



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁶ : C12N 15/12, C07K 14/52, C12N 5/10, A61K 38/19</p>	A3	<p>(11) International Publication Number: WO 98/49300</p> <p>(43) International Publication Date: 5 November 1998 (05.11.98)</p>																																										
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top; padding: 5px;"> <p>(21) International Application Number: PCT/US98/07801</p> <p>(22) International Filing Date: 20 April 1998 (20.04.98)</p> <p>(30) Priority Data: 08/842,984 25 April 1997 (25.04.97) US</p> <p>(71) Applicant: COLLATERAL THERAPEUTICS [US/US]; Suite 110, 9360 Towne Centre Drive, San Diego, CA 92121 (US).</p> <p>(72) Inventor: BOHLEN, Peter; 2237 Cortina Circle, Escondido, CA 92029 (US).</p> <p>(74) Agent: SILVERSTEIN, Sheryl, R.; Lyon & Lyon LLP, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071-2066 (US).</p> </td> <td style="width: 50%; vertical-align: top; padding: 5px;"> <p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, 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, ML, MR, NE, SN, TD, TG).</p> <p>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></p> <p>(88) Date of publication of the international search report: 11 March 1999 (11.03.99)</p> </td> </tr> </table>			<p>(21) International Application Number: PCT/US98/07801</p> <p>(22) International Filing Date: 20 April 1998 (20.04.98)</p> <p>(30) Priority Data: 08/842,984 25 April 1997 (25.04.97) US</p> <p>(71) Applicant: COLLATERAL THERAPEUTICS [US/US]; Suite 110, 9360 Towne Centre Drive, San Diego, CA 92121 (US).</p> <p>(72) Inventor: BOHLEN, Peter; 2237 Cortina Circle, Escondido, CA 92029 (US).</p> <p>(74) Agent: SILVERSTEIN, Sheryl, R.; Lyon & Lyon LLP, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071-2066 (US).</p>	<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, 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, ML, MR, NE, SN, TD, TG).</p> <p>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></p> <p>(88) Date of publication of the international search report: 11 March 1999 (11.03.99)</p>																																								
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<p>(54) Title: TRUNCATED VEGF-RELATED PROTEINS</p> <div style="text-align: center; margin: 10px 0;"> <p>VEGF-B</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 10%; vertical-align: top;">F/L</td> <td style="width: 40%;"></td> <td style="width: 50%; text-align: right; vertical-align: top;">PVSQFDGFSHQKKVVPWIDVYTRAT</td> </tr> <tr> <td>(1)</td> <td></td> <td style="text-align: right;">PVSQFDGFSHQKKVVPWIDVYTRAT</td> </tr> <tr> <td>(2)</td> <td></td> <td style="text-align: right;">KVVFPWIDVYTRAT</td> </tr> <tr> <td>(3)</td> <td></td> <td style="text-align: right;">PWIDVYTRAT</td> </tr> <tr> <td>(4)</td> <td></td> <td style="text-align: right;">IDVYTRAT</td> </tr> <tr> <td>(5)</td> <td></td> <td style="text-align: right;">YTRAT</td> </tr> <tr> <td>(6)</td> <td></td> <td style="text-align: right;">RAT</td> </tr> </table> </div> <table style="width: 100%; border: none; margin-top: 10px;"> <tr> <td style="width: 10%; vertical-align: top;">F/L</td> <td style="width: 40%;"></td> <td style="width: 50%; text-align: right; vertical-align: top;"> CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC </td> </tr> <tr> <td>(1)</td> <td></td> <td style="text-align: right;">RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK</td> </tr> <tr> <td>(2)</td> <td></td> <td style="text-align: right;">RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK</td> </tr> <tr> <td>(3)</td> <td></td> <td style="text-align: right;">RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK</td> </tr> <tr> <td>(4)</td> <td></td> <td style="text-align: right;">RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK</td> </tr> <tr> <td>(5)</td> <td></td> <td style="text-align: right;">RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK</td> </tr> <tr> <td>(6)</td> <td></td> <td style="text-align: right;">RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK</td> </tr> </table>			F/L		PVSQFDGFSHQKKVVPWIDVYTRAT	(1)		PVSQFDGFSHQKKVVPWIDVYTRAT	(2)		KVVFPWIDVYTRAT	(3)		PWIDVYTRAT	(4)		IDVYTRAT	(5)		YTRAT	(6)		RAT	F/L		CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC CQPREVVVPLSMELMGNVVKQLVPSCVTVQRCGGCCPDDGLECVPTGQHQVRMQLMIQYPSQLGEMSLEEHSQCEC	(1)		RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK	(2)		RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK	(3)		RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK	(4)		RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK	(5)		RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK	(6)		RPKKESAVKPDSPRILCPPTQRRQRPDPTCRRCRRRRFLHCQGRGLELNPDTCRCKPRK
F/L		PVSQFDGFSHQKKVVPWIDVYTRAT																																										
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<p>(57) Abstract</p> <p>The present invention provides novel truncated forms of vascular endothelial growth factor-related proteins (VRPs or VRPs) which are useful for the stimulation of angiogenesis <i>in vitro</i> and <i>in vivo</i>. The invention also provides nucleic acids encoding such novel truncated VRPs and methods of producing truncated VRPs. Pharmaceutical compositions comprising truncated VRPs and methods of gene therapy using the nucleic acids which code for truncated VRPs may be useful for the treatment of heart disease and for wound healing.</p>																																												

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EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/07801

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C07K14/52 C12N5/10 A61K38/19

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 C12N C07K 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 27007 A (AMRAD OPERATIONS PTY LTD (AU); HAYWARD NK; WEBER G; GRIMMOND S ET AL.) 6 September 1996	1-5, 17-23, 25, 28-30, 43-46, 48,49, 60,61
Y	see abstract see page 6, line 24-25 see page 10, line 17-21; figure 10 see page 19 - page 23; example 4 Seq.ID:4 see page 41 -/-	15,16, 32-36, 38, 40-42, 47, 50-59, 62-67

☒ 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.

Z document member of the same patent family

Date of the actual completion of the international search

28 September 1998

Date of mailing of the international search report

15. 01. 1999

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

Authorized officer

Macchia, G

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/07801

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Seq.ID:6 see page 43 - page 44 see page 52 - page 53; claims 11,12,15,16,19 ---	
X	WO 96 39421 A (HUMAN GENOME SCIENCES INC (US); HU J.-S.; OLSEN H. (US); ROSEN C.A.) 12 December 1996 cited in the application	1-3,5,6, 15-23, 28-30, 32-36, 40-49, 56,59-61
Y	see abstract see page 4, paragraph 6 see page 6, paragraph 4 see page 10, paragraph 3 - page 12, paragraph 3 see page 18, paragraph 4 - page 20, paragraph 1 see page 22, paragraph 2 see page 25, paragraph 3 - page 27, paragraph 2 see page 38 - page 39; example 2 Seq.ID:2 see page 44 ---	15,16, 32-36, 38, 40-42, 47,56,59
Y	WO 96 26736 A (LUDWIG INST FOR CANCER RESEARCH (US); UNIV HELSINKI LICENSING LTD (FI)) 6 September 1996 see abstract see page 9, line 18-27 see page 10, line 29 - page 11, line 11 see page 18, line 3-26 see page 22 - page 23; example 4 see page 31 - page 33; example 9 see page 47, line 21 - page 48, line 30 see page 49, line 26 - page 50, line 5 Seq.ID:11,15 see page 59 - page 62 see figure 16 ---	15,32, 33,56,59
Y	WO 96 26742 A (UNIVERSITY CALIFORNIA; HAMMOND H.K.; GIORDANO F.J.; DILLMAN W.H. (US)) 6 September 1996 cited in the application see abstract see page 5, line 16 - page 8, line 19 see page 38 - page 44; claims ---	32-36, 38, 40-42, 47,62-67

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/07801

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	PEPPER M.S. ET AL.: "Potent synergism between vascular endothelial growth factor and basic fibroblast growth factor in the induction of angiogenesis in vitro" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 189, no. 2, 15 December 1992, pages 824-831, XP002078851 see the whole document	50-55, 57,58
A	WO 97 05250 A (UNIV HELSINKI LICENSING LTD OY (FI); ALITALO K.; JOUKOV V.) 13 February 1997 see page 7, line 12-28 see page 8, line 28 - page 11, line 1 see page 15, line 11 - page 16, line 4 see page 27, line 14 - page 29, line 12 see page 30, line 21-31 see page 44 - page 45; example 7 see page 50, line 26 - page 53, line 15 see page 68 - page 74; examples 21,22 see page 84 - page 88; example 28 Seq.ID:33 see page 112 - page 113	1-3,5-7, 9,11,15, 17-23, 28-30, 43-49, 56,59-61
A	WO 92 06194 A (CONSIGLIO NAZIONALE RICERCHE (IT); PERSICO M.; MAGLIONE D.) 16 April 1992 see page 6, paragraph 3 see page 21; claims 4,6 see page 24; claims 29,31	1-3,5-7, 9,11, 17-23, 28-30, 43-46, 48,49,60
A	WO 94 11506 A (ARCH DEVELOPMENT CORPORATION; LEIDEN J.M.; BARR H. (US)) 26 May 1994 see abstract	32-36, 38, 40-42, 47,62-67

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/ 07801

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 claim(s) 45, 47-52, 56-67
is(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:

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.:

4 totally ; 1-3, 5-67 partially.

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

International Application No. PCT/US 98/07801

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 4 totally; 1-3, 5-67 all partially.

Truncated VEGF-B, VRF-2 or VEGF-3 subunit having a deletion of at least one of the aminoacid residues N-terminal to the first cysteine of the core sequence of said subunit, homodimers and heterodimers thereof. Nucleic acid molecule encoding said truncated subunit, recombinant vector comprising said nucleic acid molecule and transformed host cell thereof. Delivery vector comprising said nucleic acid molecule. Method for producing said truncated subunit. Pharmaceutical composition comprising said truncated subunit or delivery vector, therapeutical applications thereof.

2. Claims: 1-3, 5-67 all partially.

As invention 1 but concerning VEGF-C.

3. Claims: 1-3, 6-67 all partially.

As invention 1 but concerning PlGF.

4. Claims: 1-3, 5-67 all partially.

As invention 1 but concerning poxvirus ORF-1.

5. Claims: 1-3, 5-67 all partially.

As invention 1 but concerning poxvirus ORF-2.

INTERNATIONAL SEARCH REPORT

Inform. on patent family members

International Application No

PCT/US 98/07801

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9627007 A	06-09-1996	AU 4708396 A	18-09-1996
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