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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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(54) Title: HUMAN CYR61

(57) Abstract: Polynucleotides encoding mammalian ECM signaling molecules affecting the cell adhesion, migration, and proliferation activities characterizing such complex biological processes as angiogenesis, chondrogenesis, and oncogenesis, are provided. Polypeptide compositions are also provided. The polypeptide compositions comprise mammalian ECM signaling molecules, peptide fragments, inhibitory peptides capable of interacting with receptors for ECM signaling molecules, and antibody products recognizing Cyr61. Also provided are methods for producing mammalian ECM signaling molecules, methods for using mammalian ECM signaling molecules to screen for, and/or modulate, conditions and disorders associated with angiogenesis, chondrogenesis, and oncogenesis; and ex vivo methods for using mammalian ECM signaling molecules to prepare blood products. Additionally, modulators, such as peptide modulators, of an ECM signaling molecule activity are provided. Further provided are methods for screening for modulators of a Cyr61 polypeptide-integrin receptor interaction, as well as methods of treating conditions and disorders associated with such an interaction.

INTERNATIONAL SEARCH REPORT

ional Application No
PCT/US 01/03267

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/475 G01N33/68 C12N15/63 A01K67/027 A61P19/04
A61P9/00 A61P21/00 A61K48/00

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 C07K G01N C12N A01K A61P A61K

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, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 33995 A (MUNIN CORP (US)) 18 September 1997 (1997-09-18) page 10, column 1 -page 18, column 9; claims 1,22-37,49-56,58 ---	1
X	JEDSADAYANMATA A. ET AL.: "Activation-dependent Adhesion of Human Platelets to Cyr61 and Fisp12/Mouse Connective Tissue Growth Factor Is Mediated through Integrin alphaIIb beta3" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 34, 20 August 1999 (1999-08-20), pages 24321-24327, XP002175431 figures 1-5 --- -/--	1

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

[X] 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	Date of mailing of the international search report
21 August 2001	19. 11. 01

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	Schönwasser, D

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BABIC A. ET AL.: "CYR61, a product of a growth factor-inducible immediate early gene, promotes angiogenesis and tumor growth" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, USA, vol. 95, May 1998 (1998-05), pages 6355-6360, XP002175432 page 6355, column 1, line 13 - line 17 ---	1
P,X	CHEN N. ET AL.: "Adhesion of Human Skin Fibroblasts to Cyr61 Is Mediated through Integrin alpha6beta1 and Cell Surface Heparan Sulfate Proteoglycans" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 275, no. 32, 11 August 2000 (2000-08-11), pages 24953-24961, XP002175433 the whole document -----	1-3

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US 01/03267

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:

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:

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.:

1-3

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: 1-3

   A method of screening for a modulator of cell adhesion involving human Cyr61, or a fragment, analog, or derivative thereof.

2. Claims: 4-8

   A method of screening for a modulator of cell migration involving Cyr61.

3. Claims: 9-11

   A method of screening for a modulator of cell prolferation involving human Cyr61, or a fragment, analog, or derivative thereof.

4. Claims: 12 (completely); 13,14 (both partially)

   Methods of screening for a modulator of angiogenesis involving Cyr61.

5. Claims: 13,14 (partially)

   Methods of screening for a modulator of angiogenesis involving Fisp12.

6. Claims: 13,14 (partially)

   Methods of screening for a modulator of angiogenesis involving CTGF.

7. Claims: 13,14 (partially)

   Methods of screening for a modulator of angiogenesis involving NOV.

8. Claims: 13,14 (partially)

   Methods of screening for a modulator of angiogenesis involving ELM-1 (WISP-1).

9. Claims: 13,14 (partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Methods of screening for a modulator of angiogenesis involving WISP-3.

10. Claims: 13,14 (partially)

Methods of screening for a modulator of angiogenesis involving COP-1 (WISP-2).

11. Claims: 15,16 (partially)

A method of screening for a modulator of wound healing involving Cyr61.

12. Claims: 15,16 (partially)

A method of screening for a modulator of wound healing involving a member of the CCN family except Cyr61.

13. Claim : 17

A method of screening for a modulator of macrophage adhesion involving Cyr61.

14. Claims: 18-23

A mammalian cell comprising a cyr61 mutation.

15. Claims: 24-27

Isolated human Cyr61 fragments.

16. Claim : 28

A method for modulating gene expression comprising the step of administering a biologically effective amount of a human Cyr61 fragment.

17. Claims: 29-51

A method of screening for a modulator of binding between a Cyr61 polypeptide and a Cyr61 receptor integrin, said modulator and its use for preparation of a medicament and for treating various conditions.

18. Claims: 52,53

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A kit for assaying for Cyr61-integrin receptor interactions, said kit comprisin a Cyr61 polypeptide and a composition comprising an integrin receptor.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 01/03267

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9733995 A	18-09-1997	AU 733382 B2	10-05-2001
		AU 2329697 A	01-10-1997
		CA 2248549 A1	18-09-1997
		EP 0888452 A2	07-01-1999
		JP 2000506732 T	06-06-2000
		WO 9733995 A2	18-09-1997