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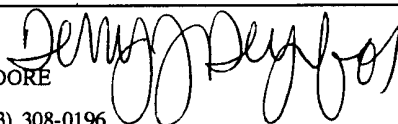
WO 00/68247 A3

(54) Title: SERINE PROTEASES

(57) Abstract: The present invention relates to novel human serine protease polypeptides and isolated nucleic acids containing the coding regions of the genes encoding such polypeptides. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human serine protease polypeptides. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human serine protease polypeptides.

INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/12207

<p><b>A. CLASSIFICATION OF SUBJECT MATTER</b>                  IPC(7) : C12N 9/64, 15/57, 15/85; C12Q 1/37                  US CL : 435/226, 23, 69.1, 252.3, 320.1; 536/23.2                  According to International Patent Classification (IPC) or to both national classification and IPC</p>													
<p><b>B. FIELDS SEARCHED</b>                  Minimum documentation searched (classification system followed by classification symbols)                  U.S. : 435/226, 23, 69.1, 252.3, 320.1; 536/23.2                  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 practicable, search terms used)                  GenBank &amp; EMBL EST &amp; GSS databases, GenEMBL1-58, N-GeneSeq36, issued U.S. patent nucleotide and amino acid sequences, A-GeneSeq36, SPTREMBL12, Swiss-Prot38, and PIR63</p>													
<p><b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b></p> <table border="1"> <thead> <tr> <th>Category*</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X,P --- Y,P</td> <td>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" The Journal of Biological Chemistry. 22 October 1999. Vol. 274. No. 43. pages 30784-30893, especially Figure 7A and pages 30788-30792.</td> <td>1-3, 5-8, and 11 ----- 9, 10, 12, and 14-21</td> </tr> <tr> <td>X --- Y</td> <td>Database Genbank, Accession No. AI280891. NCI-CGAP. "National Cancer Institute, Cancer Genome Anatomy Project (CGAP), Tumor Gene Index." Gene Sequence, Unpublished, 28 January 1999.</td> <td>1, 2, 5-8 and 11 ----- 3, 4, 9, 10, 12, and 14-21</td> </tr> <tr> <td>Y</td> <td>WO 98/33812 A1 (BRIGHAM AND WOMEN'S HOSPITAL, INC.) 06 August 1998, pages 18-32.</td> <td>3, 4, 9, 10, 12 and 14-21</td> </tr> </tbody> </table>		Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X,P --- Y,P	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" The Journal of Biological Chemistry. 22 October 1999. Vol. 274. No. 43. pages 30784-30893, especially Figure 7A and pages 30788-30792.	1-3, 5-8, and 11 ----- 9, 10, 12, and 14-21	X --- Y	Database Genbank, Accession No. AI280891. NCI-CGAP. "National Cancer Institute, Cancer Genome Anatomy Project (CGAP), Tumor Gene Index." Gene Sequence, Unpublished, 28 January 1999.	1, 2, 5-8 and 11 ----- 3, 4, 9, 10, 12, and 14-21	Y	WO 98/33812 A1 (BRIGHAM AND WOMEN'S HOSPITAL, INC.) 06 August 1998, pages 18-32.	3, 4, 9, 10, 12 and 14-21
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<p><input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.      <input type="checkbox"/> See patent family annex.</p>													
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<p>Date of the actual completion of the international search 02 NOVEMBER 2000</p>	<p>Date of mailing of the international search report <b>07 DEC 2000</b></p>												
<p>Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230</p>	<p>Authorized officer WILLIAM W. MOORE Telephone No. (703) 308-0196</p> 												

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/12207

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	REYNOLDS. D. S. et al. "Cloning of the cDNA and Gene of Mouse Mast Cell Protease-6". The Journal of Biological Chemistry. 25 February 1991. Vol. 266. No. 6. pages 3847-3853.	1-8, 11 and 12

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/12207**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international 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:
  
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:

Please See Extra 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.:  
a single species of claims 1-12 and 14-21

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/12207

### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I includes at least nine independent species of claims 1-12 and 14-21, drawn to a first product, an isolated protease or a fragment thereof, to a first method of making the protease utilizing a nucleic acid encoding all or part of a protease, as well as vectors and host cells comprising the nucleic acid, as well as to methods of use of the polypeptide product, or its encoding nucleic acid, in treatment or diagnosis of medical conditions and methods of use of the polypeptide in assays for identifying binding partners and activity modulators.

Group III includes at least nine independent species of claims 1-11, 16, 17, 19, and 20, drawn to a second product, an epitope of a polypeptide, to a first method of making the epitope using an isolated nucleic acid encoding an epitope, as well as to methods of use of the epitope of a polypeptide in treatment and diagnosis of medical conditions and assays for identifying binding partners.

Group III includes at least nine independent species of claim 13, drawn to a sixth product, an antibody.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

In Group I, there are at least nine species of polypeptides having amino acid sequences of SEQ IDs NOs: 11-19 in Table I of the specification encoded by their corresponding nucleic acids enumerated as SEQ IDs NOs: 2-10 in Table I. The claims are deemed to correspond to the species listed above in the following manner: Claim 1's clauses (a), (b) and (d) describe polypeptides having a amino acid sequences of SEQ IDs NOs: 11-19 encoded by the corresponding polynucleotides having nucleic acid sequences of SEQ IDs NOs: 2-10. Each of claims 1-12 and 14-21 are generic.

In Group II, there are at least nine species of peptide or polypeptide epitopes constituting as yet undesignated regions within polypeptides of SEQ IDs NOs: 11-19 in Table I encoded by undesignated regions of nucleic acids of SEQ IDs NOs: 2-10. The claims are deemed to correspond to species listed above in the following manner: Clause (c) of claim 1 wherein a peptide or polypeptide epitope constitutes an amino acid sequence in SEQ IDs NOs: 11-19 encoded by polynucleotide regions within one of SEQ IDs NOs: 2-10. Each of claims 1-10 are generic.

In Group III, the at least nine species are antibodies capable of recognizing any of the polypeptides enumerated in Table I of the specification as SEQ IDs NOs: 11-19. The claims are deemed to correspond to the species listed above in the following manner: Claim 13 embraces an antibody that will bind to at least any one SEQ IDs NOs: 11-19, thus is a generic claim.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The invention of Group I lacks a same or corresponding special technical feature with the invention of Group II because an invention of Group II need not encode a product having any vestige of protease activity, disclosed to be a special technical feature of Group I. The invention of Group I lacks a same or corresponding special technical feature with the invention of Groups III because the invention of Group III, an antibody, has neither a structural nor functional relationship to a protease of Group I thus can not share a same, nor a corresponding, nor a special technical feature with an invention of Group I.

The invention of Group II lacks a same or corresponding special technical feature with the inventions of Group because an invention of Group III, an antibody, has neither a structural nor a functional relationship to an epitope of Group I thus cannot share a same, nor a corresponding, nor a special technical feature with an invention of Group II.

The species listed above, combining the nucleic acids of SEQ IDs NOs: 2-10 with the corresponding polypeptides of SEQ IDs NOs: 11-19, do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each species either encodes or represents a protease which has no special structural or other relationship with the other proteases because, as disclosed, all are serine proteases or portions thereof, therefore the claims define a generic, rather than a special, technical feature.