Abstract:
The present invention relates to methods for the detection and quantification of apolipoproteins and isoforms thereof in a sample, as well as to predictive methods of the probability of neurodegenerative or cardiovascular disease development based on apolipoprotein levels as determined by the detection methods of the invention.
# INTERNATIONAL SEARCH REPORT

**INTERNATIONAL APPLICATION**

**No.**

PCT/EP2016/076457

**A. CLASSIFICATION OF SUBJECT MATTER**

INV. G01N33/68 G01N33/92

**ABD.**

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, WPI Data, BIOSIS, EMBASE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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</table>

Further documents are listed in the continuation of Box C.

See patent family annex.

**Date of the actual completion of the international search**

21 February 2017

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

09/05/2017

**Name and mailing address of the ISA/Authorized officer**

European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016

Chretien, Eva Maria
<table>
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<th>Relevant to claim No.</th>
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<td>A</td>
<td>DAVID B POLIS ET AL: &quot;ISOLATION OF A CRYSTALLINE ALBUMIN FROM MILK&quot;, J BIOL CHEM, vol. 187, 1 November 1950 (1950-11-01), pages 349-354, XP055347922, whole document, in particular abstract and discussion</td>
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<td>X</td>
<td>WO 2011/109246 AI (DAVID GLADSTONE INST [US]; HUANG YADONG [US]; XU QIN [US]; BIEN-LY NGA) 9 September 2011 (2011-09-09) whole document, in particular par. 92, 198, 199, 203</td>
<td>1,2,8,9</td>
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<td>X</td>
<td>WO 00/55635 AI (SEREX INC [US]) 21 September 2000 (2000-09-21) whole document, in particular p. 11, 1. 26 - p. 12, 1. 5; p. 14, 1. 7-9, p. 18, 1. 16-33</td>
<td>1,2,8,9</td>
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## 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:

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see additional sheet
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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.:

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1, 2(completely) ; 8, 9(partially)
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**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 Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1, 2 (completely); 8, 9 (partially)

An in vitro method for the detection and/or quantification of an apolipoprotein n selected from the group consisting of apoAI, apoAIV, apoCI, apoCII, apoCIII, apoE and apoJ (clusteri n) or an isoform thereof in a sample

2. Claims: 3-5 (completely); 8, 9 (partially)

An in vitro method for determining the relative amount of an isoform of a given apolipoprotein n selected from the group consisting of apoAI, apoAIV, apoCI, apoCII, apoCIII, apoE and apoJ (clusteri n) with respect to the total content of said apolipoprotein n in a sample

3. Claims: 6, 7 (completely); 8, 9 (partially)

A method for determining the allelic dosage of haplotypes associated with the expression of an apolipoprotein isoform selected from the group consisting of apoAI, apoAIV, apoCI, apoCII, apoCIII, apoE and apoJ (clusteri n) in a subject

4. Claims: 10 (completely); 12 (partially)

A method for determining the probability that a subject develops a neurodegenerative disease that comprises determining in a sample from said subject the levels of apoE E4 isoform

5. Claims: 11 (completely); 12 (partially)

A method for determining the probability that a subject develops a neurodegenerative disease that comprises determining in said subject the allelic dosage of the haplotype encoding the apoE E4 isoform

6. Claims: 13, 14

A kit comprising a polystyrene or a polycarbonate surface and an anti body specific for an apolipoprotein n or isoform thereof, wherein the kit does not comprise a second anti body specific for said apolipoprotein n or isoform thereof

7. Claims: 15, 16

Use of a kit comprising a polystyrene or a polycarbonate
surface and an anti body specific for an apolipoprotein or isoform thereof, wherein the kit does not comprise a second anti body specific for said apolipoprotein or isoform thereof for detecting and/or quantifying an apolipoprotein selected from the group consisting of apoAI, apoAIV, apoCI, apoCII, apoCIII, apoE and apoJ (clusterin) or an isoform thereof, wherein the polystyrene or polycarbonate surface is blocked with albumin.

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<td>WO 2011109246 Al</td>
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