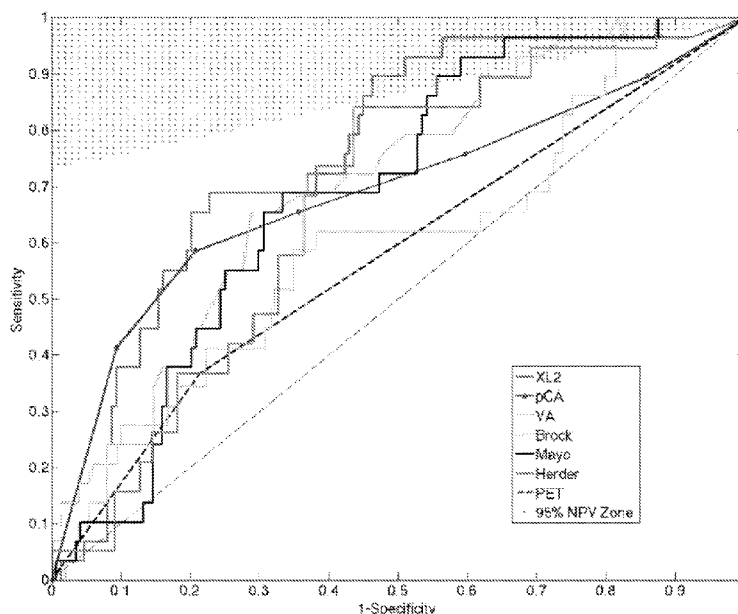




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- (74) **Agent: YU, Chun, L. et al.;** Cooley LLP, 1299 Pennsylvania Avenue, NW, Suite 700, Washington, DC 20004 (US).
- (81) **Designated States** (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, 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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(54) **Title:** COMPOSITIONS, METHODS AND KITS FOR DIAGNOSIS OF LUNG CANCER

FIGURE 34



(57) **Abstract:** Methods are provided for identifying biomarker proteins that exhibit differential expression in subjects with a first lung condition versus healthy subjects or subjects with a second lung condition. Also provided are compositions comprising these biomarker proteins and methods of using these biomarker proteins or panels thereof to diagnose, classify, and monitor various lung conditions. The methods and compositions provided herein may be used to diagnose or classify a subject as having lung cancer or a non-cancerous condition, and to distinguish between different types of cancer (e.g., malignant versus benign, SCLC versus NSCLC).



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, KM, ML, MR, NE, SN, TD, TG).

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))*
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14 December 2017 (14.12.2017)

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2017/031250

A. CLASSIFICATION OF SUBJECT MATTER
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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

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 practicable, search terms used)

EPO-Internal, 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	US 2015/219666 A1 (LI XIAO-JUN [US] ET AL) 6 August 2015 (2015-08-06) ([0130]); claims 2,5,8, 12, 14, 15,23 -----	1-13, 24-30
X	WO 2015/042454 A1 (INTEGRATED DIAGNOSTICS INC [US]) 26 March 2015 (2015-03-26) claims 1, 2, 18 -----	1-13, 24-30
X	WO 2013/096845 A2 (INTEGRATED DIAGNOSTICS INC [US]; KEARNEY PAUL EDWARD [CA]; FANG KENNET) 27 June 2013 (2013-06-27) [00105] [00104] [00107] [00101] -----	1-13, 24-30
	-/--	

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 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

23 August 2017

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07/11/2017

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2017/031250

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	<p>Kearney Paul, Li Xiao-Jun, Porter Alex, Springmeyer Steven, Mazzone Peter: "An Integrated Risk Predictor for Pulmonary Nodules",</p> <p>17 December 2016 (2016-12-17), pages 1-17, XP002773107, bioRxiv</p> <p>Retrieved from the Internet: URL:http://www.biorxiv.org/content/biorxiv/early/2016/12/17/094920.full.pdf [retrieved on 2017-08-22] the whole document</p> <p align="center">-----</p>	<p>1-13, 24-30</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/031250

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 all searchable 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 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.:

2, 13, 25(completely); 1, 3-12, 24, 26-30(partially)

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: 2, 13, 25(completely); 1, 3-12, 24, 26-30(partially)

method of determining the likelihood that a pulmonary nodule is or is not lung cancer comprising contacting a blood sample of a subject with a proteolytic enzyme to produce enzyme fragments from a panel of proteins present in the blood sample comprising C163A and LG3BP, performing mass spectrometry and the analysis of the result

- 2-36. claims: 14-23(completely); 1, 3-12, 24, 26-30(partially)

method of determining the likelihood that a pulmonary nodule is or is not lung cancer comprising contacting a blood sample of a subject with a proteolytic enzyme to produce enzyme fragments from a panel of proteins present in the blood sample comprising 2 of the claimed protein combinations, performing mass spectrometry and the analysis of the result

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2017/031250

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		WO 2013096845 A2	27-06-2013
