



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07K 14/47, 7/08, A61K 38/10, 38/17	A3	(11) International Publication Number: WO 99/37678 (43) International Publication Date: 29 July 1999 (29.07.99)
(21) International Application Number: PCT/NL99/00045 (22) International Filing Date: 26 January 1999 (26.01.99) (30) Priority Data: 1008139 27 January 1998 (27.01.98) NL (71) Applicant (for all designated States except US): STICHTING VOOR DE TECHNISCHE WETENSCHAPPEN [NL/NL]; Postbus 3021, NL-3502 GA Utrecht (NL). (72) Inventors; and (75) Inventors/Applicants (for US only): VAN NIEUW AMERON- GEN, Arie [NL/NL]; Gijsbrecht van Nijenrodestraat 136, NL-3621 GM Breukelen (NL). VEERMAN, Engelmundus, Cornelis, Ignatius [NL/NL]; Willem van den Bergstraat 27, NL-1132 TZ Volendam (NL). VAN'T HOF, Willem [NL/NL]; Schelpenkade 61, NL-2313 ZZ Leiden (NL). HELMERHORST, Eva, Josephine [NL/NL]; Egelantiers- gracht 630, NL-1015 RS Amsterdam (NL). (74) Agent: VAN SOMEREN, Petronella, Francisca, Hendrika, Maria; Arnold & Siedsma, Sweelinckplein 1, NL-2517 GK The Hague (NL).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, 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, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, 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 <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims</i> <i>and to be republished in the event of the receipt of amendments.</i> <i>In English translation (filed in Dutch).</i> (88) Date of publication of the international search report: 14 October 1999 (14.10.99)
(54) Title: ANTIMICROBIAL PEPTIDES (57) Abstract The invention relates to peptides with antimicrobial activity, consisting of an amino acid chain which contains a domain of 10 to 25 amino acids, wherein the majority of the amino acids of the one half of the domain are positively charged amino acids and the majority of the amino acids of the other half of the domain are uncharged amino acids.		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/NL 99/00045

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07K14/47 C07K7/08 A61K38/10 A61K38/17

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 6 C07K A61K

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 91 12815 A (SQUIBB BRISTOL MYERS CO) 5 September 1991 (1991-09-05) zie Seq.ID 5-12 page 3, line 20 - page 5, line 24; claims 36,38,46; examples ----	1-6, 32-39
X	WO 92 01462 A (SCRIPPS RESEARCH INST) 6 February 1992 (1992-02-06) zie Seq.ID 23 page 6, line 24 - page 9, line 16; claims; examples ----	1-7, 32-39
X	WO 93 24138 A (MAGAININ PHARMA) 9 December 1993 (1993-12-09) zie Seq.ID's 94 ff page 5, last paragraph - page 9, paragraph 1; claims; examples ----- -/--	1-7, 32-39



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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Date of the actual completion of the international search

19 August 1999

Date of mailing of the international search report

26/08/1999

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

Fuhr, C

INTERNATIONAL SEARCH REPORT

International Application No

PCT/NL 99/00045

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 08270 A (MAGAININ PHARMA) 21 March 1996 (1996-03-21) zie Seq.ID 29 page 1, paragraph 4; claims; examples page 3, paragraph 4 - page 5, last paragraph ---	1-7, 32-39
X	WO 96 40251 A (OPHIDIAN PHARM INC ; WILLIAMS JAMES A (US); SHEKHANI MOHAMMED SALEH) 19 December 1996 (1996-12-19) claims; example 39 ---	1, 32-39
A	TAKAHASHI, SHO ET AL: "Synthesis of alpha.-helices having a positively charged random coil-block on either N- or C-terminal" BULL. CHEM. SOC. JPN. (1988), 61(7), 2467-71 CODEN: BCSJA8; ISSN: 0009-2673, 1988, XP002083167 page 2467, right-hand column, paragraph 2 - page 269, left-hand column, paragraph 1 ---	1, 16-22
X	TOSSI, ALESSANDRO ET AL: "Identification and characterization of a primary antibacterial domain in CAP18, a lipopolysaccharide binding protein from rabbit leukocytes" FEBS LETT. (1994), 339(1-2), 108-12 CODEN: FEBLAL; ISSN: 0014-5793, 1994, XP002083170 page 111, left-hand column, paragraph 2 - page 112, left-hand column, paragraph 3; table 1 ---	1, 24-39
X	AOYAGI H ET AL: "SYNTHESIS OF ANTIBACTERIAL PEPTIDES, GRAMICIDIN S ANALOGS AND DESIGNED AMPHIPHILIC OLIGOPEPTIDES" TETRAHEDRON, vol. 44, no. 3, 1 January 1988 (1988-01-01), pages 877-886, XP000574054 page 881, last paragraph - page 882, paragraph 2; figure 3 ---	1, 24-39
X	MIHARA, HISAKAZU ET AL: "Design and synthesis of amphiphilic basic peptides with antibacterial activity and their interaction with model membrane" BULL. CHEM. SOC. JPN. (1987), 60(2), 697-706 CODEN: BCSJA8; ISSN: 0009-2673, 1987, XP002083171 page 703, left-hand column, paragraph 2 - page 704, left-hand column, last paragraph; figure 1 ---	1, 24-39
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/NL 99/00045

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 106, no. 25, 22 June 1987 (1987-06-22) Columbus, Ohio, US; abstract no. 214352, MIHARA, HISAKAZU ET AL: "Design and synthesis of basic amphiphilic peptides possessing antimicrobial activity and their interaction with lipids" XP002083172 abstract & PEPT. CHEM. (1986), VOLUME DATE 1985, 23RD, 223-8 CODEN: PECHDP;ISSN: 0388-3698, 1986, -----	1,24-39
X	CHEMICAL ABSTRACTS, vol. 103, no. 19, 11 November 1985 (1985-11-11) Columbus, Ohio, US; abstract no. 160837, SASAKI, TOORU ET AL: "Syntheses and properties of H-'Orn-Leu!n-OH (n = 1-12) and cyclo'Orn-Leu-!n (n = 2-8)" XP002083173 abstract & PEPT. CHEM. (1985), VOLUME DATE 1984, 22ND, 361-6 CODEN: PECHDP;ISSN: 0388-3698, 1985, -----	1,24-39

INTERNATIONAL SEARCH REPORT

International application No.

PCT/NL 99/ 00045

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:
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 II Observations where unity of invention is lacking (Continuation of item 2 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-7, 16-22 and 24-31 relate to an extremely large number of possible compounds/products. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/products 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. 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/products claimed in claims 8-15 and 23. The search has been extended to closely related peptides having the alleged i.e. antibacterial activity.

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/NL 99/00045

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