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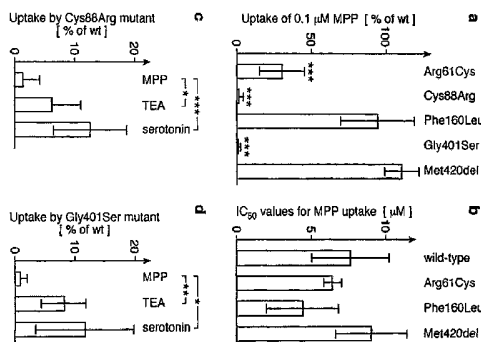
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- (88) Date of publication of the international search report: 1 July 2004

[Continued on next page]

(54) Title: POLYMORPHISMS IN THE HUMAN GENES FOR OCT1 AND THEIR USE IN DIAGNOSTIC AND THERAPEUTIC APPLICATIONS



(57) Abstract: The present invention relates to a polymorphic OCT1 polynucleotide. Moreover, the invention relates to genes or vectors comprising the polynucleotides of the invention and to a host cell genetically engineered with the polynucleotide or gene of the invention. Further, the invention relates to methods for producing molecular variant polypeptides or fragments thereof, methods for producing cells capable of expressing a molecular variant polypeptide and to a polypeptide or fragment thereof encoded by the polynucleotide or the gene of the invention or which is obtainable by the method or from the cells produced by the method of the invention. Furthermore, the invention relates to an antibody which binds specifically the polypeptide of the invention. Moreover, the invention relates to a transgenic non-human animal. The invention also relates to a solid support comprising one or a plurality of the above mentioned polynucleotides, genes, vectors, polypeptides, antibodies or host cells. Furthermore, methods of identifying a polymorphism, identifying and obtaining a pro-drug or drug or an inhibitor are also encompassed by the present invention. In addition, the invention relates to methods for producing of a pharmaceutical composition and to methods of diagnosing a disease. Further, the invention relates to a method of detection of the polynucleotide of the invention. Furthermore, comprised by the present invention are a diagnostic and a pharmaceutical composition. Even more, the invention relates to uses of the polynucleotides, genes, vectors, polypeptides or antibodies of the invention. Finally, the invention relates to a diagnostic kit.

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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.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/09356

A. CLASSIFICATION OF SUBJECT MATTER							
IPC 7	C07K14/47	C12Q1/68	G01N33/50	G01N33/53	A61K38/17		
	C07K16/18	A01K67/027	C12N15/12	A61K48/00			
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 C07K 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, MEDLINE, EMBASE, BIOSIS, WPI Data, EMBL							
C. DOCUMENTS CONSIDERED TO BE RELEVANT							
Category °	Citation of document, with indication, where appropriate, of the relevant passages				Relevant to claim No.		
X	SHU Y ET AL: "Identification and functional characterization of hOCT1 polymorphisms in ethnically diverse populations" CLINICAL PHARMACOLOGY AND THERAPEUTICS, vol. 71, no. 2, February 2002 (2002-02), page P73, XP009024430 Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics; Atlanta, Georgia, USA; March 24-27, 2002 ISSN: 0009-9236 abstract <div style="text-align: center;">----- -/--</div>				1-41		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.							
° Special categories of cited documents : <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> *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 </td> <td style="width: 50%; border: none; vertical-align: top;"> *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 </td> </tr> </table>						*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
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			Date of mailing of the international search report				
26 January 2004			19. 04. 04				
Name and mailing address of the ISA			Authorized officer				
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			Loubradou, G				

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/09356

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 EMBL 'Online! 23 March 1998 (1998-03-23), SULTON ET AL.: "Homo sapiens PAC clone RP-5-844F9 from 7, complete sequence" XP002267877 Database accession no. ac004453 The sequence comprises SEQ ID 4 abstract</p>	1,3,4,6, 8
X	<p>DATABASE EMBL 'Online! 10 September 2001 (2001-09-10), WATERSON: "Homo sapiens chromosome UNK clone RP11-112b7" XP002267878 Database accession no. ac093630 The sequence of the complementary strand comprises SEQ ID 4. abstract</p>	1,3,4,6, 8
X	<p>DATABASE EMBL 'Online! 6 February 2001 (2001-02-06), BIRREN ET AL.: "Mus musculus chromosome 12 clone RP23-283B7 map 12" XP002267879 Database accession no. ac109228 The sequence of the complementary strand comprises SEQ ID 4. abstract</p>	1,3,4,6, 8
A	<p>WO 02/059142 A (MORNHINWEG ESTHER ;HOFFMEYER SVEN (DE); BRINKMANN ULRICH (DE); EPI) 1 August 2002 (2002-08-01) claims 1-42</p>	
A	<p>DRESSER M J LEABMAN M K GIACOMINI K M: "Transporters involved in the elimination of drugs in the kidney: organic anion transporters and organic cation transporters" JOURNAL OF PHARMACEUTICAL SCIENCES, AMERICAN PHARMACEUTICAL ASSOCIATION. WASHINGTON, US, vol. 90, no. 4, April 2001 (2001-04), pages 397-421, XP002959943 ISSN: 0022-3549 cited in the application page 415 second half of the paragraph bridging left- and right-hand columns</p>	
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/09356

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	KERB REINHOLD ET AL: "Identification of genetic variations of the human organic cation transporter hOCT1 and their functional consequences." PHARMACOGENETICS, vol. 12, no. 8, November 2002 (2002-11), pages 591-595, XP009024431 ISSN: 0960-314X the whole document -----	1-41
P,X	SHU YAN ET AL: "Evolutionary conservation predicts function of variants of the human organic cation transporter, OCT1." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. UNITED STATES 13 MAY 2003, vol. 100, no. 10, 13 May 2003 (2003-05-13), pages 5902-5907, XP002267876 ISSN: 0027-8424 the whole document -----	1-41

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/09356

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:

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. 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.:

1-41 (partially)

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: 1-41 (partially)

subject-matter related to SEQ IDs 4 and 28, and to the polymorphism position 109130.

2. claims: 1-41 (partially)

subject-matter related to SEQ ID 5 and to the polymorphism position 109211

3. claims: 1-41 (partially)

subject-matter related to SEQ ID 6 and to the polymorphism position 119220

4. claims: 1-41 (partially)

subject-matter related to SEQ ID 7 and to the polymorphism position 123551

5. claims: 1-41 (partially)

subject-matter related to SEQ ID 8 and to the polymorphism position 126806

6. claims: 1-41 (partially)

subject-matter related to SEQ ID 9 and to the polymorphism position 126846

7. claims: 1-41 (partially)

subject-matter related to SEQ ID 10 and to the polymorphism positions 126863 to 126865

8. claims: 1-41 (partially)

subject-matter related to SEQ ID 11 and to the polymorphism position 126922

9. claims: 1-41 (partially)

subject-matter related to SEQ ID 12 and to the polymorphism position 126915

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. claims: 1-41 (partially)

subject-matter related to SEQ ID 13 and to the polymorphism
position 130672

11. claims: 1-41 (partially)

subject-matter related to SEQ ID 14 and to the polymorphism
position 141819

12. claims: 1-41 (partially)

subject-matter related to SEQ ID 15 and to the polymorphism
position 142951

13. claims: 1-41 (partially)

subject-matter related to SEQ ID 16 and to the polymorphism
position 141961

14. claims: 1-41 (partially)

subject-matter related to SEQ ID 17 and to the polymorphism
position 142993

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/09356

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02059142	A	01-08-2002	WO 02059142 A2	01-08-2002