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- 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))

(88) Date of publication of the international search report:
14 April 2011

(54) Title: sPLA2 IIA POLYMORPHISM ANALYSIS FOR THE DIAGNOSIS/PROGNOSIS OF A CARDIOVASCULAR DISEASE/EVENT

(57) Abstract: The invention relates to a method of identifying a subject having or at risk of having or developing a cardiovascular disease and/or a cardiovascular event, comprising determining, in a sample obtained from said subject, the presence or absence of a variant allele of nucleotide polymorphism (SNP) of the sPLA2 type IIA nucleic acid, wherein the SNP is selected from the group consisting of rs11573156 and rs2236771, wherein the presence of the minor allele (G) of SNP rs11573156 indicates an increased risk of having or being at risk of having or developing a cardiovascular disease and/or cardiovascular event, and the presence of the minor allele (C) of SNP rs2236771 indicates a decreased risk of having or being at risk of having or developing a cardiovascular disease and/or cardiovascular event.



WO 2011/020906 A3

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. 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)
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, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WOOTTON PETER T E ET AL: "Tagging-SNP haplotype analysis of the secretory PLA2IIa gene PLA2G2A shows strong association with serum levels of sPLA2IIa: results from the UDACS study." HUMAN MOLECULAR GENETICS 15 JAN 2006 LNKD-PUBMED:16368710, vol. 15, no. 2, 15 January 2006 (2006-01-15), pages 355-361, XP002607836 ISSN: 0964-6906 the whole document	1-5
A	----- -/--	6

Further documents are listed in the continuation of Box C.

See patent family 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.

"&" document member of the same patent family

Date of the actual completion of the international search 11 November 2010	Date of mailing of the international search report 24/02/2011
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Persson, Anna

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2010/062144

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 NCBI Probe [Online] 27 December 2005 (2005-12-27), "Sequence-specific oligonucleotide (SSO) probe for Homo sapiens variation rs11573156" XP002607837 Database accession no. Pr001824682 the whole document</p>	5
A	<p>-----</p> <p>FISCHER MARCUS ET AL: "Genetic variants within the PLA2G2A gene encoding secretory phospholipase A2 group IIA are related to the risk of myocardial infarction" Circulation, [Online] October 2006 (2006-10), XP002607838 & 79TH ANNUAL SCIENTIFIC SESSION OF THE AMERICAN-HEART-ASSOCIATION; CHICAGO, IL, USA; NOVEMBER 12 -15, 2006 American Heart Association Retrieved from the Internet: URL:http://circ.ahajournals.org/cgi/content/meeting_abstract/114/18_MeetingAbstracts/II_887-c?maxtoshow=&hits=10&RESULTFORMAT=&fulltext=abstract+4111&searchid=1&FIRSTINDEX=0&volume=114&issue=18+Supplement&resourcetype=HWCIT abstract</p>	1-6
A	<p>-----</p> <p>WOOTTON PETER T E ET AL: "Tagging SNP haplotype analysis of the secretory PLA2-V gene, PLA2G5, shows strong association with LDL and oxLDL levels, suggesting functional distinction from sPLA2-IIA: results from the UDACS study." HUMAN MOLECULAR GENETICS 15 JUN 2007 LNKD- PUBMED:17545304, vol. 16, no. 12, 15 June 2007 (2007-06-15), pages 1437-1444, XP002607839 ISSN: 0964-6906 the whole document</p>	1-6
A	<p>-----</p> <p>DIVCHEV DIMITAR ET AL: "The secretory phospholipase A2 group IIA: a missing link between inflammation, activated renin-angiotensin system, and atherogenesis?" VASCULAR HEALTH AND RISK MANAGEMENT 2008 LNKD- PUBMED:18827909, vol. 4, no. 3, 2008, pages 597-604, XP002607840 ISSN: 1176-6344 the whole document</p> <p>-----</p> <p style="text-align: center;">-/--</p>	1-6

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2010/062144

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>KOENIG WOLFGANG ET AL: "Association between type II secretory phospholipase A2 plasma concentrations and activity and cardiovascular events in patients with coronary heart disease" EUROPEAN HEART JOURNAL (ONLINE), OXFORD UNIVERSITY PRESS, GB, US, NL LNKD- DOI:10.1093/EURHEARTJ/EHP302, vol. 30, no. 22, 7 August 2009 (2009-08-07), pages 2742-2748, XP002565770 ISSN: 1522-9645 [retrieved on 2009-08-07] the whole document</p> <p style="text-align: center;">-----</p>	1-6
A	<p>SIMON TABASSOME ET AL: "Genetic Determinants of Response to Clopidogrel and Cardiovascular Events" NEW ENGLAND JOURNAL OF MEDICINE, THE, MASSACHUSETTS MEDICAL SOCIETY, WALTHAM, MA, US LNKD- DOI:10.1056/NEJMOA0808227, vol. 360, no. 4, 22 January 2009 (2009-01-22), pages 363-375, XP002603681 ISSN: 0028-4793 the whole document</p> <p style="text-align: center;">-----</p>	6
X,P	<p>SIMON TABASSOME ET AL: "Impact of Secretory PLA2-IIa Gene Polymorphisms on sPLA2 Activity and Cardiovascular Events Following an AMI: Results From the French Registry of Acute ST Elevation or Non-ST-elevation Myocardial Infarction (FAST-MI) Registry" Circulation, [Online] November 2009 (2009-11), XP002607841 & 82ND SCIENTIFIC SESSION OF THE AMERICAN-HEART-ASSOCIATION; ORLANDO, FL, USA; NOVEMBER 14 -18, 2009 American Heart Association Retrieved from the Internet: URL:abstract">http://circ.ahajournals.org/cgi/content/meeting_abstract/120/18_MeetingAbstracts/S1174-c?maxtoshow=&hits=10&RESULTFORMAT=&fulltext=abstract+5908&searchid=1&FIRSTIND EX=0&volume=120&issue=18+Supplement&resource=HWCIT>abstract</p> <p style="text-align: center;">----- -/--</p>	1-6

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2010/062144

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	EXETER H ET AL: "FUNCTIONALITY OF PLA2G2A PROMOTER VARIANTS ASSOCIATED WITH SPLA2-IIA LEVELS" ATHEROSCLEROSIS SUPPLEMENTS, ELSEVIER, vol. 11, no. 2, MS15, June 2010 (2010-06), page 112, XP027097377 ISSN: 1567-5688 [retrieved on 2010-06-01] abstract	1-6
X,P	----- GUARDIOLA M ET AL: "P156 PLA2G2A, PLA2G5 AND PLA2G10 VARIANTS, SPLA2 ACTIVITY AND MASS AND CHD RISK: RESULTS FROM GRACE AND EPIC-NORFOLK" ATHEROSCLEROSIS SUPPLEMENTS, ELSEVIER, vol. 11, no. 2, June 2010 (2010-06), page 49, XP027097084 ISSN: 1567-5688 [retrieved on 2010-06-01] abstract -----	1-6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2010/062144

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:

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 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.:

6(completely); 1-5(partially)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 6(completely); 1-5(partially)

Methods of identifying a subject having or at risk of developing a cardiovascular disease and/or a cardiovascular event comprising analysing (a haplotype comprising) the sPLA2 type IIA SNP rs11573156. A method of predicting the responsiveness of a subject at risk of having or developing a cardiovascular disease and/or a cardiovascular event to a drug decreasing the quantity and/or inhibiting the activity of sPLA2 type IIA comprising analysing (a haplotype comprising) rs11573156. Related kit.

2. claims: 1-5(partially)

Methods of identifying a subject having or at risk of developing a cardiovascular disease and/or a cardiovascular event comprising analysing (a haplotype comprising) the sPLA2 type IIA SNP rs2236771. Related kit.
