

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

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
3 January 2002 (03.01.2002)

PCT

(10) International Publication Number
WO 02/000702 A3

(51) International Patent Classification⁷: **C12N 15/57**,
9/64, 1/19, C12Q 1/68, G01N 33/68, A61K 48/00, C12N
15/62, A61K 39/395, 31/7088, C12Q 1/37

(21) International Application Number: PCT/EP01/07292

(22) International Filing Date: 26 June 2001 (26.06.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/214,259 26 June 2000 (26.06.2000) US

(71) Applicant (for all designated States except US): **BAYER
AKTIENGESELLSCHAFT** [DE/DE]; 51368 Lev-
erkusen (DE).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **RAMAKRISHNAN,
Shyam** [IN/US]; 76 Euston Road, Apt. #10, Brighton, MA
02135 (US).

(74) Common Representative: **BAYER AKTIENGE-
SELLSCHAFT**; 51368 Leverkusen (DE).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, 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, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
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, TR), 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:
13 February 2003

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: REGULATION OF HUMAN EPIDERMIS-SPECIFIC SERINE PROTEASE

(57) Abstract: Reagents which regulate human epidermis-specific serine protease activity and reagents which bind to human epi-
dermis-specific serine protease gene products can be used to regulate extracellular matrix degradation. Such regulation is particularly
useful for treating metastasis of malignant cells, tumor angiogenesis, inflammation, atherosclerosis, neurodegenerative diseases, and
pathogenic infections.



WO 02/000702 A3

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 01/07292

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/57 C12N9/64 C12N1/19 C12Q1/68 G01N33/68
A61K48/00 C12N15/62 A61K39/395 A61K31/7088 C12Q1/37

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

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)

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	DATABASE EMBL 'Online! Sequence 14 from Patent W00112788, 28 February 2001 (2001-02-28) PRESNELL SR AND TAFT DW: "Tryptase-like polypeptide ztrypl" retrieved from E.B.I., HINXTON, U.K. Database accession no. AX082990 XP002215253 99% identical over 418 nucleotides (see nts 724-1141) abstract	1-17
P, X	-& DATABASE EMBL 'Online! Sequence 15 from Patent W00112788, 28 February 2001 (2001-02-28) PRESNELL SR AND TAFT DW: "Tryptase-like polypeptide ztrypl" retrieved from E.B.I., HINXTON, U.K. Database accession no. AX082991 XP002215254 -/--	1-17

☒ 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

23 October 2002

Date of mailing of the international search report

15/11/2002

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

Brouns, G

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 01/07292

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X P, Y	98% identical over 82 amino acids (see aa 231-312) abstract -& WO 01 12788 A (ZYMOGENETICS INC.) 22 February 2001 (2001-02-22) pages 36-45, 52, 53, 58-60, 66, 78; claims 5-7, 10-14	1-17, 68-71 21-67
X	--- DATABASE EMBL 'Online! 3 August 1999 (1999-08-03) NCI-CGAP: "wd26a04.x1 Soares_NFL_T_GBC_S1 Homo sapiens cDNA clone IMAGE:2329230 3' similar to SW:MCT7_MOUSE Q02844 MAST CELL PROTEASE 7 PRECURSOR mRNA sequence." retrieved from E.B.I., HINXTON, U.K. Database accession no. AI935051 XP002215255	19,20
Y	100% identical to SEQ ID NO:3 over all 82 nucleotides abstract	21-67
P, A	--- MIN HAE-KI ET AL: "Human mouse mast cell protease 7-like tryptase genes are pseudogenes." JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, vol. 107, no. 2 Part 2, February 2001 (2001-02), pages 315-321, XP008008869 ISSN: 0091-6749 page 319-321; figure 1B	1
A	--- VANDERSLICE P ET AL: "HUMAN MAST CELL TRYPTASE: MULTIPLE CDNAS AND GENES REVEAL A MULTIGENE SERINE PROTEASE FAMILY" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 87, 1 May 1990 (1990-05-01), pages 3811-3815, XP002073694 ISSN: 0027-8424 page 3815	1
A	--- PALLAORO MICHELE ET AL: "Characterization of genes encoding known and novel human mast cell tryptases on chromosome 16p13.3." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 6, 5 February 1999 (1999-02-05), pages 3355-3362, XP002177260 ISSN: 0021-9258 abstract; figures 5,6 --- -/--	1

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 01/07292

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WONG G W ET AL: "Identification of a new member of the tryptase family of mouse and human mast cell proteases which possesses a novel COOH-terminal hydrophobic extension" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 274, no. 43, 22 October 1999 (1999-10-22), pages 30784-30793, XP002177259 ISSN: 0021-9258 abstract -----	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 01/07292

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:
Although claims 16, 17, 52-57, 59 and 68-71 are directed to a method of treatment of the human or animal body, the search has been carried out and based on the alleged effects of the compounds that appear clear to the person skilled in the art.
2. ☒ Claims Nos.: 14, 68-71, in part: 15-17, 52, 58-60, 62
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

Claims Nos.: 14, 68-71, in part: 15-17, 52, 58-60, 62

Present claims 14-17, 52, 58-60, 62 and 68-71 relate to a reagent defined by reference to a desirable characteristic or property, namely that it or modulates the activity of a epidermis-specific serine protease or a polynucleotide encoding said protein, or specifically binds to aforementioned protein or polynucleotide.

The claims cover all reagents having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT or disclosure within the meaning of Article 5 PCT for any of such products. 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 reagent 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 to the person skilled in the art, namely said reagent being a polypeptide, an antibody, RNA, a ribozyme or an antisense oligonucleotide.

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.