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- (72) Inventors; and
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| PCT/US00/00376 | 6 January 2000 (06.01.2000)   | US |
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| PCT/US00/06884 | 15 March 2000 (15.03.2000)    | US |
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[Continued on next page]

(54) Title: INTERLEUKIN-1-RECEPTOR ASSOCIATED KINASE-3 (IRAK3)

(57) Abstract: Compositions and methods are disclosed for stimulating or inhibiting angiogenesis and/or cardiovascularization in mammals, including humans. Pharmaceutical compositions are based on polypeptides or antagonists thereto that have been identified for one or more of these uses. Disorders that can be diagnosed, prevented, or treated by the compositions herein include trauma such as wounds, various cancers, and disorders of the vessels including atherosclerosis and cardiac hypertrophy. In addition, the present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.



**(84) Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, 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), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

— *With (an) indication(s) in relation to deposited biological material furnished under Rule 13bis separately from the description.*

**Published:**

— *With international search report.*  
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# INTERNATIONAL SEARCH REPORT

Inter:   nal Application No
PCT/US 00/13705

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7	C12N15/12	C07K14/47	C07K14/52	A61K38/17	C07K16/18
	G01N33/53	C12Q1/68	C12N15/11	C12N15/86	

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   C07K   A61K   G01N   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)

EPO-Internal, BIOSIS, STRAND

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 25834 A (GENENTECH INC) 27 May 1999 (1999-05-27)  the whole document	1-24, 29, 31-34, 38, 40-48, 59-80
X	WO 98 07880 A (HUMAN GENOME SCIENCES INC ;NI JIAN (US); ROSEN CRAIG A (US); YU GU) 26 February 1998 (1998-02-26)  the whole document	1-4, 11-24, 47, 48, 59-80
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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

13 September 2000

Date of mailing of the international search report

22. 12. 00

Name and mailing address of the ISA

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Smalt, R

# INTERNATIONAL SEARCH REPORT

International Application No PCT/US 00/13705
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>GURNEY A L ET AL: "Identification of a new member of the tumor necrosis factor family and its receptor, a human ortholog of mouse G1TR" CURRENT BIOLOGY,CURRENT SCIENCE,,GB, vol. 9, no. 4, 25 February 1999 (1999-02-25), pages 215-218, XP000938588 ISSN: 0960-9822 the whole document</p>	1-4,6, 11-24, 59-80
X	<p style="text-align: center;">---</p> <p>KWON BYUNGSUK ET AL: "Identification of a novel activation-inducible protein of the tumor necrosis factor receptor superfamily and its ligand." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 10, 5 March 1999 (1999-03-05), pages 6056-6061, XP002147323 ISSN: 0021-9258 the whole document</p>	1-4, 11-24, 47,48, 59-80
A	<p style="text-align: center;">---</p> <p>KLAGSBRUN M: "REGULATORS OF ANGIOGENESIS: STIMULATORS, INHIBITORS, AND EXTRACELLULAR MATRIX" JOURNAL OF CELLULAR BIOCHEMISTRY,US,LISS, NEW YORK, NY, vol. 47, no. 3, 1 November 1991 (1991-11-01), pages 199-200, XP000616588 ISSN: 0730-2312 the whole document</p>	
A	<p style="text-align: center;">---</p> <p>WO 95 29242 A (CHILDRENS MEDICAL CENTER) 2 November 1995 (1995-11-02) the whole document</p>	
A	<p style="text-align: center;">---</p> <p>EP 0 335 243 A (HARVARD COLLEGE) 4 October 1989 (1989-10-04) the whole document</p>	
P,X	<p style="text-align: center;">---</p> <p>WO 99 40196 A (GENENTECH INC) 12 August 1999 (1999-08-12)</p> <p style="text-align: center;">-----</p> <p>examples 2,10,11</p>	1,2,6,7, 10,11, 13-15, 17,18, 31-34, 38,42, 45-48, 59-65, 67, 70-73, 79,80

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/13705

## 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 31-45 and 49-58 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/composition.
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:  
  
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:

see additional 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.:  
  
1-49, 52, 59-80

### 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

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: claims 1-49,52,59-80, all partially

Composition comprising PRO175 polypeptide or (ant)agonist thereof, fusion proteins comprising a portion of said protein, antibody against said protein, method for identifying (ant)agonists of said protein or compounds which modulate the expression level or the activity of said protein, methods for modulating the activity of said protein using said (ant)agonists or modulators, methods for diagnosis comprising assessing the protein or expression levels of said polypeptide, retroviral particle encoding said protein or (ant)agonist, and producer cell of said protein or (ant)agonist comprising said retroviral particle, use of said protein, (ant)agonists thereof or nucleic acids encoding said protein in the manufacture of a composition for the treatment of angiogenesis or cardiovascularization related disorder.

2. Claims: Inventions 2-17: claims 1-80,  
all partially and in as far as applicable

Idem as subject 1 but limited to the respective proteins PRO200, PRO198, PRO364, PRO356, PRO535, PRO819, PRO1002, PRO1308, PRO1304, PRO183, PRO202, PRO861, PRO877, PRO879, PRO882, and PRO1710.

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

A meaningful search for the full scope of claims 1,2,5-7,10,17-19,31-35,38,42, and 45-54, referring to (ant)agonists of the claimed proteins and compounds inhibiting the expression thereof, could not be performed due to insufficient characterization of the (ant)agonists and/or expression inhibitors in the description (lack of disclosure, support, clarity, and conciseness, PCT articles 5 & 6). It is clear from e.g. claims 3,4 and 20, however, that the claimed (ant)agonists could be agonistic antibodies against proteins defined in the application, and that the expression inhibiting compound could be an antisense molecule. The search for the above claims, in as far as they relate to (ant)agonists and expression inhibitors, was therefore limited to (ant)agonistic antibodies and antisense molecules only.

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.

# INTERNATIONAL SEARCH REPORT

information on patent family members

Inter. . . . .nal Application No

PCT/US 00/13705

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