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(54) **NOVEL PHOSPHORYLATION OF CARDIAC TROPONIN I AS A MONITOR FOR CARDIAC INJURY**

(57) This invention relates to novel phosphorylation sites in cardiac Troponin I that are associated with the onset of heart failure. The phosphorylation sites, i.e., serine 5, tyrosine 26, threonine 51, serine 166, threonine 181 and/or serine 199, can be used as biomarkers for (i) identifying subjects at risk for the development of heart failure, (ii) treating subjects having a higher than normal level of the biomarker, and (iii) monitoring therapy of a subject at risk for the development of heart failure. Also described are antibodies, reagents, and kits for carrying out a method of the present invention.

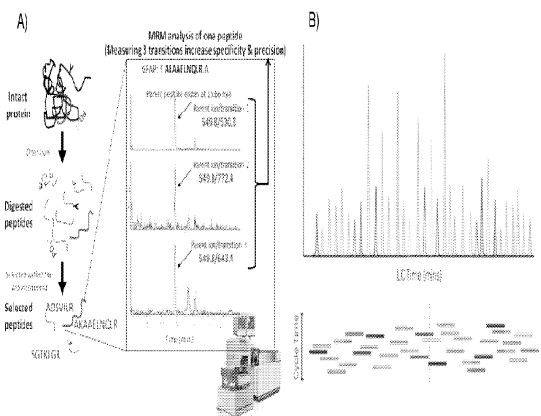


Figure 1. An illustration of MRM assay A) MRM measures peptides unique to a target protein; B) Scheduled MRM™ Algorithm.



EUROPEAN SEARCH REPORT

Application Number
EP 17 15 2485

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	US 2004/072255 A1 (VAN EYK JENNIFER E [CA] ET AL) 15 April 2004 (2004-04-15) * paragraph [0016] * * paragraph [0038] * * claims 5,6 *	1-15	INV. C07K16/18 G01N33/53 G01N33/531 A61K39/395 A61P9/00
A	----- ANDREW E. MESSER ET AL: "The use of phosphate-affinity SDS-PAGE to measure the cardiac troponin I phosphorylation site distribution in human heart muscle", PROTEOMICS - CLINICAL APPLICATIONS, 13 October 2009 (2009-10-13), pages NA-NA, XP055353458, DE ISSN: 1862-8346, DOI: 10.1002/prca.200900071 * the whole document *	1-15	
A	----- BAR-OR D ET AL: "Diagnostic potential of phosphorylated cardiac troponin I as a sensitive, cardiac-specific marker for early acute coronary syndrome: Preliminary report", CLINICA CHIMICA ACTA, ELSEVIER BV, AMSTERDAM, NL, vol. 362, no. 1-2, 1 December 2005 (2005-12-01), pages 65-70, XP027648665, ISSN: 0009-8981 [retrieved on 2005-12-01] * the whole document *	1-15	
----- -The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 9 March 2017	Examiner Schwachtgen, J
CATEGORY OF CITED DOCUMENTS 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 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			

EPO FORM 1503 03.02 (P04C01)



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CLAIMS INCURRING FEES

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

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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):

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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.

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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:

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see sheet B

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

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

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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:

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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:

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1-15(partially)

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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 17 15 2485

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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:

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1. claims: 1-15(partially)

means and methods of detecting cardiac troponin I
phosphorylated at serine 166

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2. claims: 1-15(partially)

means and methods of detecting cardiac troponin I
phosphorylated at threonine 181

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3. claims: 1-15(partially)

means and methods of detecting cardiac troponin I
phosphorylated at serine 5

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4. claims: 1-15(partially)

means and methods of detecting cardiac troponin I
phosphorylated at tyrosine 26

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5. claims: 1-15(partially)

means and methods of detecting cardiac troponin I
phosphorylated at threonine 51

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6. claims: 1-15(partially)

means and methods of detecting cardiac troponin I
phosphorylated at serine 199

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

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5 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.

09-03-2017

10	Patent document cited in search report	Publication date	Patent family member(s)	Publication date
	US 2004072255 A1	15-04-2004	AU 2003273674 A1	04-05-2004
			CA 2501756 A1	22-04-2004
			EP 1554587 A2	20-07-2005
15			JP 2006502203 A	19-01-2006
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			WO 2004034060 A2	22-04-2004

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EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

专利名称(译)	心肌肌钙蛋白i的新磷酸化作为心脏损伤的监测		
公开(公告)号	EP3178846A3	公开(公告)日	2017-07-26
申请号	EP2017152485	申请日	2011-02-17
[标]申请(专利权)人(译)	雪松-西奈医学中心 高等教育科学研究及疾病护理协会		
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IPC分类号	C07K16/18 G01N33/53 G01N33/531 A61K39/395 A61P9/00		
代理机构(译)	J A KEMP		
优先权	61/305298 2010-02-17 US PCT/US2011/025301 2011-02-17 WO		
其他公开文献	EP3178846A2 EP3178846B1		
外部链接	Espacenet		

摘要(译)

本发明涉及心脏肌钙蛋白I中与心力衰竭发作有关的新磷酸化位点。磷酸化位点，即丝氨酸5，酪氨酸26，苏氨酸51，丝氨酸166，苏氨酸181和/或丝氨酸199，可用作生物标记物，用于(i) 鉴定具有发生心力衰竭风险的受试者，(ii) 治疗具有高于正常水平的生物标志物的受试者，和(iii) 监测具有发生心力衰竭风险的受试者的治疗。还描述了用于实施本发明方法的抗体，试剂和试剂盒。

