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(74) Agent: LANDRUM, Charles, P.; Fulbright & Jaworski
L.L.P., 600 Congress Avenue, Suite 2400, Austin, TX
78701 (US).

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(71) Applicant (for all designated States except US): ASUR-
AGEN, INC. [US/US]; 2150 Woodward St., Suite 100,
Austin, TX 78744 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BADER, Andreas,
G. [US/US]; 2150 Woodward St., Suite 100, Austin, TX
78744 (US). BYROM, Mike [US/US]; 2150 Woodward
St., Suite 100, Austin, TX 78744 (US). JOHNSON,
Charles, D. [US/US]; 2150 Woodward St., Suite 100,
Austin, TX 78744 (US). BROWN, David [US/US]; 2150
Woodward St., Suite 100, Austin, TX 78744 (US).

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(54) Title: MIR-200 REGULATED GENES AND PATHWAYS AS TARGETS FOR THERAPEUTIC INTERVENTION

(57) Abstract: The present invention concerns methods and compositions for identifying genes or genetic pathways modulated by miR-200, using miR-200 to modulate a gene or gene pathway, using this profile in assessing the condition of a patient and/or treating the patient with an appropriate miRNA.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/078894

A. CLASSIFICATION OF SUBJECT MATTER
INV. 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)
C12N C07K

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 , BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MENG ET AL: "Involvement of Human Micro-RNA in Growth and Response to Chemotherapy in Human Choi angiocarcinoma Cell Lines" GASTROENTEROLOGY, ELSEVIER, PHILADELPHIA, PA, US, vol. 130, no. 7, June 2006 (2006-06), pages 2113-2129, XP005475314 ISSN: 0016-5085 cited in the application the whole document</p> <p style="text-align: center;">----- -/-</p>	<p>1-24, 45, 46</p>

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents *

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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.</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search 1 February 2008	Date of mailing of the international search report 14/04/2008
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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, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <p style="text-align: center;">Herrmann, Kl aus</p>
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/078894

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MICHAEL M Z ET AL: "REDUCED ACCUMULATION OF SPECIFIC MICRORNAS IN COLORECTAL NEOPLASIA" MOLECULAR CANCER RESEARCH, XX, XX, vol. 1, no. 12, October 2003 (2003-10), pages 882-891, XP009051992 ISSN: 1541-7786 table 2</p> <p>-----</p>	1-24,45, 46
A	<p>WO 2005/013901 A (ISIS PHARMACEUTICALS INC [US]; ESAU CHRISTINE [US]; LOLLO BRIDGET [US]) 17 February 2005 (2005-02-17) the whole document</p> <p>-----</p>	1-24,45, 46
P, X	<p>WO 2006/128245 A (SOUTHERN ADELAIDE HEALTH SERVI [AU]; MICHAEL MICHAEL ZENON [AU]) 7 December 2006 (2006-12-07) claims 1,9,60-70</p> <p>-----</p>	1-24,45, 46

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2 007/ 078894

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material

a sequence listing

table(s) related to the sequence listing

b. format of material

on paper

in electronic form

c. time of filing/furnishing

J contained in the international application as filed

J filed together with the international application in electronic form

furnished subsequently to this Authority for the purpose of search

2. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

FURTHER INFORMATION CONTINUED FROM PCT/ASA/ 210

Continuation of Box II.1

Although claims 1-40 and 45 are directed to a diagnostic method practised on the human/animal body or 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.1

sss

Continuation of Box II.2

Claims Nos.: 25-44 and partially claims 1-24, 45 and 46

No. search report was established for the subject-matter of claims 25-40 for the following reasons: Claims 25-40 have not been searched and examined because a pathological condition or disease related to a gene designated "ABCC1" and modulated by a miRNA is neither disclosed nor supported within the terms of Art. 5 and 6 PCT, respectively (Art. 17(2)(a)(ii) PCT). Furthermore, the cellular pathway or physiologic pathway is not defined in any way (Art. 6 PCT).

Claims 1-24, 45 and 46 fail to comply with the requirements of Art. 6 PCT (clarity) to such an extent that a meaningful search could not be carried out over the whole scope of the claims (Art. 17(2)(a)(ii) PCT). "miR-200" is not a clear definition. Numerous sequences fall under said term (see e.g. p. 5, l. 29-p. 12, l. 28 of the application). Furthermore, according to p. 6, l. 6-10 of the application the "miR-200" sequence can be as short as 5 nucleotides and those 5 nucleotides must only be at least 75% identical to one of the sequences defined in SEQ ID NO: 1-108. Thus, the search has been restricted to the vague term "miR-200" since no core sequence could be identified which all "miR-200" sequences share.

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

overcome.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/078894

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:
see FURTHER INFORMATION sheet PCT/ISA/210
- 2. Claims Nos.: 25-44 and partially claims 1-24, 45 and 46
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 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 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.:
1-40, 45, 46 all 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:

Invention 1: claims 1-40, 45 and 46 (all partially)

A method of modulating gene expression in a cell comprising administering an amount of an isolated nucleic acid comprising a "miR-200" in an amount sufficient to modulate the expression of the sequences given under accession number NM_004996, NM_019862, NM_019898, NM_019899, NM_019900 or NM_019901 ("ABCC1") (line 1 of Table 1), and subject-matter relating thereto.

Inventions 2-2105: claims 1-40, 45 and 46 (all partially)

Idem as subject 1 but limited to each of the sequences given under the accession numbers and gene symbols, respectively, listed in Tables 1 and 3-5 of this application.

Invention 2106: claims 39-42

A method of selecting a miRNA to be administered to a subject as defined in independent claim 41.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/078894

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005013901 A	17-02-2005	CA 2533701 A1	17-02-2005
		EP 1648914 A2	26-04-2006
		US 2006252722 A1	09-11-2006
		US 2005261218 A1	24-11-2005
WO 2006128245 A	07-12-2006	AU 2006254732 A1	07-12-2006
		CA 2610702 A1	07-12-2006
		EP 1904110 A1	02-04-2008