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(54) Title: METHODS AND COMPOSITIONS FOR ACTIVATING OR INHIBITING VEGF-D AND VEGF-C

(57) Abstract: Methods for activating endothelial growth factors VEGF-C or VEGF-D with plasmin, and methods of treatment comprising administering a pharmaceutical compositions comprising plasmin. Also disclosed are methods of screening for inhibitors of activation of the growth factors by plasmin, and method of treatment by blocking activation of VEGF-C/D activation by plasmin. Further disclosed are methods for screening for other proteases that activate VEGF-CD, and for inhibitors of such activation. The invention further includes inhibitors of plasmin activity and methods of treating patients in need thereof with said inhibitors.

INTERNATIONAL SEARCH REPORT

International application No. _____

PCT/US03/22521

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/43, 38/49, 38/55, 39/395; C12Q 1/37, 1/25; C12S 3/00
 US CL : 424/94.64, 145.1; 435/4, 7.1; 436/501

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)
 U.S. : 424/94.64, 145.1; 435/4, 7.1; 436/501

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
 none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	OLOFSSON et al. Proc. Natl. Acad. Sci. USA. September 1998, Vol. 95, pages 11709-11714, especially abstract and page 11712, column 1, paragraph 2.	1-17
Y	PLOUET et al. J. Biol. Chem. May 1997, Vol. 272, No. 20, pages 13390-13396, especially abstract and page 13393.	1-17
Y	STACKER et al. J. Biol. Chem. November 1999, Vol. 274, No. 45, pages 32127-32136, especially abstract, page 32127, column 2 to page 32128, paragraph 1, and page 32130.	1-17
Y	ENHOLM et al. Trends in Cardiovascular Medicine. 1998, Vol. 8, No. 7, pages 292-297, especially Figure 2 at page 294.	1-17

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"&"	document member of the same patent family
"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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 Authorized officer: Christine J. Saoud (signature), Telephone No. 703-308-0196 (signature).

INTERNATIONAL SEARCH REPORT

Continuation of B. FIELDS SEARCHED Item 3:

WEST, MEDLINE, EMBASE, BIOSIS

search terms: VEGF, activat?, plasmin, VEGF?, serine protease, VHD, VEGFC, VEGFD, VEGF-C, VEGF-D, activation, process?