TRANSGENIC MICE CONTAINING Kir2.3 POTASSIUM K+ CHANNEL GENE DISRUPTIONS

Abstract: The present invention relates to transgenic animals, as well as compositions and methods relating to the characterization of gene function. Specifically, the present invention provides transgenic mice comprising mutations in a Kir2.3 gene. Such transgenic mice are useful as models for disease and for identifying agents that modulate gene expression and gene function, and as potential treatments for various disease states and disease conditions.
GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent
(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG).

Published:
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report: 28 August 2003

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.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 C12N15/00 A01K67/027 C07K14/47 C12N5/10 A61K49/00

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 A01K 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)

BIOSIS, WPI Data, EPO-Internal

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
<thead>
<tr>
<th>Category *</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
</table>

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.
  - **Z** document member of the same patent family

**Data of the actual completion of the international search**

24 March 2003

**Data of mailing of the international search report**

04 JUL 2003

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. 31 851 epc nl, Fax: (+31-70) 340-0816

Authorized officer
CHAMONNET, F
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>BANNISTER J P A ET AL: &quot;Conserved extracellular cysteine residues in the inwardly rectifying potassium channel Kir2.3 are required for function but not expression in the membrane&quot; FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 458, no. 3, 24 September 1999 (1999-09-24), pages 393-399, XP004260298 ISSN: 0014-5793 the whole document</td>
<td>1</td>
</tr>
</tbody>
</table>
# INTERNATIONAL SEARCH REPORT

**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. **X** Claims Nos.: 21  
   because they relate to subject matter not required to be searched by this Authority, namely:  
   Rule 39.1(v) PCT - Presentation of information

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:

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. **X** 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.:  
   1-12, 14-18, 21

**Remark on Protest**

□ The additional search fees were accompanied by the applicant's protest.  
□ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-12 14-18 21

A targeting construct comprising (a) a first polynucleotide sequence homologous to a first portion of a Kir2.3 gene, (b) a second polynucleotide sequence homologous to at least a second portion of a Kir2.3 gene, and (c) a selectable marker; a method of producing said targeting construct; a cell comprising a disruption in a Kir2.3 gene; a non-human transgenic animal comprising a disruption in a Kir2.3 gene; a method for producing said transgenic animal; methods of identifying an agent that modulates the expression or function of a Kir2.3 gene using said animal or cell or ameliorates a phenotype associated with a disruption in a Kir2.3 gene; phenotypic data associated with said transgenic mouse wherein the data is in an electronic database.

2. Claims: 16, 37, 39

An agent modulating the expression or function of a Kir2.3 gene; an agonist or antagonist of Kir2.3;