



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US98/25398 (22) International Filing Date: 30 November 1998 (30.11.98) (30) Priority Data: 60/067,690 4 December 1997 (04.12.97) US (71) Applicant (for all designated States except US): CREATIVE BIOMOLECULES, INC. [US/US]; 45 South Street, Hopkinton, MA 01748 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): NAKAOKA, Takashi [JP/JP]; Fourth Dept. of Internal Medicine, School of Medicine, University of Tokyo, 3-28-6, Mejiro-dai, Bunkyo-ku, Tokyo 112 (JP). MIYAZONO, Kohei [JP/JP]; Dept. of Biochemistry, The Cancer Institute, Tokyo, Japanese Foundation of Cancer Research, 1-37-1, Kami-ikebukuro, Toshima-ku, Tokyo 170 (JP). SAMPATH, Kuber, T. [US/US]; 6 Spring Street, Medway, MA 02053 (US). (74) Agent: CHIU, Jerrie, L.; Testa, Hurwitz & Thibault, LLP, High Street Tower, 125 High Street, Boston, MA 02110 (US).		(81) Designated States: AU, CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 5 August 1999 (05.08.99)
(54) Title: MAINTENANCE OF SMOOTH MUSCLE INTEGRITY BY MORPHOGENIC PROTEINS (57) Abstract Disclosed are compositions and methods for maintaining the integrity of smooth muscle, particularly vascular smooth muscle. Vascular diseases are characterized by an excessive build-up of vascular smooth muscle cells, resulting in an occlusion of a blood vessel, and/or by loss of elasticity in the blood vessels. Causes of blood vessel occlusion include smooth muscle cell proliferation and inflammatory responses. Inhibition of the proliferation of smooth muscle cells or inflammatory responses represents an effective treatment for vascular disorders, such as atherosclerosis and restenosis. Treatment may include administration of a morphogenic protein. The protein itself may be delivered to the site of vascular occlusion or the protein may be delivered by a vector, such as an adenoviral vector containing a DNA insert encoding a morphogenic protein. Such compositions and methods may also inhibit the responses of smooth muscle cells to various traumas, such as exposure to toxic agents. All of these treatments operate to preserve the cell phenotype by inhibiting an increase in extracellular matrix proteins, such as collagen, or by maintaining the normal balance of extracellular matrix proteins, such as Types I and III collagen.		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/25398

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/86 C07K14/51

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 C07K

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,P	WO 98 34655 A (CREATIVE BIOMOLECULES INC) 13 August 1998 see abstract see page 12, line 23 - page 13, line 21 see page 16, line 4 - page 22, line 2 ---	1,2,7-9
X	WO 97 07135 A (CREATIVE BIOMOLECULES INC ;LUDWIG INST CANCER RES (US)) 27 February 1997 see abstract see page 2, line 3 - page 3, line 9 see page 41, line 12 - page 42, line 29 ---	1,2,5-9, 38-46, 56,57, 60-66
X	WO 95 33502 A (CREATIVE BIOMOLECULES INC) 14 December 1995 see abstract see page 22, line 4 - page 26, line 24 ---	1,2,7-9
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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 :

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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

"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

1 June 1999

Date of mailing of the international search report

09/06/1999

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INTERNATIONAL SEARCH REPORT

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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	WO 96 26737 A (CREATIVE BIOMOLECULES INC) 6 September 1996 see abstract see page 2, line 24 - line 25 see page 4, line 26 - page 5, line 7 see page 15, line 10 - page 22, line 4 ---	1,2,5-9, 38-46
X	WO 91 05802 A (CREATIVE BIOMOLECULES INC) 2 May 1991 see abstract see page 30, line 1 - page 37, line 4 ---	1,2,4-9
X	WO 94 03600 A (CREATIVE BIOMOLECULES INC) 17 February 1994 see abstract see page 3, line 26 - page 7, line 4 see table 1 ---	1,2,4-9
X	WO 97 41881 A (CREATIVE BIOMOLECULES INC) 13 November 1997 see abstract see page 39, line 19 - line 28 ---	1,2,4-9, 20-28, 38-46
X	WO 97 34626 A (CREATIVE BIOMOLECULES INC ;GEN HOSPITAL CORP (US)) 25 September 1997 see abstract see page 14, line 14 - page 23, line 25 see examples 1,2 -----	1,2,5-9, 38-46

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/ 25398

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:
Remark: Although claims 10-80
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:
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

Information on patent family members

International Application No

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