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A61K 38/17

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Filed on	1 November 1999 (01.11.1999)
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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: TWIK POTASSIUM CHANNEL MOLECULES AND USES THEREFOR

(57) Abstract: The invention provides isolated nucleic acid molecules, designated TWIK nucleic acid molecules, which encode proteins involved in potassium channel mediated activities. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing TWIK nucleic acid molecules, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a TWIK gene has been introduced or disrupted. The invention still further provides isolated TWIK proteins, fusion proteins, antigenic peptides and anti-TWIK antibodies. Diagnostic methods utilizing compositions of the invention are also provided.

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INTERNATIONAL SEARCH REPORT

International Application No

PC, US 00/30024

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/705 C07K16/28 G01N33/53 G01N33/68
C12Q1/68 A61K38/17

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 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, EMBL, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL [Online] 11 September 1997 (1997-09-11) ROBERT STRAUSBERG: "1 Homo sapiens cDNA clone IMAGE:1015480" retrieved from EBI Database accession no. AA553991 XP002163999	1-7
Y	abstract	8-22
X	--- DATABASE EMBL [Online] 28 June 1999 (1999-06-28) ROBERT STRAUSBERG: "Homo sapiens cDNA clone IMAGE:2365922" retrieved from EBI Database accession no. AI740592 XP002164000	1-7
Y	abstract	8-22

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☒ 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

19 April 2001

Date of mailing of the international search report

20-07-01

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PC, US 00/30024

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL [Online] 30 September 1998 (1998-09-30) ADAMS M.D. ET AL.: "Homo sapiens genomic clone 2385B13" retrieved from EBI Database accession no. AQ240175 XP002164001	1-7
Y	abstract ---	8-22
X	DATABASE EMBL [Online] 23 December 1998 (1998-12-23) ADAMS M.D. ET AL.: " Homo sapiens genomic clone 2384B13" retrieved from EBI Database accession no. AQ310967 XP002164002	1-7
Y	abstract ---	8-22
Y	EP 0 930 364 A (SYNTHELABO) 21 July 1999 (1999-07-21) page 18 -page 20; claims 1,4; figure SEQ.ID.1 ---	8-22
Y	LESAGE F ET AL: "TWIK-1, A UBIQUITOUS HUMAN WEAKLY INWARD RECTIFYING K+ CHANNEL WITH A NOVEL STRUCTURE" EMBO JOURNAL,GB,OXFORD UNIVERSITY PRESS, SURREY, vol. 15, no. 5, 1996, pages 1004-1011, XP002017569 ISSN: 0261-4189 cited in the application the whole document ---	8-22
A	REYES R ET AL: "Cloning and expression of a novel pH-sensitive two pore domain K+ channel from human kidney" JOURNAL OF BIOLOGICAL CHEMISTRY,AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD,US, vol. 273, no. 47, 20 November 1998 (1998-11-20), pages 30863-30869, XP002141714 ISSN: 0021-9258 the whole document ---	1-22
P,X	WO 00 52164 A (CURTIS RORY A J ;MILLENNIUM PHARM INC (US)) 8 September 2000 (2000-09-08) page 136 -page 138; claims 1-19; figures 1A-C,3 -----	1-22

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/30024

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 claim 30 is 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.: 21
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, 30 partly

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.2

Claims Nos.: 21

Claim 21 relating to modulators to polypeptides of claim 8 , has not been searched as its subject-matter is insufficiently disclosed .

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.

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 ,30 partly

Twik-3 polypeptide with amino acid sequence with seq.id.5. and antibody selectively binding to this polypeptide. Nucleic acid molecules with nucleotide sequences with seq.id.4,6 encoding said polypeptide and host cells containing said nucleic acid molecule. Methods for either producing or detecting said polypeptide and related kit, and methods for identifying a compound which binds to this polypeptide. Methods for detecting the presence of a nucleic acid encoding said polypeptide. Method of treatment involving an anti-TWIK-3 antibody .

2. Claims: 1-22 ,30 partly

Twik-4 polypeptide with amino acid sequence with seq.id.8 and antibody selectively binding to this polypeptide. Nucleic acid molecules with nucleotide sequences with seq.id.7,9 encoding said polypeptide and host cells containing said nucleic acid molecule. Methods for either producing or detecting said polypeptide and related kit, and methods for identifying a compound which binds to this polypeptide. Methods for detecting the presence of a nucleic acid encoding said polypeptide. Method of treatment involving an anti-TWIK-4 antibody .

3. Claims: 1-22 ,30 partly

Twik-5 polypeptide with amino acid sequence with seq.id.11 and antibody selectively binding to this polypeptide. Nucleic acid molecules with nucleotide sequences with seq.id.10,12 encoding said polypeptide and host cells containing said nucleic acid molecule. Methods for either producing or detecting said polypeptide and related kit, and methods for identifying a compound which binds to this polypeptide. Methods for detecting the presence of a nucleic acid encoding said polypeptide. Method of treatment involving an anti-TWIK-5 antibody .

4. Claims: 30 partly and 23-29 31-39

Method of treatment involving TWIK modulators ,like e.g. anti-TWIK antibodies as long as not provided in inventions 1-3 , or TWIK-2 proteins with amino acid sequence seq.id.2 and nucleotide sequences with seq.1 , or antisense TWIK nucleic acid molecule or ribozymes .

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT, US 00/30024

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0930364 A	21-07-1999	AU 2717399 A WO 9936529 A	02-08-1999 22-07-1999
WO 0052164 A	08-09-2000	AU 3509100 A	21-09-2000