Title: EXOSOMAL BIOMARKERS FOR PREDICTING CARDIOVASCULAR EVENTS

Abstract: The present invention relates to a method of predicting the risk of a subject developing a cardiovascular event, comprising determining the presence of a biomarker that is indicative of the risk of developing a cardiovascular event in an exosome sample from the subject. The exosomes are suitably isolated from a body fluid selected from serum, plasma, blood, urine, amniotic fluid, malignant ascites, bronchoalveolar lavage fluid, synovial fluid, breast milk, saliva, in particular serum. Alternatively, the exosomes are present in a body fluid, in particular serum. The biomarker is selected from the proteins Vronectin, Serpin F2, CD14, Cystatin C, Plasminogen, Nidogen 2, Serpin G1 or any combination of two or more of these proteins. The invention further relates to a method of diagnosing the occurrence of acute coronary syndrome in a subject, comprising determining the presence of a biomarker that is indicative of the occurrence of acute coronary syndrome in an exosome sample from the subject. In this method the biomarker is selected from Serpin F2, CD14, Cystatin C or combinations thereof.
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:
7 February 2013
# A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N33/68

ADD.

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)

G01N

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 practicable, search terms used)

EPO-Internal, BIOSIS, WPI Data

# C. DOCUMENTS CONSIDERED TO BE RELEVANT

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See patent family annex.

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
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  * A* document member of the same patent family

Date of the actual completion of the international search: 16 November 2012

Date of mailing of the international search report: 10/12/2012

Name and mailing address of the ISA:
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NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax. (+31-70) 340-3016

Authorized officer: Giry, Murielle
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<td>ROBBI E L.A. ET AL.: &quot;Inhibitors of fibrinolysis are elevated in atherosclerotic plaque&quot;, ARTERIOSCLER. THROMB. VASC. BIOL., vol. 16, no. 4, April 1996 (1996-04), pages 539-545, XP009164641 abstract page 544, column 1, last paragraph - column 2, paragraph 1</td>
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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).

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.: I-16(partially)

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

1. claims: 1-4, 8-16 (all partially)
   Method of predicting the risk of a cardiovascular event based on detecting vitronectin in an exosome sample and kit therefor
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2. claims: 1-16 (partially)
   Method of predicting the risk of a cardiovascular event, such as acute coronary syndrome, based on detecting serpin F2 in an exosome sample and kit therefor
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3. claims: 1-16 (partially)
   Method of predicting the risk of a cardiovascular event, such as acute coronary syndrome, based on detecting CD14 in an exosome sample and kit therefor
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4. claims: 1-16 (partially)
   Method of predicting the risk of a cardiovascular event, such as acute coronary syndrome, based on detecting cystatins C in an exosome sample and kit therefor
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5. claims: 1-4, 8-16 (all partially)
   Method of predicting the risk of a cardiovascular event based on detecting plasminogen in an exosome sample and kit therefor
   ---

6. claims: 1-4, 8-16 (all partially)
   Method of predicting the risk of a cardiovascular event based on detecting tenasin 2 in an exosome sample and kit therefor
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7. claims: 1-4, 8-16 (all partially)
   Method of predicting the risk of a cardiovascular event based on detecting serpin G in an exosome sample and kit therefor
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