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Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

[Continued on next page]

(54) Title: NOVEL PEPTIDES THAT PROMOTE LIPID EFFLUX

ABCA1-dependent Cholesterol Efflux

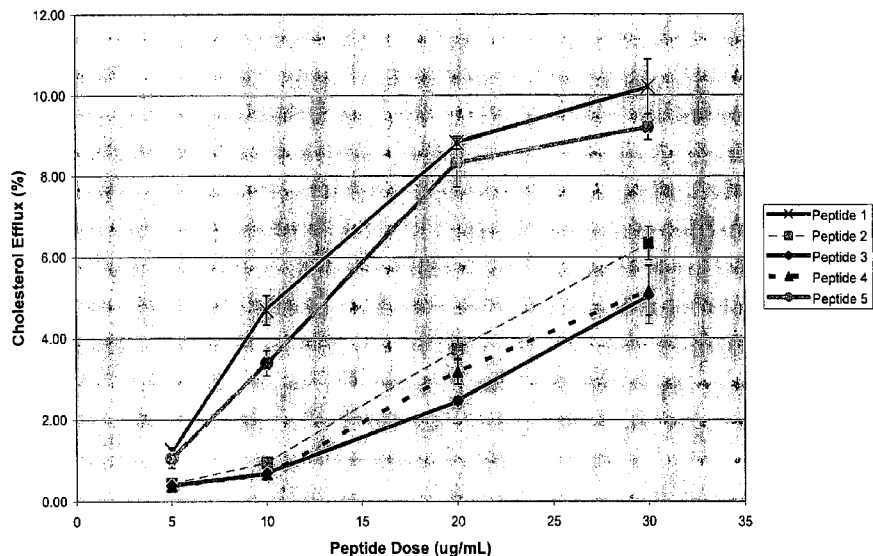


FIG. 4

(57) Abstract: Disclosed herein are peptides with domains that promote lipid efflux from cells and optionally possess at least one anti-inflammatory domain and/or a domain that stimulates LCAT activity. The present invention provides the use of the peptides disclosed herein in the preparation of a medicament. Provided herein are methods of using the peptides to treat or inhibit diseases including dyslipidemic disorders, stroke and myocardial infarction. Also provided are methods of detecting plaque in vessels using the labeled peptides of the present invention.

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— *with information concerning authorization of rectification  
of an obvious mistake under Rule 91.1*

**(88) Date of publication of the international search report:**  
4 December 2008

**(15) Information about Correction:**

**Previous Correction:**  
see Notice of 24 July 2008

INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2007/014135

A. CLASSIFICATION OF SUBJECT MATTER  
INV. C07K14/775

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)  
C12N 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, Sequence Search, WPI Data, CHEM ABS Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/008775 A (ISTITUTO BIOCHIMICO NAZ SAVIO [IT]; D ANDREA LUCA [IT]; PEDONE CARLO []) 26 January 2006 (2006-01-26) sequence 1	1-6,9-20
A	WO 2005/058938 A (UNIV CALIFORNIA [US]; BIELICKI JOHN K [US]; NATARAJAN PRADEEP [US]) 30 June 2005 (2005-06-30) sequence 39	1-6,9-20
A	US 2006/088524 A1 (MORRISSEY JAMES H [US] ET AL) 27 April 2006 (2006-04-27) sequence 31	1-6,9-20
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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.
- \* & \* document member of the same patent family

Date of the actual completion of the international search

2 October 2008

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13/10/2008

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## INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>NAVAB M ET AL: "ORAL D-4F CAUSES FORMATION OF PRE-BETA HIGH-DENSITY LIPOPROTEIN AND IMPROVES HIGH-DENSITY LIPOPROTEIN-MEDIATED CHOLESTEROL EFFLUX AND REVERSE CHOLESTEROL TRANSPORT FROM MACROPHAGES IN APOLIPOPROTEIN E-NULL MICE" CIRCULATION, AMERICAN HEART ASSOCIATION, DALLAS, TX, vol. 109, no. 25, 29 June 2004 (2004-06-29), pages 3215-3220, XP009049368 ISSN: 0009-7322 abstract page 3215, left-hand column</p>	1-6,9-20
A	<p>-----</p> <p>MENDEZ ARMANDO J ET AL: "Synthetic amphipathic helical peptides that mimic apolipoprotein A-I in clearing cellular cholesterol" JOURNAL OF CLINICAL INVESTIGATION, vol. 94, no. 4, 1994, pages 1698-1705, XP002479089 ISSN: 0021-9738 abstract page 1698, right-hand column, paragraph 2 table 1</p>	1-6,9-20
A	<p>-----</p> <p>REMALEY ALAN T ET AL: "Synthetic amphipathic helical peptides promote lipid efflux from cells by an ABCA1-dependent and an ABCA1-independent pathway" JOURNAL OF LIPID RESEARCH, BETHESDA, MD, US, vol. 44, no. 4, 1 April 2003 (2003-04-01), pages 828-836, XP002383068 ISSN: 0022-2275 abstract</p>	1-6,9-20
A	<p>-----</p> <p>NEUFELD EDWARD B ET AL: "The ABCA1 transporter functions on the basolateral surface of hepatocytes" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 297, no. 4, October 2002 (2002-10), pages 974-979, XP002479090 ISSN: 0006-291X the whole document</p> <p>-----</p>	1-6,9-20

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2007/014135

## 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:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable 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.:  
  
1-6 and 9-20 (all partially; SEQ ID NOs 1, 130 and 624)
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 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.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-6 and 9-20 (all partially)

An isolated peptide of formula (A-B-C)<sub>n</sub>, wherein A is GEEMRDRARAHVDALRTH (SEQ ID NO:1 of present application), C comprises helix 8 of ApoA-I, B is a linking group between A and C and n is an integer from 1-10, and subject-matter relating thereto.

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Inventions 2-100: claim 1-6 and 9-20 (all partially)

Idem as subject 1 but limited to each of the polypeptides as in SEQ ID NO:2-14 and combinations thereof, respectively. Due to the high number of possible peptides, an arbitrary number of 100 inventions has been chosen. The Applicant is asked to indicate for which sequence(s) or combination(s) of sequences a further search is to be carried out.

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Invention 101: claims 7 and 9-20 (all partially)

An isolated peptide of formula D-I-W, wherein D is absent, I is GABA and W is absent, and subject-matter relating thereto.

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Inventions 102-200: claims 7 and 9-20 (all partially)

Idem as subject 3 but limited to each of the polypeptides as in SEQ ID NO:15, 16, GABA, Pro, 7, 25, 26, 21, 22 and combinations thereof, respectively. Due to the high number of possible peptides, an arbitrary number of 100 inventions has been chosen. The Applicant is asked to indicate for which sequence(s) or combination(s) of sequences a further search is to be carried out.

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Invention 201: claims 8 and 9-20 (all partially)

An isolated peptide of formula D-R-S-W-T-N-O-(X<sub>n</sub>-Y<sub>z</sub>-Z<sub>m</sub>)S-O'-N'-T'-W'-S'-R'-D')<sub>r</sub>, wherein D, D', R, R', S, S', W, W', T, T', N, N', O, O' and Y are absent, X and Y are each comprised of 5-25 amino acid residues, provided an amphipathic alpha helix is obtained, and subject-matter relating thereto.

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Inventions 202-300: claims 8 and 9-20 (all partially)

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Idem as subject 5 but limited to each of the polypeptides as in SEQ ID NO:15, 16, GABA, 21, 22, etc., and combinations thereof, respectively. Due to the high number of possible peptides, an arbitrary number of 100 inventions has been chosen. The Applicant is asked to indicate for which sequence(s) or combination(s) of sequences a further search is to be carried out.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/014135

Patent document cited in search report	Publication date	Publication date	Patent family member(s)
WO 2006008775	A	26-01-2006	NONE
WO 2005058938	A	30-06-2005	AU 2004299486 A1
			CA 2549529 A1
			EP 1706131 A2
US 2006088524	A1	27-04-2006	NONE