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(54) Title: METHODS FOR PREDICTING DRUG EFFICACY IN PATIENTS AFFLICTED WITH HYPERTENSION

(57) Abstract: Methods are disclosed for predicting the efficacy of a drug for treating hypertension in a patient, including: obtaining a sample of cells from the patient; obtaining a gene expression profile from the sample in the absence and presence of in vitro modulation of the cells with specific mediators; and comparing the gene expression profile of the sample with a reference gene expression profile, wherein similarity between the sample expression profile and the reference expression profile predicts the efficacy of the drug for treating hypertension in the patient.



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INTERNATIONAL SEARCH REPORT

Interr Application No
PCT/IB2004/001947

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 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)

IPC 7 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, PAJ, WPI Data, MEDLINE, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/020220 A (PROCACCIO VINCENT ; WALLACE DOUGLAS C (US); KERSTANN KEITH (US); LEVY) 13 March 2003 (2003-03-13) page 5, paragraph 2 page 29; example 1 table 3; sequences 33,2452,2453,2596,2597	14
X	WO 00/52204 A (ORNTOT, TORBEN, F) 8 September 2000 (2000-09-08) page 112 page 117 table 8	14

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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
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- *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

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INTERNATIONAL SEARCH REPORT

Inter

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/070742 A (EPIGENOMICS AG) 12 September 2002 (2002-09-12) page 23 page 25 page 27 page 31 page 38 -----	14
Y	WO 02/053769 A (WIESNER RUDOLF) 11 July 2002 (2002-07-11) page 12, lines 5-10 page 12, lines 20-27 claim 1 claim 4 page 10, lines 4,5,15,16,23,24,28,29 page 12, lines 20-27 -----	1,3-13
Y	US 2003/096782 A1 (BRISTOW MICHAEL R ET AL) 22 May 2003 (2003-05-22) claims 25,28 -----	1,3-13
A	WO 03/021261 A (DECODE GENETICS EHF ; HAKONARSON HAKON (IS)) 13 March 2003 (2003-03-13) claim 1 -----	1-14
P,X	WO 03/083140 A (ST.JUDE CHILDREN'S RESEARCH HOSPITAL, INC; DOWNING, JAMES, R; YEOH, EN) 9 October 2003 (2003-10-09) the whole document -----	14
P,X	US 2004/018522 A1 (BRIGHAM AND WOMEN'S HOSPITAL, INC) 29 January 2004 (2004-01-29) the whole document -----	14

INTERNATIONAL SEARCH REPORT

International application No.
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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. ☐ 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 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 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.:
1-14 (partially)
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.

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 1-14 (partially)

A method for predicting the efficacy of a drug for treating hypertension in a patient, comprising:

- i) determining the gene expression profile from a sample obtained from cells of the patient in the absence and presence of in vitro modulation of the cells with specific mediators; and
- ii) comparing the gene expression profile of the sample with the reference gene expression profile, wherein similarity between the sample expression profile and the reference expression profile predicts the efficacy of the drug for treating hypertension in the patient, and in particular wherein the said gene and the said reference gene encode the protein kinase (cAMP-dependent, catalytic) inhibitor gamma (PKIG).

A microarray consisting of one gene as listed in Fig. 2-4, namely of the protein kinase (cAMP-dependent, catalytic) inhibitor gamma (PKIG) gene.

Inventions 2-46: claims 1-14 (partially)

The same method as herein above wherein the said gene and the said reference gene encode one of the 45 other genes disclosed in Fig. 2-4.

The same microarray as herein above consisting of one of the other genes disclosed in Fig. 2-4.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter Application No
PCT/IB2004/001947

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