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(54) **Fibrin(ogen) degradation and clot lysis by fibrinolytic metalloproteinase**

(57) The invention provides a method of causing the degradation of fibrin(ogen) (i.e., fibrin, fibrinogen, and related substances) by means of a fibrinolytic matrix metalloproteinase, preferably an MT1-MMP. The method of the invention can be performed *in vitro* to provide diagnostic information characterizing fibrin(ogen) and fibrinolytic physiology. The method can also be performed *in vivo* as a method of thrombolytic therapy in which a fibrinolytic matrix metalloproteinase is adminis-

tered to a subject to degrade thrombus *in situ*. The fibrinolytic matrix metalloproteinase can be administered in conjunction with other active agents, preferably with agents having thrombolytic activity to improve thrombolytic and fibrinolytic therapy. The invention further provides compositions containing a fibrinolytic matrix metalloproteinase for the performance of fibrinolytic or thrombolytic procedures. Also provided are kits that include a fibrinolytic matrix metalloproteinase for performing fibrinolytic or thrombolytic procedures.



European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	WO 98 52601 A (THE NEW YORK BLOOD CENTER, INC.) 26 November 1998 (1998-11-26)	1-45	A61K38/48 C12Q1/56
Y	* page 6, line 24 - page 9, line 22; claims *	1-45	G01N33/53 A61K48/00 A61P7/02
Y	N. HIRAOKA ET AL.: "Matrix metalloproteinases regulate neovascularization by acting as pericellular fibrinolysins." CELL, vol. 95, 30 October 1998 (1998-10-30), pages 365-377, XP002179644 CAMBRIDGE, MA, US * page 365, summary *	1-45	/(A61K38/48, 38:49)
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
			A61K G01N A61L
INCOMPLETE SEARCH			
<p>The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.</p> <p>Claims searched completely :</p> <p>Claims searched incompletely :</p> <p>Claims not searched :</p> <p>Reason for the limitation of the search: see sheet C</p>			
Place of search		Date of completion of the search	Examiner
THE HAGUE		9 October 2001	Ryckebosch, A
CATEGORY OF CITED DOCUMENTS			
<p>X : particularly relevant if taken alone</p> <p>Y : particularly relevant if combined with another document of the same category</p> <p>A : technological background</p> <p>O : non-written disclosure</p> <p>P : intermediate document</p>		<p>T : theory or principle underlying the invention</p> <p>E : earlier patent document, but published on, or after the filing date</p> <p>D : document cited in the application</p> <p>L : document cited for other reasons</p> <p>& : member of the same patent family, corresponding document</p>	

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Although claims 1-8,10,11 (all as far as being related to an in vivo method) and claims 9,12-22,43-45 are directed to a method of treatment of the human/animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition.



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PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 00 20 2122

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
Y	T.L. HAAS ET AL.: "Transcriptional upregulation of membrane type 1 matrix metalloproteinase (MT1-MMP) in endothelium via the transcription factor Egr1." FASEB JOURNAL FOR EXPERIMENTAL BIOLOGY, ABSTRACTS, PART I, vol. 13, no. 4, 12 March 1999 (1999-03-12), page A204 XPO02179645 BETHESDA, MD, US * abstract # 187.2 *	1-45	
P,X	A. BINI ET AL.: "Characterization of stromelysin (MMP-3), matrilysin (MMP-7), and membrane type 1 matrix metalloproteinase (MT1-MMP) derived fibrin(ogen) fragments D-dimer and D-like monomer: NH2-terminal sequences of late-stage digest fragments." BIOCHEMISTRY., vol. 38, 19 October 1999 (1999-10-19), pages 13928-13936, XPO02928681 EASTON, PA, US * the whole document *	1-45	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
E	WO 00 63700 A (THE NEW YORK BLOOD CENTER, INC.) 26 October 2000 (2000-10-26) * page 9, line 16 - line 23; claims; example 1 *	1-5,10, 11,34-38	

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**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 00 20 2122

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

09-10-2001

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		WO 9852601 A1	26-11-1998
WO 0063700 A	26-10-2000	AU 4344800 A	02-11-2000
		WO 0063700 A1	26-10-2000

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

