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- (71) Applicant (for all designated States except US): PARKER HUGHES INSTITUTE [US/US]; 2665 Long Lake Road, St. Paul, MN 55113 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): UCKUN, Fatih, M. [US/US]; 12590 Ethan Avenue North, White Bear Lake, MN 55110 (US). ZHU, De-Min [US/US]; 8386 Pleasantview Drive, Mounds View, MN 55112 (US).
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(54) Title: CATHEPSIN INHIBITORS IN CANCER TREATMENT

(57) Abstract: Embodiments of the present invention provide methods for inhibiting tumor cell growth, or treating cancer cells, in a subject through the administration of a cathepsin inhibitor or inhibitors. Methods for inhibiting inflammatory disease cells as well as other cathepsin expressing cells in a subject with a cathepsin inhibitor or inhibitors are also within the present invention. Furthermore, the present invention relates to inducing cytotoxicity or apoptosis in cells by administering a cytotoxic or an apoptotic dose of a cathepsin inhibitor or inhibitors to the cell. Finally, the present invention relates to the administering of cathepsin expressing vectors to tumor cells so as to inhibit the tumor cells growth.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/10196

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/06 A61K48/00 A61P35/00

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)

IPC 7 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)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, CHEM ABS Data, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 49190 A (CORTECH INC ;LEIMER AXEL H (US); SPRUCE LYLE W (US); CHERONIS JOHN) 5 November 1998 (1998-11-05)	1-4,6,7, 9-15, 17-20, 23-30
Y	page 1, line 24 - line 30 page 2, line 29 - line 31 page 9, line 28 -page 11, line 22 page 14, line 28 - line 30 page 15, line 19 - line 22 page 16, line 4 - line 6 page 17, line 20 - line 26 page 23, line 26 - line 27 page 24, line 29 -page 26, line 10 page 28, line 8 - line 18 claims 24-51,110,120-122,137-139 --- -/--	5,8,16, 21,22

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
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- *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

17 October 2001

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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

Stein, A

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/10196

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>DEMUTH H-U ET AL: "N-PEPTIDYL O-ACYL HYDROXAMATES: COMPARISON OF THE SELECTIVE INHIBITION OF SERINE AND CYSTEINE PROTEINASES" BBA - PROTEIN STRUCTURE AND MOLECULAR ENZYMOLOGIE, ELSEVIER SCIENCE BV, AMSTERDAM, NL, vol. 1295, no. 2, 18 July 1996 (1996-07-18), pages 179-186, XP000876878 ISSN: 0167-4838 cited in the application the whole document</p> <p style="text-align: center;">---</p>	5,8,16, 21,22
X	<p>US 5 883 121 A (KATUNUMA NOBUHIKO ET AL) 16 March 1999 (1999-03-16)</p> <p>column 2, line 34 - line 57 column 10, line 9 - line 31</p> <p style="text-align: center;">---</p>	1-4,6,7, 9-15, 18-20, 23-30
X	<p>KRUEGER SABINE ET AL: "Inhibitory effects of antisense cathepsin B cDNA transfection on invasion and motility in a human osteosarcoma cell line" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 59, no. 23, 1 December 1999 (1999-12-01), pages 6010-6014, XP000942232 ISSN: 0008-5472 the whole document</p> <p style="text-align: center;">---</p>	18,19, 23-30, 33,34
X	<p>ISAHARA K ET AL: "Regulation of a novel pathway for cell death by lysosomal aspartic and cysteine proteinases." NEUROSCIENCE, vol. 91, no. 1, 7 April 1999 (1999-04-07), pages 233-249, XP001030652 ISSN: 0306-4522 cited in the application the whole document</p> <p style="text-align: center;">---</p>	31,32
E	<p>WO 01 44464 A (BRODT PNINA ;UNIV MCGILL (CA); NAVAB ROYA (CA)) 21 June 2001 (2001-06-21)</p> <p>the whole document</p> <p style="text-align: center;">---</p>	1-4,6,7, 9-13, 18-20, 23-34
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/10196

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	ZHU D M ET AL: "Z - Phe - Gly - NHO - Bz, an inhibitor of cysteine cathepsins, induces apoptosis in human cancer cells." CLINICAL CANCER RESEARCH, (2000 MAY) 6 (5) 2064-9. , XP001030668 the whole document ---	1-37
T	ZHU D M ET AL: "Cathepsin inhibition induces apoptotic death in human leukemia and lymphoma cells." LEUKEMIA AND LYMPHOMA, (2000 OCT) 39 (3-4) 343-54. , XP001030704 the whole document -----	1-37

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-4,6,7,9-15,17-20,23-34 (all partially)

Present claims 1-4,6,7,9-15,17-20 and 23-34 relate to a compound defined by reference to a desirable characteristic or property, namely its inhibitory effect on cathepsins. These claims however do not contain any structural or essential characteristics of the compound.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. 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. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compound CATI-1 mentioned in the description at page 5 lines 7-11, in the examples and in claims 5, 8,16, 21-22 and 35-37. Additionally the general term cathepsin inhibitor has been searched.

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/US 01/10196

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