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see PCT Gazette No. 32/2004 of 5 August 2004, Section II

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: DIAGNOSTIC MARKERS FOR THERAPEUTIC TREATMENT

(57) Abstract: A method for monitoring the effectiveness of an administered agent that interacts with the A3 adenosine receptor (A3AR) in treatment of a disease state in an individual is provided. The level of at least one parameter of a biological marker is determined and compared to a control level, the control level being the level of the parameter without treatment, which is determined either as the level of the parameter in the individual prior to treatment or the level of the parameter in untreated control subject having the disease state. Monitoring a change in these parameters versus control, may also be used for screening agents that interact with the A3AR for such that can be used for a treating a disease state.



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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/50 G01N33/573

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 G01N

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, PAJ, 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	US 2002/115635 A1 (FISHMAN PNINA ET AL) 22 August 2002 (2002-08-22) page 1, paragraph 13 - page 3, paragraph 15; figures; examples	1-10, 12, 16-25
X	FISHMAN PNINA ET AL: "Evidence for involvement of Wnt signaling pathway in IB-MECA mediated suppression of melanoma cells." ONCOGENE. 6 JUN 2002, vol. 21, no. 25, 6 June 2002 (2002-06-06), pages 4060-4064, XP002284081 ISSN: 0950-9232 cited in the application the whole document	1-10, 12, 16-25

☒ 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
- *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

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL 03/00857

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MADI L ET AL: "HIGH EXPRESSION OF A3ARS IN MELANOMA AND COLON CARCINOMA CEL LINES: A TARGET FOR TUMOR CELL GROWTH INHIBITION" DRUG DEVELOPMENT RESEARCH, NEW YORK, NY, US, vol. 56, no. 4, August 2002 (2002-08), page 560, XP002284082 ISSN: 0272-4391 #72 abstract	1-4, 7-10,12, 16-21, 24,25
X	FISHMAN PNINA ET AL: "The A3 adenosine receptor: A new target for cancer therapy and chemoprotection" INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, vol. 6, no. Supplement 1, 2000, page S60, XP009024523 & JOINT MEETING OF THE 5TH WORLD CONGRESS ON ADVANCES IN ONCOLOGY AND THE 3RD INTERNATIONAL SYMPOSIUM; CRETE, GREECE; OCTOBER 19-21, 2000 ISSN: 1107-3756 #76 abstract	1,2,5-8, 13-15, 19,22-25
X	BAHARAV E ET AL: "THE EFFECT OF ADENOSINE AND THE A3 ADENOSINE RECEPTOR AGONIST IB-MECA ON JOINT INFLAMMATION AND AUTOIMMUNE DISEASES MODELS" INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, SPANDIDOS, ATHENS, GR, vol. 10, no. SUPPL 1, 10 October 2002 (2002-10-10), page S104, XP009026428 ISSN: 1107-3756 #499 abstract	1,2,5,7, 8,11,12, 16,17, 19,22-25
X	FISHMAN P ET AL: "ADENOSINE ACTS AS A CHEMOPROTECTIVE AGENT BY STIMULATING G-CSF PRODUCTION: A ROLE FOR A1 AND A3 ADENOSINE RECEPTORS" JOURNAL OF CELLULAR PHYSIOLOGY, LISS, NEW YORK, NY, US, vol. 183, no. 3, June 2000 (2000-06), pages 393-398, XP001003004 ISSN: 0021-9541 page 395, right-hand column, last paragraph - page 396, left-hand column, paragraph 1	1,2,5,8, 13,14, 16,18, 19,22,25

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IL 03/00857

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HASKÓ G ET AL: "Adenosine receptor agonists differentially regulate IL-10, TNF-alpha, and nitric oxide production in RAW 264.7 macrophages and in endotoxemic mice." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD. : 1950) 15 NOV 1996, vol. 157, no. 10, 15 November 1996 (1996-11-15), pages 4634-4640, XP002284385 ISSN: 0022-1767 page 4637, left-hand column, line 18 - line 25; table 1 -----	1,2,5,7, 8,11,12, 16,17, 19,22-25
X	BAR-YEHUDA SARA ET AL: "Agonists to the A3 adenosine receptor induce G-CSF production via NF-kappaB activation: A new class of myeloprotective agents" INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, vol. 10, no. Supplement 1, 10 October 2002 (2002-10-10), page S100, XP008031645 & 7TH WORLD CONGRESS ON ADVANCES IN ONCOLOGY AND THE 5TH INTERNATIONAL SYMPOSIUM ON MOLECULAR MEDICINE; HERSONISSOS, CRETE, GREECE; OCTOBER 10-12, 2002 ISSN: 1107-3756 abstract -----	1-8, 13-17, 19-25

INTERNATIONAL SEARCH REPORT

national application No.
PCT/IL 03/00857

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.:
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 II Observations where unity of invention is lacking (Continuation of item 2 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 1-17 and 19-25 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claims 1-17 and 19-25 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 I.1

Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body.

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IL 03/00857

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2002115635 A1	22-08-2002	EP 1363644 A2	26-11-2003
		WO 02066020 A2	29-08-2002
		US 2002165197 A1	07-11-2002