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- (74) Agent: GUTERMAN, Sonia, K.; Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, MA 02111 (US).
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US 60/314,329 (CIP)
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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.*

(54) Title: COMPOSITIONS AND METHODS FOR DETECTION AND REGULATION OF GENES ASSOCIATED WITH RUPTURED ATHEROSCLEROTIC PLAQUE

(57) Abstract: Compositions and methods for detecting tissue specificity for expression of perilipin, Hormone Sensitive Lipase (HSL) and Adipocyte Differentiation Related Protein (ADRP) mRNA and polypeptide are provided, and show that perilipin mRNA is located in plaques containing a thrombus, and perilipin polypeptide is found in foam cells of intimal xanthomas, in the shoulder area of stable lesions, and near the site of cap rupture in lesions containing a thrombus. HSL expression increases during plaque progression, and co-localizes to the same sites as perilipin. ADRP is expressed in all stages of human atherosclerosis, and is most important during the initial phases of lipid uptake. Perilipin expression increases in more lipid-laden macrophage derived foam cells, and replaces ADRP on the surface of the lipid droplet, thereby regulating accessibility to the lipolytic enzyme HSL. Perilipin and HSL are markers for progression of atherosclerosis associated with ruptured plaque.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/26913

A. CLASSIFICATION OF SUBJECT MATTER				
IPC(7) : A61B 5/055; C07K 7/00, 16/40; C12N 5/20; C07H 21/04; A01K 67/027				
US CL : 424/9.341; 530/326, 388.26, 435/326; 536/23.5; 800/14				
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) U.S. : 424/9.341; 530/326, 388.26, 435/326; 536/23.5; 800/14				
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) Medline, WEST, STN				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X,P	FABER et al. Identification of genes potentially involved in rupture of human atherosclerotic plaques. Circ. Res. 14 September 2001, Vol. 89, No. 6, pages 547-554.	1-11		
X	GREENBERG et al. Perilipin, a major hormonally regulated adipocyte-specific phosphoprotein associated with the periphery of lipid storage droplets. J. Biol. Chem. 15 June 1991, Vol. 266, No. 17, pages 11341-11346.	18, 22-23, 25-26 and 28		
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Y		24, 27 and 33-36		
X	BLANCHETTE-MACKIE et al. Perilipin is located on the surface layer of intracellular lipid droplets in adipocytes. J. Lipid Res. June 1995, Vol. 36, No. 6, pages 1211-1226.	22-23, 25-26 and 28		
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Y		24, 27 and 33-36		
A	MEIJER JD. Hormone sensitive lipase: structure, function and regulation. Thesis written at the Biochemical Physiology Research Group, Department of Experimental Zoology, University of Utrecht, March 1998. See entire document.	1-15, 17-36		
X,P	SCHWARTZ et al. Molecular markers, fibrous cap rupture, and the vulnerable plaque: New experimental opportunities. Circ Res. 14 September 2001, Vol. 89, No. 6, pages 471-473.	1-11		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"> * 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 application or patent 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 </td> <td style="width: 50%; border: none;"> "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 </td> </tr> </table>			* 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 application or patent 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
* 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 application or patent 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		Date of mailing of the international search report		
23 November 2003 (23.11.2003)		13 FEB 2004		
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230		Authorized officer <i>Telicia D. Roberts for</i> Maher M. Haddad Telephone No. (703) 308-0196		

INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,585,462 A (LONDOS et al) 17 December 1996 (17.12.1996), entire document.	22-23, 25-27 and 28 ----- 24 and 33-36

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/26913

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claim 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. Claim Nos.: 16
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

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.