

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

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
19 April 2001 (19.04.2001)

PCT

(10) International Publication Number
WO 01/27154 A3

(51) International Patent Classification⁷: **C07K 14/50**,
A61K 47/42, 47/48

(21) International Application Number: PCT/IB00/01491

(22) International Filing Date:

27 September 2000 (27.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/156,246 27 September 1999 (27.09.1999) US

(71) Applicants and

(72) Inventors: O'MAHONY, Daniel, J. [IE/IE]; 75 Avoca
Park, Avoca Avenue, Blackrock, Dublin (IE). LAMBKIN,
Imelda, J. [IE/IE]; 9 Station Street, Sutton, Dublin 13 (IE).

(81) Designated States (national): AG, AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, BZ, CA, CH, CN, CU, CZ, DE, DK,

DZ, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,
VN, YU, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

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

20 June 2002

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.

(54) Title: MEMBRANE TRANSLOCATING PEPTIDE DRUG DELIVERY SYSTEM

(57) Abstract: The present invention relates to a novel membrane translocating full-length peptide sequence, fragment, motif, derivative, analog or peptidomimetic thereof (MTLPs), to nucleotide sequences coding therefor, and to compositions comprising a MTLP-active agent complex and a MTLP-active particle complex. The MTLP or the nucleotide sequence coding therefor enhance movement of the active agent or of the active particle across a lipid membrane. More particularly, the present invention relates to an MTLP-active agent complex and an MTLP-active particle complex, wherein the MTLP enhances uptake of the active agent into a cell, into or out of an intracellular compartment and across a cell layer. Methods of making and methods of using MTLPs also are included.



WO 01/27154 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 00/01491

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/50 A61K47/42 A61K47/48

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)

IPC 7 A61K 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)

CHEM ABS Data, SEQUENCE SEARCH, EPO-Internal, WPI 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	ROJAS M ET AL.: "Genetic engineering of proteins with cell membrane permeability" NATURE BIOTECHNOLOGY, vol. 16, April 1998 (1998-04), pages 370-375, XP002182596 cited in the application	2,4,7,9, 10
Y	the entire document, particularly page 374, paragraph 4, page 375, column 1, figure 1A	1,3,5,6, 8,11
	---	-/--

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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

13 November 2001

Date of mailing of the international search report

29/11/2001

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

Schmidt, H

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 00/01491

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EASON PD & IMPERIALI B: "A Potent Oligosaccharyl Transferase Inhibitor That Crosses the Intracellular Endoplasmic Reticulum Membrane" BIOCHEMISTRY, vol. 38, 4 August 1999 (1999-08-04), pages 5430-5437, XP002182597	2,4,7,9,10
Y	page 5433, column 2, paragraph 1; figure 2B	1,3,5,6,8,11
Y	US 4 675 189 A (KENT ET AL.) 23 June 1987 (1987-06-23) claims 1,10; example 1	6,8,11
X	LIN YZ ET AL.: "Inhibition of Nuclear Translocation of Transcription Factor NK-kappaB by a synthetic peptide containing a Cell Membrane-permeable Motif and Nuclear Localization Sequence" THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 270, no. 24, 16 June 1995 (1995-06-16), pages 14255-14258, XP002050723 page 14255, column 2, paragraph 4 -page 14256, column 1, paragraph 3; figure 2	7,9,10
A	NEZIL FA & BLOOM M: "Combined influence of cholesterol and synthetic amphiphilic peptides upon bilayer thickness in model membranes" BIOPHYSICAL JOURNAL, vol. 61, May 1992 (1992-05), pages 1176-1183, XP001031328 page 1176, column 2, paragraph 2	1-11
P,X	WO 99 49879 A (VANDERBILT UNIVERSITY) 7 October 1999 (1999-10-07) the entire document, particularly page 1, line 11- line 21, page 30, line 25 - page 35, line 25, SEQ ID NO 1-9	2,4,6-11
P,Y	WO 99 64449 A (THE QUEENS UNIVERSITY OF BELFAST) 16 December 1999 (1999-12-16) page 2, line 5 - line 33; figure 6A	1,3,5

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-6 (partially)

Present claims 1-6 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. It is unclear in the sense of Article 6 PCT what is meant by "a derivative, fragment, motif, analog or peptidomimetic" of SEQ ID NOs 2-24 (claims 1 and 2). These expressions may comprise a wide range of peptides and modifications and are therefore speculative, embracing a great variety of possibilities not yet explored by the applicant, the effect of which cannot be expected by the skilled person using the teaching disclosed in the current application and his technical knowledge to be able to reproduce without undue burden all the possibilities which are actually claimed.

Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds of SEQ ID NOs 2-24.

The applicant's attention is drawn to the fact that claims, or parts of 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 00/01491

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4675189	A	23-06-1987	MX 9202840 A1 AT 21624 T AU 556754 B2 AU 7756081 A CA 1176565 A1 DE 3175230 D1 DE 52510 T1 EP 0052510 A2 HK 20489 A IE 52003 B1 IL 64298 A JP 1901277 C JP 4040329 B JP 57118512 A MY 83587 A NZ 198982 A PH 19942 A SG 94487 G ZA 8107973 A	30-06-1992 15-09-1986 20-11-1986 27-05-1982 23-10-1984 02-10-1986 20-03-1986 26-05-1982 17-03-1989 13-05-1987 31-07-1985 27-01-1995 02-07-1992 23-07-1982 31-12-1987 31-05-1985 14-08-1986 06-05-1988 27-07-1983
WO 9949879	A	07-10-1999	US 6248558 B1 AU 3462899 A EP 1067949 A1 WO 9949879 A1	19-06-2001 18-10-1999 17-01-2001 07-10-1999
WO 9964449	A	16-12-1999	AU 4281999 A EP 1086126 A1 WO 9964449 A2	30-12-1999 28-03-2001 16-12-1999