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60/983,944 31 October 2007 (31.10.2007) US
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(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.
INTERNATIONAL SEARCH REPORT

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

<table>
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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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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
  * "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
3 February 2009

Date of mailing of the international search report
14/05/2009

Name and mailing address of the ISA/
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV RUISWIK
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Authorized officer
Botz, Oürgen
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<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
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<td>A</td>
<td>MCMANUS MICHAEL T: &quot;MicroRNAs and cancer&quot; 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</td>
<td>1-37</td>
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</table>
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).

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.:

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.
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;
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<tr>
<td>WO 2005078139 A</td>
<td>25-08-2005</td>
<td>CA 2554818 A1</td>
<td>25-08-2005</td>
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<tr>
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<td></td>
<td>EP 1713938 A2</td>
<td>25-10-2006</td>
</tr>
<tr>
<td>WO 2005118806 A</td>
<td>15-12-2005</td>
<td>AU 2005250432 A1</td>
<td>15-12-2005</td>
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<tr>
<td></td>
<td></td>
<td>CA 2572450 A1</td>
<td>15-12-2005</td>
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<td></td>
<td>JP 2008500837 T</td>
<td>17-01-2008</td>
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<td></td>
<td>EP 1959012 A2</td>
<td>20-08-2008</td>
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<td>JP 2005296014 A</td>
<td>27-10-2005</td>
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<tr>
<td></td>
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<td>US 2006134639 A</td>
<td>22-06-2006</td>
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