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8 March 2007

For two-letter codes and other abbreviations, refer to the “Guidance Notes on Codes and Abbreviations” appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title:  
COMPOSITION AND METHODS FOR CANCER DIAGNOSIS UTILIZING THE MIR 17-92 CLUSTER

(57) Abstract:  
The application relates to methods and compositions for the diagnosis, prevention, and treatment of tumors and cancers in mammals, for example, humans, utilizing the mir 17-92 cluster. The application further relates to screening methods to identify compounds and reagents useful in cancer diagnosis, prevention, and therapy.
A. CLASSIFICATION OF SUBJECT MATTER

INV. C12Q1/68  C12N15/11

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, MEDLINE, EMBASE, BIOSIS, CHEM ABS Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<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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<tbody>
<tr>
<td>X</td>
<td>MOURELATOS Z. ET AL.,: &quot;miRNPs: a novel class of ribonucleoproteins containing numerous microsnars&quot; GENES &amp; DEVELOPMENT, vol. 16, 2002, pages 720-728, XP002408176 see whole doc. esp. Tab.1</td>
<td>40-45</td>
</tr>
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<td>X</td>
<td>LAGOS-QUINTANA M. ET AL.,: &quot;identification of novel genes coding for small expressed rnas&quot; SCIENCE, vol. 294, 26 October 2001 (2001-10-26), pages 853-858, XP002408177 see whole doc. esp. Tab.2</td>
<td>40-45</td>
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</table>

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.
  * F* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

21 November 2006

12/12/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk
Tel: (+31-70) 340-2040, Tx: 31 851 epo nl, Fax: (+31-70) 340-3016

Form PCT/ISA/210 (second sheet) (April 2008)

Authorized officer

Mueller, Frank
<table>
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<th>Category</th>
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<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>X</td>
<td>OTA AKINOBU ET AL: &quot;Identification and characterization of a novel gene, CI3orf25, as a target for 13q31-q32 amplification in malignant lymphoma&quot; CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 64, no. 9, 1 May 2004 (2004-05-01), pages 3087-3095, XP002339401 ISSN: 0008-5472 cited in the application see whole doc. esp. Fig.7</td>
<td>1-45</td>
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<tr>
<td>X</td>
<td>W0 03/029459 A2 (MAX PLANCK GES ZUR [DE]; TUSCHL THOMAS [DE]; LAGOS-QUINTANA MARIANA [D]) 10 April 2003 (2003-04-10) see whole doc. esp. Fig.7, Fig 2b, claims and pages 14, 1.13-22 and p.41</td>
<td>1-45</td>
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<tr>
<td>X</td>
<td>EIS P. S. ET AL.,: &quot;accumulation of miR-155 and BIC RNA in human B cell lymphomas&quot; PNAS, vol. 102, no. 10, 8 March 2005 (2005-03-08), pages 3627-3632, XP002408178 the whole document</td>
<td>1-45</td>
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</table>
Continuation of Box II.1

Although claims 26-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Claims Nos.: 26-45 (part)

The present claims 26,40,45 relate to an extremely large number of possible compounds/methods. Support and disclosure in the sense of Article 6 and 5 PCT is to be found however for only a very small proportion of the compounds/methods claimed, see namely seq ids 11 and 12, and claims 38,39,42,43. The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of claims 26,40,45 (PCT Guidelines 9.19 and 9.23).

The search of claims 26,40,45 was restricted to those claimed compounds/methods which appear to be supported and a generalisation of their structural formulae, namely seq ids 11 and 12.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.
Box 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. X Claims Nos.: 26-45 (part)
   because they relate to subject matter not required to be searched by this Authority, namely:
   Although claims 26-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. X Claims Nos.: 26-45 (part)
   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:
   see FURTHER INFORMATION sheet PCT/ISA/210

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 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.
☐ No protest accompanied the payment of additional search fees.
<table>
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<tr>
<th>Patent document cited in search report</th>
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<td>US 2005059005 A1</td>
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<tr>
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