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60/521,384 15 April 2004 (15.04.2004) US(71) Applicant (for all designated States except US): **ATHERA BIOTECHNOLOGIES AB** [SE/SE]; Fogdevreten 2B, S-17177 Stockholm (SE).

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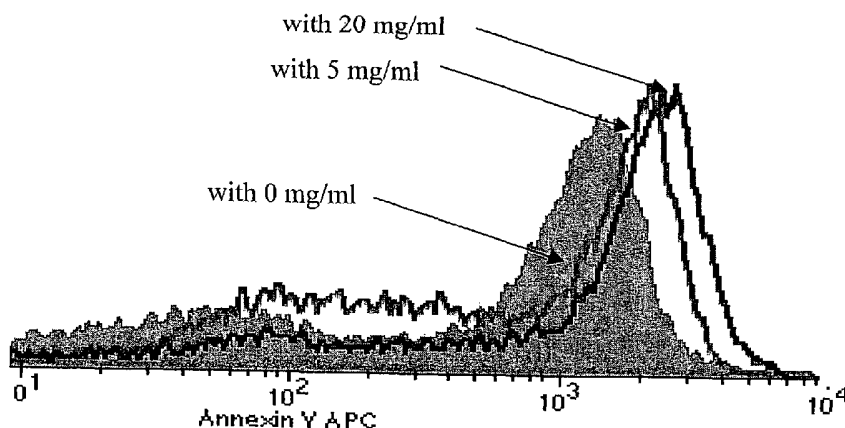
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(54) Title: PHOSPHORYLCHOLINE CONJUGATES AND CORRESPONDING ANTIBODIES



(57) **Abstract:** IgG and IgM autoantibody levels against phosphorylcholine in subjects with hypertension (diastolic pressure >95 mmHg) were determined at baseline in order to determine the importance of antibodies for the development of atherosclerosis. The results show that increases in intima-media thickness (IMT) at a follow-up four years after baseline were significantly less prevalent in subjects having high autoantibodies particularly high IgM autoantibodies, to phosphorylcholine. The presence or absence of autoantibodies, particularly IgM autoantibodies, against phosphorylcholine is thus related to an increased or decreased risk of developing ischemic cardiovascular diseases. A method to determining antibodies, particularly IgM antibodies, toward phosphorylcholine is proposed in this invention to identify subjects at risk of developing ischemic cardiovascular diseases. Animal experiments show that medium to high levels of antibodies, particularly IgM antibodies, can be detected in plasma after active immunization with a keyhole limpet hemocyanin (KLH-phosphorylcholine conjugate). A pharmaceutical composition comprising a phosphorylcholine conjugate (active immunization) or an antibody preparation, for example a monoclonal antibody, with specificity to a phosphorylcholine conjugate (passive immunization) is proposed and the use of these compositions as active or passive immunogen is the treatment or prevention of atherosclerosis.



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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

national application No
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A. CLASSIFICATION OF SUBJECT MATTER C07K16/44 A61K47/48 G01N33/92 G01N33/68		
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) A61K G01N C07K		
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, DISSERTATION ABS, CHEM ABS Data, EMBASE, BIOSIS		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE DISSERTATION ABSTRACTS 'Online! ProQuest Info&Learning; 2002, BINDER, CHRISTOPH JOHANNES: "Defining innate and adaptive immune mechanisms in the atheroprotective effect of immunization with oxidized low-density lipoproteins" XP002355546 retrieved from DIALOG accession no. 01907366 Database accession no. AADAA-I3064459 abstract & DISSERTATION ABSTRACTS INTERNATIONAL, vol. 63, no. 09-b, 2002, page 4109, -/--	1-9
☒ 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. *G* document member of the same patent family		
Date of the actual completion of the international search 10 February 2006		Date of mailing of the international search report 24/02/2006
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Dullaart, A

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X	ROSE N ET AL: "Autoimmunity: Busting the atherosclerotic plaque" NATURE MEDICINE 01 JUN 2003 UNITED STATES, vol. 9, no. 6, 1 June 2003 (2003-06-01), pages 641-642, XP002355526 ISSN: 1078-8956 page 641, left-hand column, paragraph 3 -----	1-9
X	BINDER C J ET AL: "Innate and acquired immunity in atherogenesis" NATURE MEDICINE 01 NOV 2002 UNITED STATES, vol. 8, no. 11, 1 November 2002 (2002-11-01), pages 1218-1226, XP002355527 ISSN: 1078-8956 figure 3 page 1224, right-hand column, paragraph 2 -----	1-9
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Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Box 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:

Although claim 9 is directed to a method of treatment of the human/animal body, a search has been carried out, based on the alleged effects of the compound/composition.
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 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 fee, this Authority did not invite payment of any additional fee.
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.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ 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: 1-3 and 9 in part, and 4-8

Use of a phosphorylcholine conjugate in the treatment of atherosclerosis or related disease, and corresponding method of prophylactic or therapeutic treatment.

2. claims: 1-3 and 9 in part

Use of an antibody specific for a phosphorylcholine conjugate in the treatment of atherosclerosis or related disease, and corresponding method of prophylactic or therapeutic treatment.

3. claims: 10-15

Method of diagnosing the presence or absence of IgM or IgG antibodies as defined in these claims.

4. claim: 16

Use of a phosphorylcholine conjugate for assessing a patient's risk of developing or progression of ischemic cardiovascular disease as defined in this claim.

INTERNATIONAL SEARCH REPORT

Information on patent family members

national application No

T/GB2005/001463

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