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(54) Risk Markers For Cardiovascular Disease

(57) Provided herein methods for determining whether a subject, particularly a human subject, is at risk of developing, having, or experiencing a complication of cardiovascular disease, and methods of treating subjects who are identified by the current methods of being at risk for cardiovascular disease. In one embodiment, the method comprises determining levels of one or more oxidized apolipoprotein A-I related biomolecules in a bodily sample from the subject. Also, provided are kits and reagents for use in the present methods. Also provided are methods for monitoring the status of cardiovascular disease in a subject or the effects of therapeutic agents on subjects with cardiovascular disease. Such method comprising determining levels of one or more oxidized apolipoprotein A-I related molecules in bodily samples taken from the subject over time or before and after therapy.

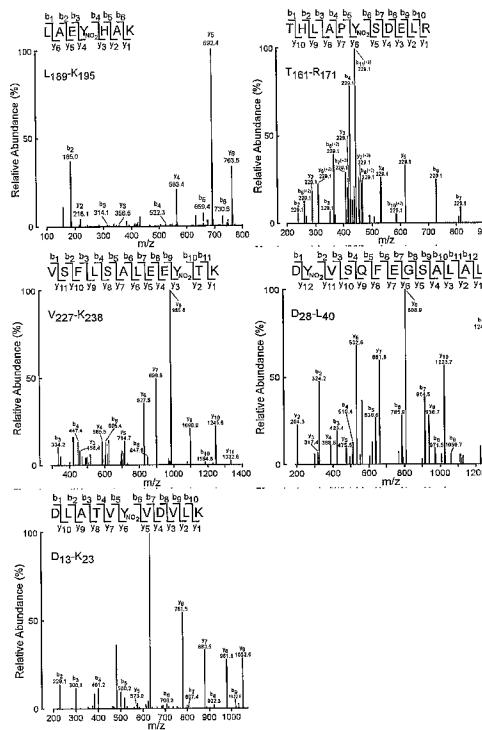


Figure 1



EUROPEAN SEARCH REPORT

Application Number
EP 10 18 1021

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (IPC)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	WO 01/38395 A1 (HEART RES INST LTD [AU]; STOCKER ROLAND [AU]; WANG XING LI [US]; WILCK) 31 May 2001 (2001-05-31) * pages 7-8 * * pages 17-18 *	1-8, 11-15 9,10	INV. G01N33/53 G01N33/92 G01N33/68
X	----- EP 0 722 086 A1 (YAMASA CORP [JP]) 17 July 1996 (1996-07-17) * example 9 * * columns 1-2 * * columns 15-16 *	1-8, 11-15 9,10	
X	----- BERGT CONSTANZE ET AL: "Tyrosine chlorination in apo A-I is directed by lysine residues when hypochlorous acid oxidizes HDL.", FREE RADICAL BIOLOGY & MEDICINE, vol. 35, no. Supplement 1, 20 November 2003 (2003-11-20), - 24 November 2003 (2003-11-24), page S101, XP008081307, & 10TH ANNUAL MEETING OF THE SOCIETY FOR FREE RADICAL BIOLOGY AND MEDICINE; SEATTLE, WA, USA; NOVEMBER 20-24, 2003 ISSN: 0891-5849 * abstract *	12,13 9,10	
Y	----- -/-		TECHNICAL FIELDS SEARCHED (IPC)
			G01N
1 The present search report has been drawn up for all claims			
Place of search		Date of completion of the search	Examiner
The Hague		9 March 2011	Lunter, Pim
CATEGORY OF CITED DOCUMENTS		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			



EUROPEAN SEARCH REPORT

Application Number

EP 10 18 1021

DOCUMENTS CONSIDERED TO BE RELEVANT					
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)		
X	BERGT C ET AL: "Lysine Residues Direct the Chlorination of Tyrosines in YXXK Motifs of Apolipoprotein A-I When Hypochlorous Acid Oxidizes High Density Lipoprotein", JOURNAL OF BIOLOGICAL CHEMISTRY 20040227 AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY INC. US, vol. 279, no. 9, 3 December 2003 (2003-12-03), pages 7856-7866, XP002627284, DOI: DOI:10.1074/jbc.M309046200 * abstract * -----	12,13			
Y		9,10			

TECHNICAL FIELDS SEARCHED (IPC)					

The present search report has been drawn up for all claims					
Place of search	Date of completion of the search	Examiner			
The Hague	9 March 2011	Lunter, Pim			
CATEGORY OF CITED DOCUMENTS					
X : particularly relevant if taken alone	T : theory or principle underlying the invention				
Y : particularly relevant if combined with another document of the same category	E : earlier patent document, but published on, or after the filing date				
A : technological background	D : document cited in the application				
O : non-written disclosure	L : document cited for other reasons				
P : intermediate document	& : member of the same patent family, corresponding document				



CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

- Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

1-15

The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).



**LACK OF UNITY OF INVENTION
SHEET B**

Application Number
EP 10 18 1021

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-15

Methods for characterizing subject's risks, comprising determining levels of oxidized HDL, oxidized apoAI or an oxidized apoAI-peptide fragment; antibodies and kits for said methods

Methods for characterizing a subject's risks profile; for evaluating therapy; for monitoring cardiovascular disease over time, comprising determining levels of apoAI-related biomolecules

2. claims: 16-18

Agents for use in methods of treating a subject to reduce the risk of a cardiovascular disease

ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.

EP 10 18 1021

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

09-03-2011

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专利名称(译)	心血管疾病的风险标记		
公开(公告)号	EP2306192A3	公开(公告)日	2011-08-10
申请号	EP2010181021	申请日	2004-12-06
[标]申请(专利权)人(译)	克里夫兰诊所基金会		
申请(专利权)人(译)	克里夫兰诊所基金会		
当前申请(专利权)人(译)	克里夫兰诊所基金会		
[标]发明人	HAZEN STANLEY PENN MARC S SMITH JONATHAN ZHANG RENLIANG ZHENG LEMIN		
发明人	HAZEN, STANLEY PENN, MARC S SMITH, JONATHAN ZHANG, RENLIANG ZHENG, LEMIN		
IPC分类号	G01N33/53 G01N33/92 G01N33/68 A61B C07K16/18		
CPC分类号	A61P3/06 A61P7/02 A61P9/00 A61P9/10 A61P29/00 A61P43/00 G01N33/6893 G01N33/92 G01N2333/775 G01N2800/32 C07K16/18 G01N33/561		
优先权	60/527178 2003-12-05 US 60/600527 2004-08-11 US 60/600551 2004-08-11 US 60/619044 2004-10-15 US		
其他公开文献	EP2306192A2 EP2306192B1		
外部链接	Espacenet		

摘要(译)

本文提供了用于确定受试者，特别是人受试者是否有发展，患有或经历心血管疾病并发症的风险的方法，以及治疗通过目前存在心血管疾病风险的方法鉴定的受试者的方法。在一个实施方案中，该方法包括测定来自受试者的身体样品中一种或多种氧化的载脂蛋白A-I相关生物分子的水平。此外，提供了用于本方法的试剂盒和试剂。还提供了用于监测受试者中心血管疾病状态或治疗剂对患有心血管疾病的受试者的影响的方法。这种方法包括确定随时间或在治疗之前和之后取自受试者的身体样品中一种或多种氧化载脂蛋白A-1相关分子的水平。

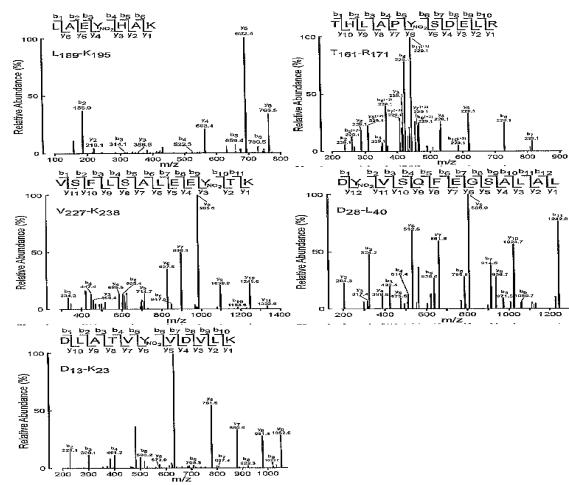


Figure 1