



(51) International Patent Classification:

C12Q 1/68 (2006.01) *C12N 15/11* (2006.01)
C12N 13/00 (2006.01)

(21) International Application Number:

PCT/US2012/038077

(22) International Filing Date:

16 May 2012 (16.05.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/488,631 20 May 2011 (20.05.2011) US

(71) Applicant (for all designated States except US): **FRED HUTCHINSON CANCER RESEARCH CENTER** [US/US]; 1100 Fairview Avenue North, Seattle, WA 98109 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **STIREWALT, Derek, L.** [US/US]; 739 West Etruria Street, Seattle, WA 98119 (US). **POGOSOVA-AGADJANYAN, Era** [US/US]; 15930 131st Place SE, Renton, WA 98058 (US).

RADICH, Jerald, P. [US/US]; 26327 Southeast 33rd Street, Sammamish, WA 98075 (US). **FAN, Wenhong** [CN/US]; 12206 Southeast 47th Street, Bellevue, WA 98006 (US). **HELTON, Bret** [US/US]; 7547 19th Avenue NW, Seattle, WA 98117 (US).

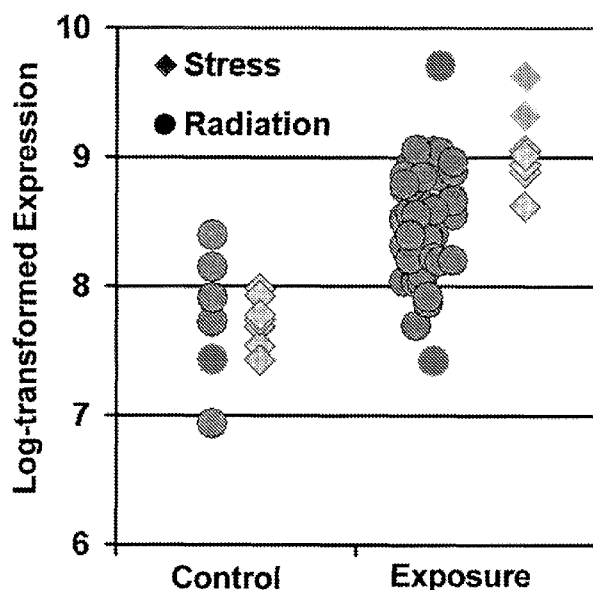
(74) Agent: **POOR, Brian, W.**; Christensen O'Connor Johnson Kindness PLLC, 1420 Fifth Avenue, Suite 2800, Seattle, WA 98101 (US).

(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.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,

[Continued on next page]

(54) Title: METHODS AND COMPOSITIONS FOR MEASURING RADIATION EXPOSURE IN A SUBJECT

FIGURE 1A

(57) Abstract: The present disclosure provides a method for assessing exposure to ionizing radiation comprising the steps of (a) measuring the RNA expression level of certain biomarker genes in a biological sample; (b) correcting the RNA expression level of the measured biomarker in step (a) to a reference standard or threshold value, and (c) comparing the RNA expression level of the biomarker measured in step (a) and corrected in accordance with step (b) to the corrected expression of a calibration sample or threshold value, wherein a difference in expression level between the biomarker in the biological sample and the calibration sample indicates that the source from which the biological sample is obtained was exposed to ionizing radiation. The method can further comprise classifying the source of the biological sample as either exposed or not exposed to ionizing radiation. Kits for assessing exposure to ionizing radiation are also described.



UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

- *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))*

Published:

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

(88) Date of publication of the international search report:

7 March 2013

A. CLASSIFICATION OF SUBJECT MATTER*C12Q 1/68(2006.01)i, C12N 13/00(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)

C12Q 1/68; G01N 33/50

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)

PubMed: biomarker, ionizing radiation

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	POGOSOVA-AGADJANYAN, E. L. et al. Identification of radiation-induced expression changes in nonimmortalized human T cells. Radiation Research. February 2011, Vol. 175, No. 2, pages 172-84. Epub 2010 Nov 17.	22-24, 27, 29-31
Y	See materials and methods; discussion.	25, 26, 28
X	WO 2008/030278 A2 (FRED HUTCHINSON CANCER RESEARCH CENTER) 13 March 2008.	22-24, 27, 29-31
Y	See abstract; claims 1, 9.	25, 26, 28
Y	LEE, J. H. et al. Identification of a novel ionizing radiation-induced nuclease, AEN, and its functional characterization in apoptosis. Biochemical and Biophysical Research Communications. 11 November 2005, Vol. 337, No. 1, pages 39-47.	25, 28
A	See Abstract.	22-24, 26, 27, 29-31



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

28 DECEMBER 2012 (28.12.2012)

Date of mailing of the international search report

02 JANUARY 2013 (02.01.2013)

Name and mailing address of the ISA/KR

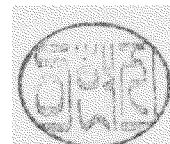
Korean Intellectual Property Office
189 Cheongsu-ro, Seo-gu, Daejeon Metropolitan
City, 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

Lee Hyun Ji

Telephone No. 82-42-481-8745



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/038077

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GROSOVSKY, A. J. et al. Base substitutions, frameshifts, and small deletions constitute ionizing radiation-induced point mutations in mammalian cells. Proceedings of the National Academy of Sciences. January 1988, Vol. 85, No. 1, pages 185-8.	26,28
A	See abstract.	22-25,27,29-31
A	WO 2011/006214 A1 (PETER MACCALLUM CANCER INSTITUTE) 20 January 2011. See claims 7-11.	22-31

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/038077**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.: 1-21
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 1-21 pertain to methods for treatment of human body by 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 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. ☐ 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/US2012/038077Patent document
cited in search reportPublication
datePatent family
member(s)Publication
date

WO 2008-030278 A2

13.03.2008

WO 2008-030278 A3

12.06.2008

WO 2011-006214 A1

20.01.2011

None