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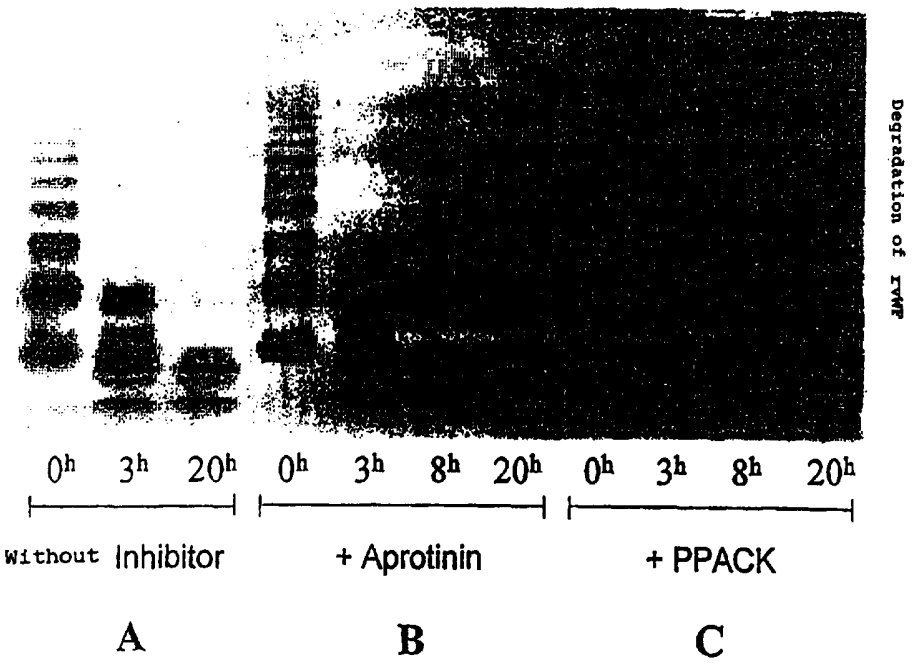
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(54) Title: VON WILLEBRAND FACTOR MULTIMERASE



(57) Abstract

There is disclosed a purified multimerase having an indirect and a direct proteolytic activity, which converts vWF having a singlet structure to vWF having a satellite structure and is active in the presence of the serine protease inhibitor DFP or the calpain protease inhibitor Z-Leu-Leu-Tyr-CHN_2, as well as a method of preparing the multimerase according to the invention.

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INTERNATIONAL SEARCH REPORT

Inter. ›nal Application No
PCT/EP 97/02131

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N9/64 C07K14/755 A61K38/48 A61K38/37 C12Q1/37
C07K16/40

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 C12N C07K A61K 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 503 991 A (CENTRE REGIONAL DE TRANSFUSION SANGUINE DE LILLE) 16 September 1992 see page 2, line 1 - line 3 see page 2, line 58 - page 3, line 18 see page 3, line 49 - page 4, line 23 ---	48-50, 55-57
A	DE 44 35 485 A (IMMUNO AG) 21 March 1996 see page 2, line 3 - line 6 see page 3, line 29 - line 36 & WO 96 10584 A cited in the application --- -/--	48-57

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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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

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"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

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Date of the actual completion of the international search	Date of mailing of the international search report
29 September 1997	23.10.97

Name and mailing address of the ISA	Authorized officer
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	MONTERO LOPEZ B.

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INTERNATIONAL SEARCH REPORT

Intern ıal Application No
PCT/EP 97/02131

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	THOMAS J. KUNICKI ET AL.: "Cleavage of human von Willebrand factor by platelet Calcium-activated protease" BLOOD, vol. 65, no. 2, February 1985, pages 352-356, XP002042008 see abstract see page 355, right-hand column, paragraph 2 - page 356, right-hand column, paragraph 1 ---	1-47
A	JUDITH A. DENT ET AL.: "Identification of a cleavage site directing the immunochemical detection of molecular abnormalities in type IIA von Willebrand factor" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 87, August 1990, WASHINGTON US, page 6306-6310 XP002042009 see abstract see page 6309, left-hand column, paragraph 3 - right-hand column, paragraph 3 ---	1-47
A	BERKOWITZ, SCOTT D. ET AL: "Sialic acid prevents loss of large von Willebrand factor multimers by protecting against amino-terminal proteolytic cleavage" BLOOD (1988), 72(5), 1790-6 CODEN: BLOOAW;ISSN: 0006-4971, 1988, XP002042010 see the whole document ---	1-47
P,X	FURLAN, MIHA ET AL: "Partial purification and characterization of a protease from human plasma which cleaves von Willebrand factor to fragments produced by in vivo proteolysis" BLOOD (1996), 87(10), 4223-4234 CODEN: BLOOAW;ISSN: 0006-4971, 1996, XP002042011 see abstract see page 4227, left-hand column, paragraph 2 - page 4233, left-hand column, paragraph 1 -----	1-8, 13-27

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INTERNATIONAL SEARCH REPORT

Int. ational application No.
PCT/EP 97/02131

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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

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:

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.

INTERNATIONAL SEARCH REPORT

International Application No. PCT /EP 97/02131

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Remark : Although claims 34-38 are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the compound.

INTERNATIONAL SEARCH REPORT

information on patent family members

Interr nal Application No
PCT/EP 97/02131

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