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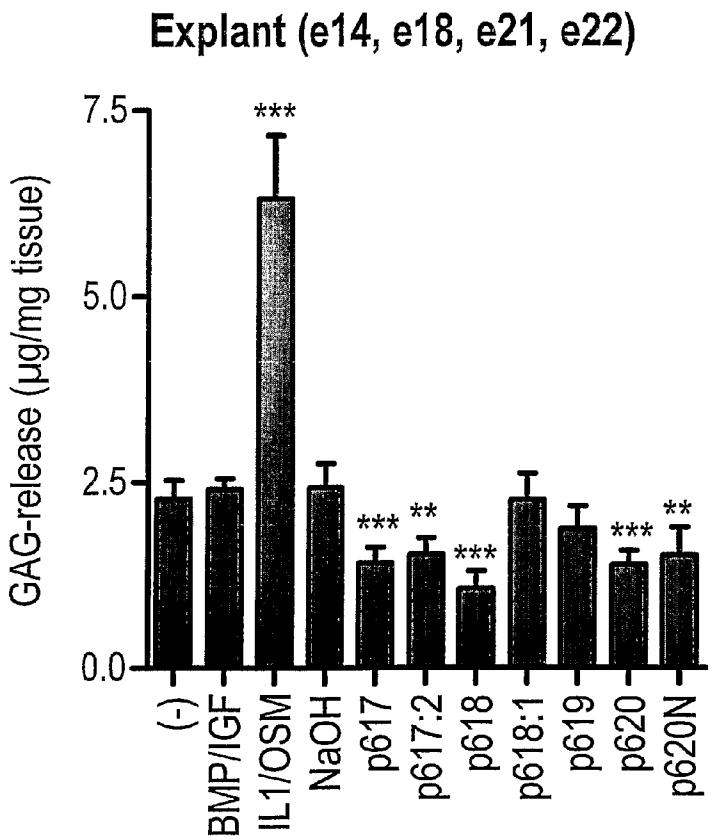
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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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[Continued on next page]

(54) Title: INTEGRIN I-DOMAIN BINDING PEPTIDES



(57) Abstract: The present invention provides novel polypeptide comprising the amino acid sequence of SEQ ID NOS: 1, 2, 3, 4 or 5, variants, fusions or derivatives thereof, and pharmaceutical formulations of the same. The peptides and formulations of the invention are useful for treating diseases or conditions capable of being treated by an agent which modulates the function of an integrin and/or a metzincin, such as arthritic diseases, inflammatory diseases and conditions and cancer. Also provided are diagnostic methods for such diseases and conditions, and methods of screening for candidate compounds with efficacy in the treatment of such diseases and conditions.

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GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:
— *of inventorship (Rule 4.17(iv))*

Published:
— *with international search report*

(88) Date of publication of the international search report:
3 May 2007

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.

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2006/003015

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K7/64 C07K7/06 G01N33/53 A61K38/08 A61K38/12

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/110477 A (CTT CANCER TARGETING TECHNOLOG [FI]; STEFANIDAKIS MICHAEL [FI]; BJOERK) 23 December 2004 (2004-12-23) the whole document	1-13,15, 17,19, 21-96
X	STEFANIDAKIS MICHAEL ET AL: "Identification of a negatively charged peptide motif within the catalytic domain of progelatinases that mediates binding to leukocyte beta2 integrins." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 36, 5 September 2003 (2003-09-05), pages 34674-34684, XP002411304 ISSN: 0021-9258 cited in the application the whole document	1-10, 21-23, 27-33, 36-96

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[X] Further documents are listed in the continuation of Box C.

[X] 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	Date of mailing of the international search report
12 December 2006	22/01/2007

Name and mailing address of the ISA/	Authorized officer
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	Madruga, Jaime

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BJORKLUND M ET AL: "Peptide Inhibition of Catalytic and Noncatalytic Activities of Matrix Metalloproteinase-9 Blocks Tumor Cell Migration and Invasion" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOCHEMICAL BIOLOGISTS, BIRMINGHAM,, US, vol. 279, no. 28, 9 July 2004 (2004-07-09), pages 29589-29597, XP002990968 ISSN: 0021-9258 cited in the application the whole document	1-10, 21-23, 27-33, 36-96
X	WO 03/022991 A2 (UNIV TEXAS [US]; PASQUALINI RENATA [US]; ARAP WADIH [US]; KOLONIN MIKH) 20 March 2003 (2003-03-20) paragraph [0044]; example 6; sequence 39	1-10, 21-23, 28,29, 36-96
A	WO 97/16557 A (BOEHRINGER INGELHEIM INT [DE]; KARLSRUHE FORSCHZENT [DE]; HEKELE ARMIN) 9 May 1997 (1997-05-09) sequence 1	
A	DATABASE Geneseq [Online] 4 February 2002 (2002-02-04), "Peptide #1939 encoded by human foetal liver single exon probe." XP002411307 retrieved from EBI accession no. GSN:ABB34433 Database accession no. ABB34433 abstract & WO 01/57277 A2 (MOLECULAR DYNAMICS INC [US]; PENN SHARRON G [US]; HANZEL DAVID K [US];) 9 August 2001 (2001-08-09)	
A	WO 99/02551 A (HEINO JYRKI [FI]; IVASKA JOHANNA [FI]; KAEPYLAE JARMO [FI]) 21 January 1999 (1999-01-21) the whole document	
A	NYMALM YVONNE ET AL: "Jararhagin-derived RKKH peptides induce structural changes in alpha1I domain of human integrin alpha1beta1." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 279, no. 9, 27 February 2004 (2004-02-27), pages 7962-7970, XP002411305 ISSN: 0021-9258 the whole document	

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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	PASQUALINI R ET AL: "A PEPTIDE ISOLATED FROM PHAGE DISPLAY LIBRARIES IS A STRUCTURAL AND FUNCTIONAL MIMIC OF AN RGD-BINDING SITE ON INTEGRINS" THE JOURNAL OF CELL BIOLOGY, ROCKEFELLER UNIVERSITY PRESS, US, vol. 130, no. 5, September 1995 (1995-09), pages 1189-1196, XP000944635 ISSN: 0021-9525 the whole document	
A	GULLBERG ET AL: "Collagen-binding I domain integrins - what do they do?" PROGRESS IN HISTOCHEMISTRY AND CYTOCHEMISTRY, GUSTAV FISCHER VERLAG, STUTTGART, DE, vol. 37, no. 1, 2002, pages 3-54, XP005032609 ISSN: 0079-6336 the whole document	

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 58-66 and 83 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Claims Nos.: -

Present claims 90-92 relate to a compound which has a given desired property or effect, namely a compound which competes with the binding of a polypeptide accoding to the invention to an integrin I-domain. However, the description does not provide support and disclosure in the sense of Article 6 and 5 PCT for any such compound having the said property or effect and there is no common general knowledge of this kind available to the person skilled in the art. This non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of the claim (PCT Guidelines 9.19 and 9.20).

The search of claims 90-92 was consequently restricted to the broad concept of a compound having the desired property or effect.

Present claims 93-96 relate to a product or a method defined by a general reference to the description. In the present context is considered to lead to a lack of clarity because the claims do not clearly identify the products encompassed as the features cannot be clearly and reliably determined. This makes it impossible to compare the claims to the prior art. As a result, the application does not comply with the requirement of clarity under Article 6 PCT.

The lack of clarity is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of claims 93-96.
The search of claims 93-96 was
restricted to the examples clearly defined in claims 1-89, which is the subject-matter supported and disclosed by the description.

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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/GB2006/003015

Box 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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 58-66 and 83 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] 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:

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 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:

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2006/003015

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004110477 A	23-12-2004	EP 1644031 A1	12-04-2006
		EP 1644032 A1	12-04-2006
		WO 2004110478 A1	23-12-2004
WO 03022991 A2	20-03-2003	CA 2458047 A1	20-03-2003
		EP 1497314 A2	19-01-2005
WO 9716557 A	09-05-1997	AU 7494696 A	22-05-1997
		DE 19540515 C1	06-02-1997
		ZA 9609077 A	24-06-1998
WO 0157277 A2	09-08-2001	AU 3087801 A	14-08-2001
		AU 3087901 A	14-08-2001
		AU 3088001 A	14-08-2001
		AU 3088101 A	14-08-2001
		AU 3088201 A	14-08-2001
		AU 3088301 A	14-08-2001
		AU 3275701 A	14-08-2001
		AU 3275801 A	20-11-2001
		AU 3275901 A	14-08-2001
		AU 3276001 A	14-08-2001
		AU 3311401 A	14-08-2001
		AU 3658901 A	14-08-2001
		EP 1309723 A2	14-05-2003
		EP 1309724 A2	14-05-2003
		EP 1292704 A2	19-03-2003
		EP 1325149 A2	09-07-2003
		EP 1292705 A2	19-03-2003
		EP 1290216 A2	12-03-2003
		EP 1341930 A2	10-09-2003
		EP 1332224 A2	06-08-2003
		EP 1325150 A2	09-07-2003
		EP 1309725 A2	14-05-2003
		EP 1290217 A2	12-03-2003
		GB 2373500 A	25-09-2002
		GB 2374929 A	30-10-2002
		GB 2383043 A	18-06-2003
		GB 2375539 A	20-11-2002
		GB 2375111 A	06-11-2002
		GB 2374872 A	30-10-2002
		GB 2378754 A	19-02-2003
		GB 2382814 A	11-06-2003
		GB 2385053 A	13-08-2003
		GB 2376018 A	04-12-2002
		GB 2376237 A	11-12-2002
		WO 0157270 A2	09-08-2001
		WO 0157271 A2	09-08-2001
		WO 0157272 A2	09-08-2001
		WO 0157273 A2	09-08-2001
		WO 0186003 A2	15-11-2001
		WO 0157274 A2	09-08-2001
		WO 0157275 A2	09-08-2001
		WO 0157276 A2	09-08-2001
		WO 0157278 A2	09-08-2001
		WO 0157251 A2	09-08-2001
		WO 0157252 A2	09-08-2001
		US 2002081590 A1	27-06-2002

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/GB2006/003015

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9902551 A	21-01-1999	AT 235510 T	15-04-2003
		AU 748134 B2	30-05-2002
		AU 8341398 A	08-02-1999
		BR 9810586 A	05-09-2000
		CA 2295219 A1	21-01-1999
		CN 1262688 A	09-08-2000
		DE 69812630 D1	30-04-2003
		DE 69812630 T2	05-02-2004
		EP 0994898 A1	26-04-2000
		ES 2195361 T3	01-12-2003
		HU 0002789 A2	28-12-2000
		JP 2001509515 T	24-07-2001
		NO 20000126 A	10-01-2000
		NZ 501767 A	28-08-2002
		PL 338001 A1	25-09-2000
		RU 2203902 C2	10-05-2003
		US 6096707 A	01-08-2000