

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
4 March 2004 (04.03.2004)

PCT

(10) International Publication Number  
**WO 2004/018995 A3**

(51) International Patent Classification<sup>7</sup>: **A61K 38/16**

(21) International Application Number:  
PCT/US2003/026023

(22) International Filing Date: 20 August 2003 (20.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/405,494 23 August 2002 (23.08.2002) US  
10/419,462 21 April 2003 (21.04.2003) US

(71) Applicant and

(72) Inventor: **WILLIAMS, Kevin, J.** [US/US]; 425 Wister  
Road, Wynnewood, PA 19096 (US).

(74) Agent: **FRIED, Allan, H.**; Caesar, Rivise, Bernstein, Co-  
hen & Pokotilow, Ltd., 12th Floor, Seven Penn Center, 1635  
Market Street, Philadelphia, PA 19102-2212 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,

CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,  
SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,  
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,  
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,  
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

(88) Date of publication of the international search report:  
10 September 2004

*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.*



**WO 2004/018995 A3**

(54) Title: THROMBOSPONDIN FRAGMENTS AND USES THEREOF IN CLINICAL ASSAYS FOR CANCER AND GENERATION OF ANTIBODIES AND OTHER BINDING AGENTS

(57) Abstract: The invention relates to thrombospondin fragments found in plasma, their use or use of portions thereof in diagnostic methods, as method calibrators, method indicators, and as immunogens, and as analytes for methods with substantial clinical utility; and their detection in plasma or other bodily fluids for purpose of diagnostic methods, especially for cancer.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/26023

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(7) : A61K 38/16 US CL : 435/69.1, 240.2, 325, 320.1, 252.3; 514/2, 12; 530/350, 412 According to International Patent Classification (IPC) or to both national classification and IPC											
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/69.1, 240.2, 325, 320.1, 252.3; 514/2, 12; 530/350, 412  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 practicable, search terms used) WEST, GenCore databases											
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>											
Category *	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 15%; padding: 5px;">Citation of document, with indication, where appropriate, of the relevant passages</th> <th style="width: 85%; padding: 5px;">Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td style="padding: 5px;">                     X                      ---                      A                      US 5,750,502 A (JESSELL et al) 12 May 1998 (12.05.1998), columns 77 and 78, residues 1007-1021 of sequence 20 same as Applicants' SEQ ID NO: 3 and 25                 </td> <td style="padding: 5px;">                     10, 27, 28, 154 and 155                       -----                      1-9, 11-26, 29-43, 47-49, 54-67, 70-78, 80-89, 93-95, 98, 109-115, 123-127, 129-132, 134, 137-150, 152, 156-164                 </td> </tr> </tbody> </table>	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X --- A US 5,750,502 A (JESSELL et al) 12 May 1998 (12.05.1998), columns 77 and 78, residues 1007-1021 of sequence 20 same as Applicants' SEQ ID NO: 3 and 25	10, 27, 28, 154 and 155  ----- 1-9, 11-26, 29-43, 47-49, 54-67, 70-78, 80-89, 93-95, 98, 109-115, 123-127, 129-132, 134, 137-150, 152, 156-164						
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.										
X --- A US 5,750,502 A (JESSELL et al) 12 May 1998 (12.05.1998), columns 77 and 78, residues 1007-1021 of sequence 20 same as Applicants' SEQ ID NO: 3 and 25	10, 27, 28, 154 and 155  ----- 1-9, 11-26, 29-43, 47-49, 54-67, 70-78, 80-89, 93-95, 98, 109-115, 123-127, 129-132, 134, 137-150, 152, 156-164										
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.											
* Special categories of cited documents:	<table style="width: 100%;"> <tr> <td style="width: 30%;">"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td style="width: 30%;">"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</td> </tr> <tr> <td>"E" earlier application or patent published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"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</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&amp;" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>	"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"E" earlier application or patent published on or after the international filing date	"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	"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)	"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	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed	
"A" document defining the general state of the art which is not considered to be of particular relevance	"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										
"E" earlier application or patent published on or after the international filing date	"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										
"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)	"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										
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family										
"P" document published prior to the international filing date but later than the priority date claimed											
Date of the actual completion of the international search 24 May 2004 (24.05.2004)	Date of mailing of the international search report <div style="text-align: center; font-size: 1.2em; font-weight: bold;">28 JUL 2004</div>										
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 872-9306	Authorized officer Alana M. Harris, Ph.D. <i>J. Roberts for</i> Telephone No. (571) 272-1600										

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/26023

**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

- 1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
- 2.  Claim 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.  Claim Nos.: 44-46,50-53,68,69,79,90-92,96,97,99-108,116-122,128,133,135,136,151 and 153  
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.