Title: METHODS AND COMPOSITIONS FOR THE ASSESSMENT OF CARDIOVASCULAR FUNCTION AND DISORDERS

Abstract: The present invention provides methods for the assessment of risk of developing acute coronary syndrome (ACS), arterial inflammation, or ACS-associated impaired vascular function, in smokers and non-smokers using analysis of genetic polymorphisms. The present invention also relates to the use of genetic polymorphisms in assessing a subject's risk of developing ACS, arterial inflammation, or ACS-associated impaired vascular function. Nucleotide probes and primers, kits, and microarrays suitable for such assessment are also provided.
### INTERNATIONAL SEARCH REPORT

**A. CLASSIFICATION OF SUBJECT MATTER**

**Int. Cl.**

*CLQ 1/68 (2006.01)*

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)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of database and, where practicable, search terms used)

EPOQUE, MEDLINE, CAPLUS, BIOTECHABS: Complement Factor H, CFH, Complement Component Factor H, Y402H, RS1061170, Tyr402His, C/T, heart, cardiac, coronary, myocardial GENOMIQUE: TTACCTGTACAAACTTCTTCCATGATTTTGATATATCCATTTCCAAAT

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>Whole document</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>US 2005/0026169 A1 (CARGILL et al.) 3 February 2005</td>
<td></td>
</tr>
<tr>
<td></td>
<td>See SEQ ID NO: 36,141</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Whole document</td>
<td></td>
</tr>
</tbody>
</table>

[X] Further documents are listed in the continuation of Box C

- **A** special categories of cited documents:
  - document defining the general state of the art which is not considered to be of particular relevance
  - document defining the general state of the art which is not considered to be of particular relevance
  - earlier application or patent but published on or after the international filing date
  - 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)
  - document referring to an oral disclosure, use, exhibition or other means
  - 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**

27 June 2008

**Date of mailing of the international search report**

4 JUL 2008

**Name and mailing address of the ISA/AU**

AUSTRALIAN PATENT OFFICE
PO BOX 200, WODEN ACT 2606, AUSTRALIA
E-mail address: pct@ipaaustralia.gov.au
Facsimile No. +61 2 6283 7999

**Authorized officer**

**Jamie Turner**

AUSTRALIAN PATENT OFFICE
(ISO 9001 Quality Certified Service)
Telephone No.: (02) 6283 2071

Form PCT/ISA/210 (second sheet) (April 2007)
INTERNATIONAL SEARCH REPORT

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:

The claims are directed to a method for determining a subject’s risk of developing acute coronary syndrome (ACS), arterial inflammation or ACS-associated impaired vascular function by detecting, in a sample, any of 7 polymorphisms (found in 7 different unrelated genes).

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. X 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.: 1-7, 9-30, 45-69 (to the extent that they relate to Y402H polymorphism in the gene encoding Complement Factor H)

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.

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2007)
This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>US 2005026169</td>
<td>AU 2003299818</td>
</tr>
<tr>
<td></td>
<td>CA 2511012</td>
</tr>
<tr>
<td></td>
<td>CA 2518957</td>
</tr>
<tr>
<td>EP 1583771</td>
<td>EP 1608782</td>
</tr>
<tr>
<td></td>
<td>US 2007042382</td>
</tr>
<tr>
<td>WO 2004058052</td>
<td>WO 2004081187</td>
</tr>
<tr>
<td>US 2007037183</td>
<td>AU 2006220604</td>
</tr>
<tr>
<td></td>
<td>CA 2600024</td>
</tr>
<tr>
<td></td>
<td>EP 1863931</td>
</tr>
<tr>
<td>WO 2006096737</td>
<td></td>
</tr>
</tbody>
</table>

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX