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(71) Applicant (*for all designated States except US*):
ROSETTA GENOMICS LTD. [IL/IL]; 10 Plaut Street,
76706 Rehovot (IL).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **ROSENWALD, Shai** [IL/IL]; Haogen 3, 74208 Nes Ziona (IL). **BEN-JAMIN, Hila** [IL/IL]; Hazamir 10, 55507 Kiryat Uno (IL). **ROSENFELD, Nitzan** [IL/IL]; 10 Alkalai Street, 76304 Rehovot (IL).

(74) Agent: **SHOSHANI KUPITZ, Tzipora**; Rosetta genomics Ltd., 10 Plaut Street, 76706 Rehovot (IL).

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25 June 2009

(54) Title: DIAGNOSIS AND PROGNOSIS OF SPECIFIC CANCERS BY MEANS OF DIFFERENTIAL DETECTION OF MICRO-RNAS/MIRNAS

(57) Abstract: The present invention provides nucleic acid sequences that are used for identification and diagnosis of specific cancers. The nucleic acid sequences can also be used for prognosis evaluation of a subject based on the expression profile of a biological sample.



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INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2008/001428

A. CLASSIFICATION OF SUBJECT MATTER

INV. C12Q1/68

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, WPI Data, BIOSIS, EMBASE, MEDLINE, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2005/078139 A (UNIV JEFFERSON [US]; CROCE CARLO M [US]; LIU CHANG-GONG [US]; CALIN GE) 25 August 2005 (2005-08-25) paragraph [0046]; claims 1-9,32,33,36-93 -----	1-37
Y	WO 2005/118806 A (AMBION INC [US]; BROWN DAVID; CONRAD RICK; DEVROE ERIC; GOLDRICK MARIA) 15 December 2005 (2005-12-15) pages 13-15 - pages 62-67; claims 50-59 -----	1-37
Y	DATABASE Geneseq [Online] 21 September 2006 (2006-09-21), "Human probe for miRNA #194." XP002513329 retrieved from EBI accession no. GSN:AEJ21990 Database accession no. AEJ21990 the whole document -/--	1-37

☒ 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 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

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- *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

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Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Botz, Jürgen

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PCT/IL2008/001428

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 2006/069584 A (EXIQON AS [DK]; PLASTERK RONALD [NL]; WIENHOLDS ERNO [NL]; KLOOSTERMAN) 6 July 2006 (2006-07-06) ----- DATABASE EMBL [Online] 7 March 2006 (2006-03-07), "Sequence 220 from Patent EP1627925." XP002513324 retrieved from EBI accession no. EMBL:CS265478 Database accession no. CS265478 the whole document & US 2005/260648 A1 (HUFFEL CHRISTOPHE V [BE] ET AL) 24 November 2005 (2005-11-24) the whole document	1-37
Y	DATABASE EMBL [Online] 18 May 2007 (2007-05-18), "Sequence 1352 from Patent EP1777301." XP002513325 retrieved from EBI accession no. EMBL:CS548322 Database accession no. CS548322 the whole document	1-37
Y	DATABASE Geneseq [Online] 5 May 2005 (2005-05-05), "Human microRNA (miRNA) mir-192." XP002513330 retrieved from EBI accession no. GSN:ADX03136 Database accession no. ADX03136 the whole document	1-37
A	CALIN G A ET AL: "A MICRORNA SIGNATURE ASSOCIATED WITH PROGNOSIS AND PROGRESSION IN CHRONIC LYMPHOCYTIC LEUKEMIA" NEW ENGLAND JOURNAL OF MEDICINE, MASSACHUSETTS MEDICAL SOCIETY, BOSTON, MA, US, vol. 353, no. 17, 27 October 2005 (2005-10-27), pages 1793-1801, XP009058593 ISSN: 1533-4406 the whole document	1-37
A	MCMANUS MICHAEL T: "MicroRNAs and cancer" SEMINARS IN CANCER BIOLOGY, SAUNDERS SCIENTIFIC PUBLICATIONS, PHILADELPHIA, PA, US, vol. 13, no. 4, 1 August 2003 (2003-08-01), pages 253-258, XP002358494 ISSN: 1044-579X the whole document	1-37

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2008/001428

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 - 37 (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: 1-37 (partially)

Invention Number 1:

A method of diagnosing mesothelioma comprising the use of SEQ. ID. NO: 2, a method to distinguish between mesothelioma and other cancers, the method comprising the use of SEQ. ID. NO:2, as well as a kit for distinguishing between mesothelioma and other cancers, said kit comprising SEQ. ID. NO:2.

2. claims: 1-37 (partially)

IDEM for

Inventions 2 - 42, comprising SEQ. ID. NOs 10, 11, 24, 41, 1, 3-9, 12-23, 25, 26 and 58 - 72;

3. claims: 38 - 58 (partially)

Invention Number 43:

A method to distinguish between squamous non small cell lung carcinoma (NSCLC) and non-squamous NSCLC, the method comprising the use of SEQ. ID. NO: 8, a kit for distinguishing between squamous NSCLC and non-squamous NSCLC said kit comprising SEQ. ID. NO:8

4. claims: 38 - 58 (partially)

IDEM for invention number 44 - 57 comprising the SEQ. ID. NOs 21, 25, 41, 44 - 50, 52, 54, 55 and 57;

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IL2008/001428

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005078139 A	25-08-2005	CA 2554818 A1 EP 1713938 A2	25-08-2005 25-10-2006
WO 2005118806 A	15-12-2005	AU 2005250432 A1 CA 2572450 A1 EP 1771563 A2 JP 2008500837 T	15-12-2005 15-12-2005 11-04-2007 17-01-2008
WO 2006069584 A	06-07-2006	EP 1838870 A2 EP 1959012 A2	03-10-2007 20-08-2008
US 2005260648 A1	24-11-2005	EP 1627925 A1 JP 2005296014 A US 2006134639 A1	22-02-2006 27-10-2005 22-06-2006