

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
2 April 2009 (02.04.2009)

PCT

(10) International Publication Number
WO 2009/039976 A3

(51) International Patent Classification:

A61K 38/17 (2006.01) *A61P 11/00* (2006.01)
A61K 38/01 (2006.01) *A61P 25/28* (2006.01)
A61P 31/20 (2006.01) *A61P 31/00* (2006.01)
A61P 3/00 (2006.01) *A61P 35/00* (2006.01)
A61P 9/00 (2006.01) *A61P 37/00* (2006.01)

(21) International Application Number:

PCT/EP2008/007518

(22) International Filing Date:

9 September 2008 (09.09.2008)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

07017747.2 11 September 2007 (11.09.2007) EP

(71) Applicant (for all designated States except US): **MONDOBIOTECH LABORATORIES AG** [LI/LI]; Herrengasse 21, FL-9490 Vaduz (LI).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BEVEC, Dorian** [DE/DE]; Kriegerstrasse 62, 82110 Germering (DE). **CAVALLI, Fabio** [CH/CH]; Via Pasquée 23, CH-6925 Gentilino (CH). **CAVALLI, Vera** [CH/CH]; Via Pasquée, 23, CH-6925 Gentilino (CH). **BACHER, Gerald** [DE/DE]; Masurenweg 5, 82110 Germering (DE).

(74) Agent: **ARTH, Hans-Lothar**; ABK Patent & Trademark Attorneys, Jasminweg 9, 14052 Berlin (DE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, 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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

— with international search report (Art. 21(3))

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

12 November 2009

(54) Title: USE OF A PEPTIDE AS A THERAPEUTIC AGENT

(57) Abstract: The present invention is directed to the use of the peptide compound Lys-Asp-Gln-Asp-Lys-OH as a therapeutic agent for the prophylaxis and/or treatment of cancer, autoimmune diseases, fibrotic diseases, inflammatory diseases, neurodegenerative diseases, infectious diseases, lung diseases, heart and vascular diseases and metabolic diseases. Moreover the present invention relates to pharmaceutical compositions preferably in form of a lyophilisate or liquide buffer solution or artificial mother milk formulation or mother milk substitute containing the peptide Lys-Asp-Gln-Asp-Lys-OH optionally together with at least one pharmaceutically acceptable carrier, cryoprotectant, lyoprotectant, excipient and/or diluent.



WO 2009/039976 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2008/007518

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K38/17 A61K38/01 A61P31/20 A61P3/00 A61P9/00
A61P11/00 A61P25/28 A61P31/00 A61P35/00 A61P37/00

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)

A61K A61P 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, WPI Data, EMBASE, 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	QIAN ZU-YUAN ET AL: "Sheep kappa-casein peptides inhibit platelet aggregation" BIOCHIMICA ET BIOPHYSICA ACTA, vol. 1244, no. 2-3, 1995, pages 411-417, XP002537012 ISSN: 0006-3002	1,6,8-15
Y	the whole document ----- -/--	2-5

☒ 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.
- *Z* document member of the same patent family

Date of the actual completion of the international search

17 July 2009

Date of mailing of the international search report

01/09/2009

Name and mailing address of the ISA/

European Patent Office, P.O. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Hars, Jesko

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2008/007518

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BAL DIT SOLLIER CLAIRE ET AL: "Effect of kappa-casein split peptides on platelet aggregation and on thrombus formation in the guinea-pig" THROMBOSIS RESEARCH, vol. 81, no. 4, 1996, pages 427-437, XP002537013 ISSN: 0049-3848 the whole document	1,6,8-15
Y	-----	2-5
X	EP 0 343 085 A (CENTRE NAT RECH SCIENT [FR]) 23 November 1989 (1989-11-23) the whole document	1,6,8-15
A	WO 92/07874 A (BRITISH BIO TECHNOLOGY [GB]) 14 May 1992 (1992-05-14) the whole document	1-15
A	EP 0 397 571 A (CENTRE NAT RECH SCIENT [FR]; INST VAISSEAU SANG [FR]) 14 November 1990 (1990-11-14) the whole document	1-15
A	CHERKAOUI S ET AL: "DETERMINATION OF THE STABILITY OF CASEINOGLYCOMACROPEPTIDE IN A COSMETIC LOTION BY USE OF CAPILLARY ZONE ELECTROPHORESIS WITH A COATED CAPILLARY" CHROMATOGRAPHIA, WIESBADEN, DE, vol. 50, no. 5/06, 1 September 1999 (1999-09-01), pages 311-316, XP009016301 ISSN: 0009-5893 the whole document	1-15
A	NEESER J-R ET AL: "SPECIFIC AND NONSPECIFIC INHIBITION OF ADHESION OF ORAL ACTINOMYCES AND STREPTOCOCCI TO ERYTHROCYTES AND POLYSTYRENE BY CASEINOGLYCOPEPTIDE DERIVATIVES" INFECTION AND IMMUNITY, vol. 56, no. 12, 1988, pages 3201-3208, XP002537014 ISSN: 0019-9567 the whole document	1-15
A	US 4 992 420 A (NEESER JEAN-RICHARD [CH]) 12 February 1991 (1991-02-12) the whole document	1-15
A	WO 02/05839 A (NESTLE SA [CH]; NEESER JEAN RICHARD [CH]; AUZANNEAU ISABELLE [FR]) 24 January 2002 (2002-01-24) the whole document	1-15
	----- -/--	

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2008/007518

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01/37850 A (NESTLE SA [CH]; REIMER RAYLENE [CH]; DARIMONT NICOLAU CHRISTIAN [CH];) 31 May 2001 (2001-05-31) the whole document	1-15
P,A	----- DATABASE WPI Thomson Scientific, London, GB; AN 2008-J29627 XP002537019 "Method for preparing recombination human casein macropeptide" & CN 101 165 179 A ((UYBE-N) UNIV BEIJING CHEM IND) 23 April 2008 (2008-04-23) abstract	7
A	----- FRANCHINI A ET AL: "Presence of casein immunoreactive epitopes in molluscs, fish and frog" LIFE SCIENCES, vol. 59, no. 22, 1996, pages 1891-1898, XP002537015 ISSN: 0024-3205 the whole document	1-15
A	----- MIKKELSEN TRINE L ET AL: "Sialic acid-containing milk proteins show differential immunomodulatory activities independent of sialic acid" JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, vol. 53, no. 20, October 2005 (2005-10), pages 7673-7680, XP002537016 ISSN: 0021-8561 the whole document	1-15
A	----- OTANI HAJIME ET AL: "Suppression of interleukin-2 receptor expression on mouse CD4+ T cells by bovine kappa-caseinoglycopeptide" BIOSCIENCE BIOTECHNOLOGY AND BIOCHEMISTRY, vol. 60, no. 6, 1996, pages 1017-1019, XP009119657 ISSN: 0916-8451 the whole document	1-15
A	----- MATIN M A ET AL: "Release of cytotoxic glycopeptides from human acid casein fraction by the action of stomach proteinases" MILCHWISSENSCHAFT, vol. 55, no. 1, 2000, pages 6-10, XP009119756 ISSN: 0026-3788 the whole document	1-15
	----- -/--	

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2008/007518

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 1 188 767 A (KRAFT FOODS HOLDINGS INC [US]) 20 March 2002 (2002-03-20) the whole document	2-5
A	HATZOGLU ANASTASSIA ET AL: "Antiproliferative and receptor binding properties of alpha- and beta-casomorphins in the T47D human breast cancer cell line" EUROPEAN JOURNAL OF PHARMACOLOGY, vol. 310, no. 2-3, 1996, pages 217-223, XP002537306 ISSN: 0014-2999 the whole document	1-15
A	KAMPA MARILENNA ET AL: "Opioid alkaloids and casomorphin peptides decrease the proliferation of prostatic cancer cell lines (LNCaP, PC3 and DU145) through a partial interaction with opioid receptors" EUROPEAN JOURNAL OF PHARMACOLOGY, vol. 335, no. 2-3, 1997, pages 255-265, XP002537307 ISSN: 0014-2999 the whole document	1-15
A	JAKUB FICHNA ET AL: "Opioid peptides in cancer" CANCER AND METASTASIS REVIEWS, KLUWER ACADEMIC PUBLISHERS, DO, vol. 23, no. 3-4, 1 August 2004 (2004-08-01), pages 351-366, XP019205160 ISSN: 1573-7233 the whole document	1-15
A	DATABASE WPI Week 200173 Thomson Scientific, London, GB; AN 2001-629609 XP002537309 & JP 2001 213897 A (KAGOME KK) 7 August 2001 (2001-08-07) abstract	1-15
P,A	WO 2008/071755 A (LORRAINE INST NAT POLYTECH [FR]; UNIV HENRI POINCARÉ NANCY I [FR]; BAL) 19 June 2008 (2008-06-19) the whole document	1-15
A	FR 2 673 374 A (OREAL [FR]) 4 September 1992 (1992-09-04) the whole document	1-15

-/--

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2008/007518

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LOUKAS S ET AL: "OPIOID ACTIVITIES AND STRUCTURES OF ALPHA CASEIN DERIVED EXORPHINS" BIOCHEMISTRY, vol. 22, no. 19, 1983, pages 4567-4573, XP002537308 ISSN: 0006-2960 the whole document -----	1-15
Y	GOBBETTI MARCO ET AL: "Angiotensin I-converting-enzyme-inhibitory and antimicrobial bioactive peptides" INTERNATIONAL JOURNAL OF DAIRY TECHNOLOGY, & 2003 SYMPOSIUM TO MARK THE 40TH YEAR SINCE THE PUBLICATION PAPER; CORK, IRELAND; OCTOBER 22, 2003, vol. 57, no. 2-3, 1 May 2004 (2004-05-01), pages 173-188, XP002537005 the whole document -----	2-5

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2008/007518

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0343085	A	23-11-1989	FR 2631626 A1	24-11-1989
WO 9207874	A	14-05-1992	AU 8769791 A	26-05-1992
			IE 913675 A1	22-05-1992
			NZ 240307 A	26-03-1993
			PT 99293 A	30-09-1992
			ZA 9108423 A	22-04-1993
EP 0397571	A	14-11-1990	FR 2646775 A1	16-11-1990
			JP 3101625 A	26-04-1991
			US 5063203 A	05-11-1991
US 4992420	A	12-02-1991	CH 671879 A5	13-10-1989
			DE 3878951 D1	15-04-1993
			DE 3878951 T2	16-09-1993
			EP 0283675 A2	28-09-1988
			ES 2039484 T3	01-10-1993
			FI 880464 A	27-08-1988
			JP 2760429 B2	28-05-1998
			JP 63233911 A	29-09-1988
			NZ 223400 A	28-08-1990
			US 4994441 A	19-02-1991
			ZA 8800798 A	04-08-1988
WO 0205839	A	24-01-2002	AR 029829 A1	16-07-2003
			AT 339217 T	15-10-2006
			AU 8756001 A	30-01-2002
			CA 2415918 A1	24-01-2002
			DE 60123067 T2	12-04-2007
			DK 1303295 T3	02-01-2007
			EP 1303295 A1	23-04-2003
			ES 2272535 T3	01-05-2007
			JP 2004503597 T	05-02-2004
			US 2003161850 A1	28-08-2003
			UY 26835 A1	31-01-2002
WO 0137850	A	31-05-2001	AU 1516301 A	04-06-2001
			EP 1235585 A2	04-09-2002
			US 2003004095 A1	02-01-2003
CN 101165179	A	23-04-2008	NONE	
EP 1188767	A	20-03-2002	CA 2355921 A1	28-02-2002
			US 6465432 B1	15-10-2002
JP 2001213897	A	07-08-2001	NONE	
WO 2008071755	A	19-06-2008	FR 2909879 A1	20-06-2008
FR 2673374	A	04-09-1992	DE 69205154 D1	02-11-1995
			DE 69205154 T2	15-05-1996
			EP 0573554 A1	15-12-1993
			ES 2078740 T3	16-12-1995
			WO 9215279 A1	17-09-1992