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60/214,047 26 June 2000 (26.06.2000) US(71) Applicant (for all designated States except US): SUGEN,
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LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
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ZW.

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IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
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[Continued on next page]

(54) Title: NOVEL PROTEASES

>SGPR397_SEQID_1

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CGGACAGTGCTGGAAGGGTGACATCTGCCACTATGCTGCTGGGCTGCTGGTGTCTGCTGCTCTTCTCTAA

(57) Abstract: The present invention relates to protease polypeptides, nucleotide sequences encoding the protease polypeptides, as well as various products and methods useful for the diagnosis and treatment of various protease-related diseases and conditions.



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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.

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3 April 2003

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/20171

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/55 C12N9/64 C07K16/40 C12N5/10 G01N33/50
G01N33/53 C12Q1/68

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 C12N C07K G01N C12Q

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)

EP0-Internal, EMBL, BIOSIS, SEQUENCE SEARCH, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL SEQUENCE LIBRARY [Online] 22 November 1995 (1995-11-22) HILLIER, L., ET AL.: "the WachU-Merck EST Project - yt08c10.r1 Soares retina N2b5HR Homo sapiens cDNA clone IMAGE:223698 5', mRNA sequence" XP002193829 accession no. H86718 ---	1,3-8, 24-28
A	WO 98 35988 A (ZENECA LTD ;EDGE MICHAEL DEREK (GB)) 20 August 1998 (1998-08-20) the whole document ---	
A	EP 0 887 416 A (SMITHKLINE BEECHAM PLC ;SMITHKLINE BEECHAM CORP (US)) 30 December 1998 (1998-12-30) the whole document ---	
	-/--	

☒ 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

21 March 2002

Date of mailing of the international search report

12.07.02

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/20171

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 245 051 A (UNIV LELAND STANFORD JUNIOR) 11 November 1987 (1987-11-11) the whole document ---	
A	WO 99 23106 A (HUMAN GENOME SCIENCES INC ;NI JIAN (US); RUBEN STEVEN M (US)) 14 May 1999 (1999-05-14) the whole document ---	
P,X	DATABASE EMBL SEQUENCE LIBRARY [Online] 2 August 2000 (2000-08-02) GU J., ET AL.: "Novel genes expressed in hematopoietic stem/progenitor cells from Myelodysplastic Syndromes patient - Homo sapiens carboxypeptidase B precursor (CPAH) mRNA, complete cds." XP002162176 accession no. AF221594 ---	1,3-8, 24-28
P,X	WO 01 23588 A (LEXICON GENETICS INC) 5 April 2001 (2001-04-05) the whole document -----	1-30

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/20171

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.: 14-19
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:

see additional sheet

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.:
1-30 partially

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

Claims Nos.: 14-19

Present claims 14-19 relate to a method of treatment by administering a substance; said substance being defined by reference to a desirable characteristic or property, namely the modulation of the activity of a protease as characterized by SEQID60.

The claims cover all substances having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for such substances.

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 substance 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, no search has been carried out for claims 14-19.

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-30 partially

invention 1: claims 1-30 partially

Human nucleic acid molecule encoding a polypeptide as characterized by SEQID60, further comprising a vector or operatively linked promoter, a hybridizing nucleic acid molecule, a human protease polypeptide as characterized by SEQID60, an antibody binding to said polypeptide, a hybridoma producing and a kit comprising said antibody, a method for identifying a substance modulating the activity of said polypeptide by contacting a polypeptide as characterized by SEQID60 with a test substance, method for identifying a substance modulating the activity of said polypeptide by recombinantly expressing said polypeptide in a cell and adding a test substance to said cell; method for treating a disease by administering such a substance in vivo or in vitro, said method wherein said substance is a protease inhibitor, method of detection of a protease polypeptide in a sample by contacting said sample with a nucleic acid probe that hybridizes to a nucleic acid target region, an isolated nucleic acid molecule that encodes a biological domain of a protease or an amino acid sequence that is 90% identical to a protease as characterized by SEQID60, a nucleic acid molecule that is characterized by SEQID1, nucleic acid molecule consisting of about 10-30 nucleotide bases of a nucleic acid sequence of SEQID1 or of a nucleic acid sequence encoding a polypeptide of SEQID60, a recombinant cell comprising such nucleic acid sequence encoding a polypeptide of SEQID60, a method for detecting the presence or amount of a protease polypeptide in a sample by forming a protease-antibody immunocomplex.

invention 2-59: claims 1-30 partially

as invention 1 but limited to SEQIDs 61-118 and SEQIDs 2-59, respectively.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/20171

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9835988	A	20-08-1998	AU 6000698 A WO 9835988 A1	08-09-1998 20-08-1998
EP 0887416	A	30-12-1998	CA 2234418 A1 EP 0887416 A2 JP 11113579 A US 6060277 A	24-12-1998 30-12-1998 27-04-1999 09-05-2000
EP 0245051	A	11-11-1987	US 4973555 A DE 3781017 D1 DE 3781017 T2 EP 0245051 A1 JP 62285783 A US 5213977 A	27-11-1990 17-09-1992 18-03-1993 11-11-1987 11-12-1987 25-05-1993
WO 9923106	A	14-05-1999	AU 9673898 A CA 2308112 A1 EP 1036086 A1 JP 2001521730 T WO 9923106 A1	24-05-1999 14-05-1999 20-09-2000 13-11-2001 14-05-1999
WO 0123588	A	05-04-2001	AU 7989000 A EP 1220932 A1 WO 0123588 A1	30-04-2001 10-07-2002 05-04-2001