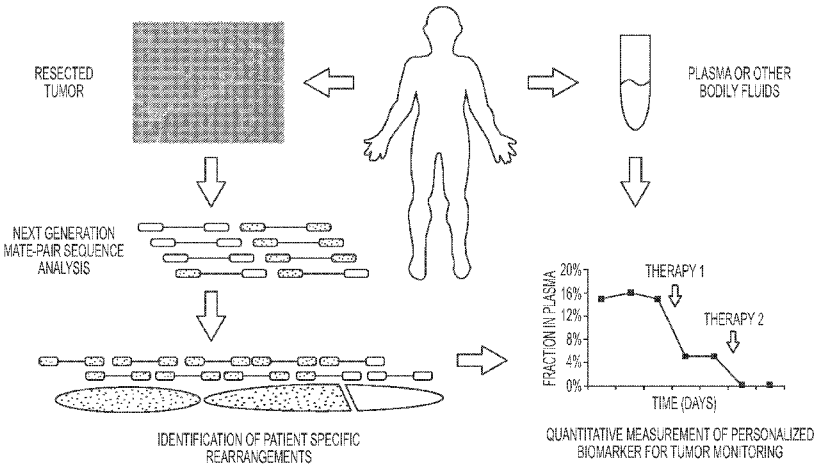


FIG. 1

(57) Abstract: Clinical management of human cancer is dependent on the accurate monitoring of residual and recurrent tumors. We have developed a method, called personalized analysis of rearranged ends (PARE), which can identify translocations in solid tumors. Analysis of four colorectal and two breast cancers revealed an average of nine rearranged sequences (range 4 to 15) per tumor. Polymerase chain reaction with primers spanning the breakpoints were able to detect mutant DNA molecules present at levels lower than 0.001% and readily identified mutated circulating DNA in patient plasma samples. This approach provides an exquisitely sensitive and broadly applicable approach for the development of personalized biomarkers to enhance the clinical management of cancer patients.

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Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

— *with sequence listing part of description (Rule 5.2(a))*

(88) Date of publication of the international search report:
9 February 2012

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2011/025152

A. CLASSIFICATION OF SUBJECT MATTER

C12Q 1/68(2006.01)i, C12N 15/11(2006.01)i, C40B 40/06(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)
C12Q 1/68; G06G 7/60; G01N 33/574

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: personalized tumor marker, cancer, breakpoint, somatic DNA, rearrangement, kit

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2010-014920 A1 (THE JOHNS HOPKINS UNIVERSITY et al.) 04 February 2010 See the whole document	38-44
A	US 2009-0275057 A1 (STEVEN P. LINKE et al.) 05 November 2009 See the whole document	38-44
A	US 2009-0061422 A1 (STEVEN P. LINKE et al.) 05 March 2009 See the whole document	38-44
A	MITCH DOWSETT et al. Emerging Biomarkers and New Understanding of Traditional Markers in Personalized Therapy for Breast Cancer. Clin Cancer Res. 2008, Vol. 14, No. 24, pp. 8019-8026 See the whole document	38-44
A	MICHAEL J. DUFFY et al. A Personalized Approach to Cancer Treatment: How Biomarkers Can Help. Clinical Chemistry. 2008, Vol. 54, No. 11, pp. 1770-1779 See the whole document	38-44

☐ 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	Date of mailing of the international search report
13 DECEMBER 2011 (13.12.2011)	**14 DECEMBER 2011 (14.12.2011)**
Name and mailing address of the ISA/KR Korean Intellectual Property Office Government Complex-Daejeon, 189 Cheongsa-ro, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer CHOI Jun-Ho Telephone No. 82-42-481-5569

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2011/025152

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.: 1-37
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 1-37 pertain to methods for treatment of the human body by surgery or therapy, as well as diagnostic methods, and thus 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:

1. ☐ As all required addtional 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. ☐ 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2011/025152

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2010-014920 A1	04.02.2010	CA 2732623 A1	04.02.2010
		EP 2315849 A1	04.05.2011
		US 2010-0041048 A1	18.02.2010
US 2009-0275057 A1	05.11.2009	None	
US 2009-0061422 A1	05.03.2009	None	