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(71) Applicants (for all designated States except US): **UNIVERSITAIR MEDISCH CENTRUM UTRECHT** [NL/NL]; Heidelberglaan 100, NL-3584 CX Utrecht (NL). **UNIVERSITEIT UTRECHT** [NL/NL]; Heidelberglaan 8, NL-3584 CS Utrecht (NL).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **MEYAARD, Linde** [NL/NL]; Waterweg 19, NL-3713 HC De Bilt (NL). **LEB-BINK, Robert Jan** [NL/US]; 550 Gene Friend Way, Apt 221, San Francisco, CA 94158 (US).

(74) Agent: **VAN LOON, C.J.J.**; Vereenigde, NL-2517 JR Den Haag (NL).

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13 March 2008

(54) Title: INTERFERING IN ACTIVATION OF AN IMMUNE CELL BY INFLUENCING INTERACTION OF LAIR AND COLLAGEN.

(57) Abstract: The invention provides a method for interfering in activation of an immune cell, comprising providing a substance which specifically interacts in the binding of leukocyte-associated immunoglobulin-like receptor (LAIR) and collagen. The invention in one aspect provides a method for down regulation of activation of an immune cell. In another aspect the invention provides a method for up regulation of activation of an immune cell. The invention further provides pharmaceutical compositions and uses thereof.



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## INTERNATIONAL SEARCH REPORT

International application No

PCT/NL2007/050093

A. CLASSIFICATION OF SUBJECT MATTER  
 INV. C12Q1/68 C07K16/00

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)

C12Q 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, EMBASE, BIOSIS, FSTA, Sequence Search

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/010197 A (GENSET SA [FR]; LUCAS JOHN [US]; SCALIA AARON [US]; DIALYNAS DENO [US]) 6 February 2003 (2003-02-06) page 2, column 35 - page 3, column 13 page 12, lines 23-32	16, 17, 20
X	WO 03/077937 A (NATIMMUNE AS [DK]; LARSEN JESPER LUND [DK]; KONGERSLEV LEIF [DK]) 25 September 2003 (2003-09-25) claims 1, 18; sequence 1	16, 17, 20
X	WO 02/098450 A (UNI MEDISCH CT UTRECHT [NL]; UNIV UTRECHT [NL]; MEYAARD LINDA [NL]) 12 December 2002 (2002-12-12) page 2, lines 4-35 page 3, line 34 - page 5, line 10 page 5, lines 12-17	1-3, 5, 7-9
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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

27 August 2007

Date of mailing of the international search report

11/01/2008

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

Leber, Thomas

## INTERNATIONAL SEARCH REPORT

International application No

PCT/NL2007/050093

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MEYAARD L ET AL: "The Epithelial Cellular Adhesion Molecule (Ep-CAM) is a ligand for the Leukocyte-associated Immunoglobulin-like Receptor (LAIR)" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 194, no. 1, 2 July 2001 (2001-07-02), pages 107-112, XP002190969 ISSN: 0022-1007 the whole document	1-3,5, 7-9
A	KNIGHT C GRAHAM ET AL: "Collagen-platelet interaction: Gly-Pro-Hyp is uniquely specific for platelet Gp VI and mediates platelet activation by collagen" CARDIOVASCULAR RESEARCH, XX, XX, vol. 41, no. 2, February 1999 (1999-02), pages 450-457, XP002425787 ISSN: 0008-6363 the whole document	
A	MEYAARD L ET AL: "Leukocyte-Associated Ig-like Receptor-1 functions as an inhibitory receptor on cytotoxic T cells" JOURNAL OF IMMUNOLOGY, THE WILLIAMS AND WILKINS CO. BALTIMORE, US, vol. 162, 1999, pages 5800-5804, XP002190968 ISSN: 0022-1767 figure 2	
A	LEBBINK ROBERT JAN ET AL: "The mouse homologue of the leukocyte-associated Ig-like receptor-1 is an inhibitory receptor that recruits Src homology region 2-containing protein tyrosine phosphatase (SHP)-2, but not SHP-1." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD. : 1950) 1 MAY 2004, vol. 172, no. 9, 1 May 2004 (2004-05-01), pages 5535-5543, XP002407123 ISSN: 0022-1767 the whole document	
A	US 2003/181392 A1 (SCHNELLMANN RICKY GENE [US] ET AL) 25 September 2003 (2003-09-25) claim 7	
A	US 6 894 029 B1 (HSIEH YUN-HWA PEGGY [US]) 17 May 2005 (2005-05-17) claim 15	
A	US 6 992 172 B1 (CHANG ROBERT C [US] ET AL) 31 January 2006 (2006-01-31)	

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# INTERNATIONAL SEARCH REPORT

International application No  
PCT/NL2007/050093

## C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 1 494 031 A (BAYER HEALTHCARE LLC [US]; MAYO FOUNDATION FOR MEDICALEDU [US]) 5 January 2005 (2005-01-05) -----	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 10-15

Claim 10 is dependent on claim 1 and refers to a specific binding body for LAIR causing up-regulation of the activation of an immune cell. The substance is thus defined by the result to be achieved only, without providing any technical features of the product as such. Thus, claim 10 lacks clarity (Art 6 PCT). Having regard to the description, it would appear that not a single binding body of LAIR is disclosed which causes upregulation of the activation of an immune cell. Thus, claim 10 lacks clarity to such an extent that no meaningful search was possible.

Claims 11-15 refer to binding bodies that cause up-regulation of the activation of an immune cell and has affinity to collagen. The substance is thus defined by the result to be achieved only, without providing any technical features of the product as such. Thus, claims 11-15 lack clarity (Art 6 PCT). Having regard to the description, it would appear that the only substance disclosed therein that would fall under the scope of claims 11-15 appears to be soluble LAIR (LAIR-2). This embodiment, however, does not fall within the range of the first invention presently searched. Thus, as far as the first invention is concerned, claims 11-15 lack clarity to such an extent (Art 6 PCT) that no meaningful search could be carried out.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/NL2007/050093

## 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.: 10-15  
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:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
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 all searchable 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.:
  
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.:  
1-5, 10-15, 20(partly); 7-9, 16, 17(fully)

### 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 1-5,10-15,20(partly); 7-9,16,17(fully)

Pharmaceutical compositions comprising a peptide G-X-Y repeats, methods of interfering in activation of immune cells using such peptides whereby the peptide is defined on the basis of the 1. peptide mentioned in claim 20.

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Invention 2-13: claims 1-5,10-15,20(partly); 7-9,16,17,21(fully)

Pharmaceutical compositions comprising a peptide G-X-Y repeats, methods of interfering in activation of immune cells using such peptides whereby the peptide is defined on the basis of the 2...13. peptide mentioned in claim 20.

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Invention 14: claims 1-5,10-15(partly); 6,18(fully)

Pharmaceutical compositions comprising a human or humanised antibody against collagen and methods of interfering in activation of immune cells using such antibodies.

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Invention 15: claims 19,22-35

LAIR-2 as pharmaceutical compositions, LAIR or soluble LAIR for medical use, compounds reducing LAIR activity, methods of treatment relating to LAIR and methods for LAIR-2 detection.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/NL2007/050093
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Patent document cited in search report	A	Publication date	Patent family member(s)	Publication date
WO 03010197	A	06-02-2003	NONE	
<hr style="border-top: 1px dashed black;"/>				
WO 03077937	A	25-09-2003	AT 337014 T	15-09-2006
			AU 2003215524 A1	29-09-2003
			CN 1652813 A	10-08-2005
			DE 60307701 T2	11-10-2007
			DK 1344533 T3	08-01-2007
			EP 1344533 A1	17-09-2003
			ES 2271515 T3	16-04-2007
			JP 2005526084 T	02-09-2005
			US 2004006009 A1	08-01-2004
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WO 02098450	A	12-12-2002	EP 1264598 A1	11-12-2002
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US 6894029	B1	17-05-2005	NONE	
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US 6992172	B1	31-01-2006	NONE	
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EP 1494031	A	05-01-2005	JP 2005046137 A	24-02-2005
<hr style="border-top: 1px dashed black;"/>				