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US 09/449,175 (CIP)
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- (71) Applicant (for all designated States except US): NEUROSCIENCES RESEARCH FOUNDATION, INC. [US/US]; 10640 John Jay Hopkins Drive, San Diego, CA 92121 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): TONONI, Giulio [IT/US]; 1127 Inspiration Lane, Escondido, CA 92025 (US). CIRELLI, Chiara [IT/US]; 1127 Inspiration Lane, Escondido, CA 92025 (US). SHAW, Paul, J. [US/US]; 911 Law Street, Apartment B, San Diego, CA 92109
- (74) Agents: WEBSTER, Melanie, K. et al.; Campbell & Flores LLP, 7th Floor, 4370 La Jolla Village Drive, San Diego, CA 92122 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AT (utility model), AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ (utility model), DE, DE (utility model), DK, DK (utility model), DM, DZ, EE, EE (utility model), ES, FI, FI (utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (utility model), SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
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(54) Title: VIGILANCE NUCLEIC ACIDS AND RELATED DIAGNOSTIC, SCREENING AND THERAPEUTIC METHODS

(57) Abstract: The invention provides methods of identifying compounds that alters vigilance, by contacting an invertebrate with a candidate compound, evaluating a vigilance property in the contacted invertebrate, and determining if the candidate compound alters the vigilance property in the contacted invertebrate. Also provided are isolated vigilance nucleic acid molecules. Methods for diagnosing and treating vigilance disorders, for determining and altering vigilance levels, and for screening for therapeutic compounds useful for treating vigilance disorders and altering vigilance level, are also provided.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/32180

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, WPI Data, PAJ, CHEM ABS Data, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>ANDRETIC ROZI ET AL: "Requirement of circadian genes for cocaine sensitization in Drosophila." SCIENCE (WASHINGTON D C), vol. 285, no. 5430, 13 August 1999 (1999-08-13), pages 1066-1068, XP002175978 ISSN: 0036-8075 page 1066 -page 1068 --- -/--</p>	<p>1-10, 12-17, 19-22</p>

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

Date of the actual completion of the international search

28 August 2001

Date of mailing of the international search report

03. 12. 2001

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

Gabriels, J

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/32180

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1986 INOUE S ET AL: "BEHAVIOR-MODULATING EFFECTS OF URIDINE IN THE RHINOCEROS BEETLE ALLOMYRINA-DICHOTOMA" Database accession no. PREV198682093248 XP002175808 abstract & ZOOLOGICAL SCIENCE (TOKYO), vol. 3, no. 4, 1986, pages 727-730, ISSN: 0289-0003</p> <p style="text-align: center;">---</p>	1-8,12, 16,17, 19-22
X	<p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1982 MICHAUD J-C ET AL: "MILD INSOMNIA INDUCED BY ENVIRONMENTAL PERTURBATIONS IN THE RAT A STUDY OF THIS NEW MODEL AND OF ITS POSSIBLE APPLICATIONS IN PHARMACOLOGICAL RESEARCH" Database accession no. PREV198376013230 XP002175809 cited in the application abstract & ARCHIVES INTERNATIONALES DE PHARMACODYNAMIE ET DE THERAPIE, vol. 259, no. 1, 1982, pages 93-105, ISSN: 0003-9780</p> <p style="text-align: center;">---</p>	1-6, 19-22
X	<p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1990 RANKIN C H ET AL: "CAENORHABDITIS-ELEGANS A NEW MODEL SYSTEM FOR THE STUDY OF LEARNING AND MEMORY" Database accession no. PREV199089105282 XP002175981 abstract & BEHAVIOURAL BRAIN RESEARCH, vol. 37, no. 1, 1990, pages 89-92, ISSN: 0166-4328</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1,2,18

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/32180

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1992 BOYNTON S ET AL: "LATHEO A NEW GENE INVOLVED IN ASSOCIATIVE LEARNING AND MEMORY IN DROSOPHILA-MELANOGASTER IDENTIFIED FROM P ELEMENT MUTAGENESIS" Database accession no. PREV199294061770 XP002175982 abstract & GENETICS, vol. 131, no. 3, 1992, pages 655-672, ISSN: 0016-6731</p> <p style="text-align: center;">---</p>	1,2,18
A	<p>ISHIDA NORIO ET AL: "Biological clocks." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 96, no. 16, 3 August 1999 (1999-08-03), pages 8819-8820, XP002175979 Aug. 3, 1999 ISSN: 0027-8424 the whole document</p> <p style="text-align: center;">---</p>	1-22
A	<p>CHEMELLI RICHARD M ET AL: "Narcolepsy in orexin knockout mice: Molecular genetics of sleep regulation." CELL, vol. 98, no. 4, 20 August 1999 (1999-08-20), pages 437-451, XP002175980 ISSN: 0092-8674 cited in the application the whole document</p> <p style="text-align: center;">---</p>	1-22
A	<p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; June 1999 (1999-06) CIRELLI CHIARA ET AL: "Differences in brain gene expression between sleep and waking as revealed by mRNA differential display and cDNA microarray technology." Database accession no. PREV200000008998 XP002175983 abstract & JOURNAL OF SLEEP RESEARCH, vol. 8, no. SUPPL. 1, June 1999 (1999-06), pages 44-52, ISSN: 0962-1105</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-22

INTERNATIONAL SEARCH REPORT

International Application No

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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.
A	<p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1992 CIRELLI CHIARA ET AL: "Modulation of desynchronized sleep through microinjection of alpha-1-adrenergic agonists and antagonists in the dorsal pontine tegmentum of the cat." Database accession no. PREV199395111422 XP002175984 abstract & PFLUEGERS ARCHIV EUROPEAN JOURNAL OF PHYSIOLOGY, vol. 422, no. 3, 1992, pages 273-279, ISSN: 0031-6768</p> <p>---</p>	1-22
A	<p>EP 0 890 578 A (SMITHKLINE BEECHAM PLC) 13 January 1999 (1999-01-13) claim 9</p> <p>---</p>	1-22
A	<p>WO 99 24610 A (MILLENNIUM PHARM INC) 20 May 1999 (1999-05-20) claims 1-19</p> <p>---</p>	1-22
A	<p>WO 99 57137 A (STAKNIS DAVID ;HARVARD COLLEGE (US); WEITZ CHARLES J (US); GEKAKIS) 11 November 1999 (1999-11-11) page 3 -page 9; claim 8</p> <p>---</p>	1-22
A	<p>US 5 885 831 A (VOSSHALL LESLIE B ET AL) 23 March 1999 (1999-03-23) the whole document</p> <p>---</p>	1-22
A	<p>US 5 968 817 A (LOVENBERG TIMOTHY W ET AL) 19 October 1999 (1999-10-19) the whole document</p> <p>-----</p>	1-22

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/32180

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:

Although claims 36 and 37 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. Claims Nos.: 36,37
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 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:

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.:
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.:

1-22 (complete)

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:

1. Claims: 1-22 (all complete)

Invention 1:

Methods for identifying compounds that modulate vigilance in an invertebrate.

2. Claims: 23-35 (all partially)

Invention 2:

An isolated nucleic acid comprising SEQ ID NO:1, kits containing said sequence, and methods using said sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

3. Claims: 23-35 (all partially)

Invention 3:

An isolated nucleic acid comprising SEQ ID NO:2, kits containing said sequence, and methods using said sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

Idem for invention 4 to 26 but limited to the sequences comprising SEQ ID NOs:3-6,8-14,16-27. (SEQ ID NO:3 represents invention number 4, ..., SEQ ID NO:6 represents invention number 7, SEQ ID NO:8 represents invention number 8, ..., SEQ ID NO:14 represents invention number 14, ..., SEQ ID NO:16 represents invention number 15, ..., SEQ ID NO:27 represents invention number 26)

4. Claims: 23-31 (all partially)

Invention 27:

An isolated nucleic acid comprising SEQ ID NO:15, kits containing said sequence.

5. Claims: 32-35 (all partially)

Invention 28:

Methods using the Fas sequence for determining/diagnosing the vigilance level of an individual or the efficiency of

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

potential vigilance modulators.

6. Claims: 32-35 (all partially)

Invention 29:

Methods using the Bip sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

7. Claims: 32-35 (all partially)

Invention 30:

Methods using the Cyp4e2 sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

8. Claims: 32-35 (all partially)

Invention 31:

Methods using the AANAT1 (Dat) sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

9. Claims: 32-35 (all partially)

Invention 32:

Methods using the Ddc sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

10. Claims: 32-35 (all partially)

Invention 33:

Methods using the Cytochrome P450 sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

11. Claims: 32-35 (all partially)

Invention 34:

Methods using the AA117313 sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

12. Claims: 32-35 (all partially)

Invention 35:

Methods using the human breast tumor autoantigen homolog sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

13. Claims: 32-35 (all partially)

Invention 36:

Methods using the aryl sulfotransferase IV sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

14. Claims: 32-35 (all partially)

Invention 37:

Methods using the KIAA313 homolog sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

15. Claims: 32-35 (all partially)

Invention 38:

Methods using the E25 sequence for determining/diagnosing the vigilance level of an individual or the efficiency of potential vigilance modulators.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 36,37

Present claims 36 and 37 relate to compounds defined by reference to a desirable characteristic or property, namely modulating vigilance.

The claims cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for any of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the claimed scope impossible.

The applicant's attention is drawn to the fact that claims, or parts of 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/32180

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
EP 0890578	A	13-01-1999	US 6100062 A	08-08-2000
			EP 0890578 A2	13-01-1999
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			WO 9421670 A1	29-09-1994
