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(54) Title: POLYMORPHISMS IN THE HUMAN GENE FOR CYP1A2 AND THEIR USE IN DIAGNOSTIC AND THERAPEUTIC APPLICATIONS

(57) Abstract: The present invention relates to a polymorphic CYP1 A2 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 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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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 02/08893

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12Q1/68 C12N9/02		
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 C12N		
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)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE GENBANK 'Online! 11 May 1998 (1998-05-11) Database accession no. AA959044 XP002228676 the whole document ---	1, 3, 6-8, 11
A	BASILE V S ET AL: "A functional polymorphism of the cytochrome P450 1A2 (CYP1A2) gene: Association with tardive dyskinesia in schizophrenia." MOLECULAR PSYCHIATRY, vol. 5, no. 4, July 2000 (2000-07), pages 410-417, XP002228674 ISSN: 1359-4184 cited in the application the whole document ---	1-48
-/--		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input type="checkbox"/> 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	"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	
"E" earlier document but published on or after the international filing date	"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	
"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)	"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.	
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	
"P" document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search 24 January 2003	Date of mailing of the international search report 24. 04. 03	
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 Wimmer, G	

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/08893

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>CHRISTIANSEN L ET AL: "Association between CYP1A2 polymorphism and susceptibility to porphyria cutanea tarda." HUMAN GENETICS, vol. 107, no. 6, December 2000 (2000-12), pages 612-614, XP002228675 ISSN: 0340-6717 cited in the application the whole document</p> <p style="text-align: center;">---</p>	1-48
A	<p>JOSEPHY P DAVID ET AL: "Activation of MeIQ (2-amino-3,4-dimethylimidazo-(4,5-f)quinoline) by sequence variants of recombinant human cytochrome P450 1A2." ENVIRONMENTAL AND MOLECULAR MUTAGENESIS, vol. 35, no. 4, 2000, pages 328-335, XP009004549 ISSN: 0893-6692 the whole document</p> <p style="text-align: center;">-----</p>	1-48

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/08893

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:

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.:

Claims 1-48 (partially)

Remark on Protest

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

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1-48 (partially)

A polynucleotide comprising a nucleic acid sequence according to SEQ ID 18.

Inventions 2-36: Claims 1-48 (partially)

Like subject 1, with SEQ ID NOS. 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 53, 54, 55, 58, 59, 60, 61, 63, 64, 65, 66, 67, 68, 70, 71, 72, 74 and 75.