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**Published**:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

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8 December 2016

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(54) Title: SYSTEM AND METHOD FOR PROCESSING GENOTYPE INFORMATION RELATING TO NSAID RISK

(57) Abstract: There are systems and methods for preparing or using prognostic information about NSAID mediated side effect risks. The information may include determining patient information, including DNA information, associated with a human subject; determining from the DNA information whether a subject genotype of the human subject includes one or more SNP diploid polymorphisms by detecting, utilizing a detection technology and the DNA information, a presence or absence of the one or more SNP diploid polymorphisms in the subject genotype, wherein each SNP diploid polymorphism of the one or more SNP diploid polymorphisms includes a combination of two SNP alleles associated with one SNP location; and determining a NSAID mediated side effect risk associated with the human subject based, at least in part, on the presence or absence of the one or more SNP diploid polymorphisms in the subject genotype.

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/29782

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12Q 1/68, G06F 19/18 (2016.01)
CPC - G06F 19/18, C12Q 1/6883
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(8) - C12Q 1/68, G06F 19/18 (2016.01)
CPC - G06F 19/18, C12Q 1/6883

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 435/6.11, 702/19

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
pubWEST; PatBase; Google Scholar
search terms - Abcb, abcb1, nonsteroidal anti-inflammatory drug, NSAID, rs1045642, C3435T, polymorphism, snp

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | US 2014/0371256 A1 (CHILDREN'S HOSPITAL MEDICAL CENTER) 18 December 2014 (18.12.2014) para [0007]; [0005]; [0067]; [0085]-[0092]; [0158]; [0161]; [0315]-[318]; Table 1. | 1, 3, 8, 10, 15, 17 |
| A | US 2014/0378351 A1 (MESHKIN) 25 December 2014 (25.12.2014) para [0008]-[0012]; [0098]. | 1, 3, 8, 10, 15, 17 |

☐ Further documents are listed in the continuation of Box C. ☐

* 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 application or patent 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 |
|---|---|
| 29 September 2016 | 17 OCT 2016 |
| Name and mailing address of the ISA/US<br>Mail Stop PCT, Attn: ISA/US, Commissioner for Patents<br>P.O. Box 1450, Alexandria, Virginia 22313-1450<br>Facsimile No. 571-273-8300 | Authorized officer:<br>Lee W. Young<br>PCT Helpdesk: 571-272-4300<br>PCT OSP: 571-272-7774 |

Form PCT/ISA/210 (second sheet) (January 2015)

# INTERNATIONAL SEARCH REPORT

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**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 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 No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I+: Claims 1-20, directed to method/apparatus for detecting SNP diploid polymorphisms associated with NSAID-mediated side effects. The method/apparatus will be searched to the extent that the SNP diploid polymorphisms encompasses the first named SNP diploid polymorphism in ABCB1 (ABCB1-ANC, ABCB1-HET, and ABCB1-NONA in the ABCB1 gene). It is believed that claims 1, 3, 8, 10, 15, 17 encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass the ABCB1 SNP diploid polymorphisms. Additional SNP diploid polymorphisms(s) will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected SNP diploid polymorphisms(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the '+' group(s) will result in only the first claimed invention to be searched. An exemplary election would be the COX1 SNP diploid polymorphisms (COXI-ANC, COXI-HET, and COXI-NONA in the COX1 gene) (claims 1, 3, 8, 10, 15, 17 ). --continued on extra sheet attached hereto--

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 additional fees, this Authority did not invite payment of additional fees.

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, 3, 8, 10, 15 and 17 (limited to an ABCB1 polymorphism)

**Remark on Protest**

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

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continuation of Box No III:

[Note. see instant Specification, para [0063], Table 1, legend. ** The naming conventions for the SNP Diploid Polymorphisms indicate the diploid is either - ANC (homozygous for the ancestral SNP), -HET (heterozygous as including one ancestral and one non-ancestral SNP in the diploid), or -NONA (homozygous for the non-ancestral SNP)]
[Note, see instant Specification, para [0004], "..A haplotype is a combination of alleles, or a combination of SNPs on the same chromosome.". Accordingly, CYP haplotype polymorphisms of claims 2, 9, and 16 is considered as an elective SNP polymorphisms, thus, excluded from the first invention.]

The inventions listed as Groups I+ do not relate to a single special technical feature under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special technical features
The inventions of Group I+ each include the special technical feature of a unique SNP diploid group, recited therein. Each SNP diploid group is considered a distinct technical feature.

Sharod technical features
The inventions of Group I+ share the common technical feature of a method and a non-transitory computer readable medium storing computer readable instructions that when executed by at least one processor perform a method, the method comprising facilitating a processing of and/or processing (1) data and/or (2) information and/or (3) at least one signal, the (1) data and/or (2) information and/or (3) at least one signal based, at least in part, on the following:
determining patient information, including DNA information, associated with a human subject;
determining from the DNA information whether a subject genotype of the human subject includes one or more SNP diploid polymorphisms by detecting, utilizing a detection technology and the DNA information, a presence or absence of the one or more SNP diploid polymorphisms in the subject genotype,
wherein each SNP diploid polymorphism of the one or more SNP diploid polymorphisms includes a combination of two SNP alleles associated with one SNP location, and
determining a nonsteroidal anti-inflammatory drug (NSAID) mediated side effect risk associated with the human subject based, at least in part, on the presence or absence of the one or more SNP diploid polymorphisms in the subject genotype.

The inventions of Group I+ further share the common technical feature of an apparatus comprising: at least one processor; and at least one memory including computer program code for one or more programs, the at least one memory and the computer program code configured to, with the at least one processor, cause the apparatus to perform the method.

However, these shared technical features do not represent a contribution over prior art, because the shared technical features are anticipated by US 2014/0378351 A1 (Meshkin).

Meshkin teaches a method comprising facilitating a processing of and/or processing (1) data and/or (2) information and/or (3) at least one signal, the (1) data and/or (2) information and/or (3) at least one signal based, at least in part, on the following:
determining patient information, including DNA information, associated with a human subject (para [0008] 'The prognostic information is derived from genotype information about the patient's genotype. The genotype information may be obtained by, inter alia, assaying a sample of genetic material associated with the patient');
determining from the DNA information whether a subject genotype of the human subject includes one or more SNP diploid polymorphisms by detecting, utilizing a detection technology and the DNA information, a presence or absence of the one or more SNP diploid polymorphisms in the subject genotype,
wherein each SNP diploid polymorphism of the one or more SNP diploid polymorphisms includes a combination of two SNP alleles associated with one SNP location (para [0010] 'The detector may be configured for detecting in the sample a presence of one or more polymorphisms in the genotype to determine an assay result. The assay result may include data describing a presence or an absence of a tested polymorphism...The polymorphisms may be selected from a group including one or more of: a SNP cytosine allele of SNP marker rs4532 in the DRD1 gene, a SNP adenine allele of SNP marker rs4680 in the COMT gene'), and
determining a nonsteroidal anti-inflammatory drug (NSAID) mediated side effect risk associated with the human subject based, at least in part, on the presence or absence of the one or more SNP diploid polymorphisms in the subject genotype (para [0082] 'The genotype information obtained from analyzing a sample of a patient's genetic material may be utilized, according to the principles of the invention, to predict whether a patient has a level of risk associated with taking a pain medication for treating chronic pain...Analgesic medications include paracetamol (known in the U.S. as acetaminophen), the non-steroidal anti-inflammatory drugs (NSAIDs) such as the salicylates').

Meshkin further teaches a non-transitory computer readable medium storing computer readable instructions that when executed by at least one processor perform the method (para [0012] 'According to a third principle of the invention, there is a non-transitory computer readable medium storing computer readable instructions that when executed by a computer system perform a method for generating genotype information...utilizing a processor, genotype information associated with the determined assay result'), and an apparatus comprising at least one processor; and at least one memory including computer program code for one or more programs, the at least one memory and the computer program code configured to, with the at least one processor, cause the apparatus to perform the method (para [0098] 'A data structure managing application, such as data structure managing application 414 provides various code components for building/updating a computer-readable system architecture, such as for a non-volatile memory, as described above. In certain examples, some or all of the processes performed by the data structure managing application 412 may be integrated into the operating system').

As the technical features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

Therefore, Group I+ inventions lack unity under PCT Rule 13 because they do not share the same or corresponding special technical feature.