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**WO 03/008637 A3**

(54) Title: USE OF GENOTYPING IN THE INDIVIDUALIZATION OF THERAPY

(57) Abstract: The invention relates to the individualization of therapy. More specifically, the present invention relates to the use of genotyping for the individualization of therapy and/or individualization of drug dosing. More specifically, the present invention relates to the use of genotyping in the individualization of therapy with a therapeutic agent or a class of therapeutic agents.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 02/01103

**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)

MEDLINE, BIOSIS, EMBASE, INSPEC, EPO-Internal, PAJ, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BROCKMÖLLER J ET AL: "Pharmacogenetic diagnostics of cytochrome P450 polymorphisms in clinical drug development and in drug treatment." PHARMACOGENOMICS. ENGLAND MAY 2000, vol. 1, no. 2, May 2000 (2000-05), pages 125-151, XP008020668 ISSN: 1462-2416 the whole document</p> <p style="text-align: center;">--- -/--</p>	1-22



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

Date of the actual completion of the international search

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## 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.
X	<p>MCELROY S ET AL: "CYP2D6 genotyping as an alternative to phenotyping for determination of metabolic status in a clinical trial setting." AAPS PHARMSCI 'ELECTRONIC RESOURCE!. UNITED STATES 2000, vol. 2, no. 4, 2000, page E33 XP002251960 ISSN: 1522-1059 the whole document</p> <p style="text-align: center;">---</p>	1-22
X	<p>MEISEL C ET AL: "HOW TO MANAGE INDIVIDUALIZED DRUG THERAPY: APPLICATION OF PHARMACOGENETIC KNOWLEDGE OF DRUG METABOLISM AND TRANSPORT" CLINICAL CHEMISTRY AND LABORATORY MEDICINE, WALTER DE GRUYTER UND CO, DE, vol. 38, no. 9, September 2000 (2000-09), pages 869-876, XP001030015 ISSN: 1434-6621 the whole document</p> <p style="text-align: center;">---</p>	1-22
X	<p>MANCINELLI L ET AL: "Pharmacogenomics: the promise of personalized medicine." AAPS PHARMSCI 'ELECTRONIC RESOURCE!. UNITED STATES 2000, vol. 2, no. 1, March 2000 (2000-03), page E4 XP002251962 ISSN: 1522-1059 See "Cytochrome P450", pages 6-7 the whole document</p> <p style="text-align: center;">---</p>	1-22
X	<p>GRIESE E-U ET AL: "ASSESSMENT OF THE PREDICTIVE POWER OF GENOTYPES FOR THE IN-VIVO CATALYTIC FUNCTION OF CYP2D6 IN A GERMAN POPULATION" PHARMACOGENETICS, CHAPMAN &amp; HALL, LONDON, GB, vol. 8, no. 1, February 1998 (1998-02), pages 15-26, XP001073429 ISSN: 0960-314X the whole document</p> <p style="text-align: center;">---</p>	1-22
X	<p>MARCH R: "PHARMACOGENOMICS: THE GENOMICS OF DRUG RESPONSE" YEAST, CHICHESTER, SUSSEX, GB, vol. 17, no. 1, 2000, pages 16-21, XP001064496 ISSN: 0749-503X See "The genetics of drug metabolizing enzymes", pages 17-18 the whole document</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-22

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/CA 02/01103

## 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>ERESHEFSKY L ET AL: "REVIEW OF THE PHARMACOKINETICS, PHARMACOGENETICS, AND DRUG INTERACTION POTENTIAL OF ANTIDEPRESSANTS: FOCUS ON VENLAFAXINE" DEPRESSION AND ANXIETY, NEW YORK, NY, US, vol. 12, no. SUPPL 1, 2000, pages 30-44, XP009000372 ISSN: 1091-4269 See "The cytochrome P450 enzyme system", pages 35-36 the whole document</p>	1-22
X	<p>LU A Y H: "Drug-metabolism research challenges in the new millennium: Individual variability in drug therapy and drug safety" DRUG METABOLISM AND DISPOSITION, WILLIAMS AND WILKINS., BALTIMORE, MD, US, vol. 26, no. 12, December 1998 (1998-12), pages 1217-1222, XP002223866 ISSN: 0090-9556 See "Genetic variations of cytochrome P450", page 1220 the whole document</p>	1-22
X	<p>INGELMAN-SUNDBERG M ET AL: "Polymorphic human cytochrome P450 enzymes: an opportunity for individualized drug treatment" TRENDS IN PHARMACOLOGICAL SCIENCES, ELSEVIER TRENDS JOURNAL, CAMBRIDGE, GB, vol. 20, no. 8, 1 August 1999 (1999-08-01), pages 342-349, XP004173660 ISSN: 0165-6147 the whole document</p>	1-22
X	<p>STREETMAN D S ET AL: "Phenotyping of drug-metabolizing enzymes in adults: a review of in-vivo cytochrome P450 phenotyping probes." PHARMACOGENETICS. ENGLAND APR 2000, vol. 10, no. 3, April 2000 (2000-04), pages 187-216, XP008020500 ISSN: 0960-314X</p>	1,4-8, 10-12
Y	the whole document	2,3,9, 13-22
X	<p>WO 00 55624 A (LEYLAND JONES BRIAN ;WONG PIERRE (CA)) 21 September 2000 (2000-09-21)</p>	1,4-8, 10-12
Y	the whole document	2,3,9, 13-22
	-/--	

## 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.
E	WO 02 088753 A (UNIV MCGILL ;LEYLAND-JONES BRIAN (US)) 7 November 2002 (2002-11-07) the whole document -----	1-22

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA 02/01103

## 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.: 23, 24  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
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.:

### 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.1

The scope of claims 1-22 also comprises diagnostic methods practised on the human/animal body. A search over the whole scope claimed was therefore not carried out (Rule 39.1(iv) PCT). The search was restricted to those diagnostic methods falling within the scope of claims 1-22 which do not comprise any steps practised on the human/animal body.

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Continuation of Box I.1

Claims Nos.: 23,24

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

## INTERNATIONAL SEARCH REPORT

on on patent family members

International Application No

PCT/CA 02/01103

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0055624	A	21-09-2000	AU 3138800 A	04-10-2000
			WO 0055624 A2	21-09-2000
			CA 2366085 A1	21-09-2000
			EP 1163518 A2	19-12-2001
			JP 2002539450 T	19-11-2002
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WO 02088753	A	07-11-2002	WO 02088753 A1	07-11-2002
			US 2003073133 A1	17-04-2003
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