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(71) Applicants (for all designated States except US): **BAXTER INTERNATIONAL INC.** [US/US]; One Baxter Parkway, Deerfield, IL 60015 (US). **BAXTER HEALTHCARE S.A.** [CH/CH]; Thurgauerstrasse 130, CH-8152 Glattpark (Opfikon) (CH). **3B PHARMACEUTICALS GMBH** [DE/DE]; Danckelmannstrasse 53, D-14059 Berlin (DE). **COSMIX MOLECULAR BIOLOGICALS GMBH** [DE/DE]; Am Rebenring 31, D-38106 Braunschweig (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DOCKAL, Michael** [AT/AT]; Mariahilferstrasse 173-175/2/54, A-1150 Vienna (AT). **EHRlich, Hartmut** [DE/AT]; Dr. Heinrich-Maier-Strasse 20/1, A-1180 Vienna (AT). **SCHEIFLINGER, Friedrich** [AT/AT]; Michelbeuerngasse 4/17, A-1090 Vienna (AT). **REIMER, Ulf** [DE/DE]; Dunckerstrasse 25, D-10437 Berlin (DE). **REINEKE, Ulrich** [DE/DE]; Danckelmannstraße 53, D-14059 Berlin (DE). **POLAKOWSKI, Thomas** [DE/DE]; Dunckerstrasse 26a, D-10437 Berlin (DE). **SCHNEIDER, Eberhard** [DE/DE]; Am Söhlberg 4, D-38321 Denkte (DE).

(74) Agents: **KISSLING, Heather, R.** et al.; MARSHALL, GERSTEIN & BORUN LLP, 233 S. Wacker Drive, Suite 6300, Sears Tower, Chicago, IL 60606-6357 (US).

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- with international search report (Art. 21(3))
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- with sequence listing part of description (Rule 5.2(a))

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(54) Title: TFPI INHIBITORS AND METHODS OF USE

(57) Abstract: The invention provides peptides that bind Tissue Factor Pathway Inhibitor (TFPI), including TFPI-inhibitory peptides, and compositions thereof. The peptides may be used to inhibit a TFPI, enhance thrombin formation in a clotting factor-deficient subject, increase blood clot formation in a subject, and/or treat a blood coagulation disorder in a subject.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/69060

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 38/00 (2010.01) USPC - 514/2; 514/13; 530/326 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(8) - A61K 38/00 (2010.01) USPC - 514/2; 514/13; 530/326 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 530/324; 530/325 Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PubWEST, GOOGLE: EPI,TFPI,LACI,Kunitz-type proteinase inhibitor domain, blood coagulation, antibody, peptide,dose, concentration, GenCore 6.3: SEQ ID NO:8-14,16-56, 164, 223, 742, 744, 968, 971, 978, 1001, 1040, 2001,1210, 1213, 1293, 2023, 2051, 2126, 2128, 2296, 2298, 2497-2498, 3001, 3048, 3051, 3053, 3055, 3057, 3064, 3066, 3108		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 7,015,194 B2 (Kjalke) 21 March 2006 (21.03.2006) Abstract, claim 5; col 7, ln 55-59; col 11, ln 45-51	95-96, 98
X	Tang, et al. Sepsis-Induced Coagulation in the Baboon Lung Is Associated with Decreased Tissue Factor Pathway Inhibitor. The American Journal of Pathology 2007, 171(3):1066-1077; Abstract, pg 1068	95-96
X	US 2008/0161425 A1 (Hackeng, et al.) 03 July 2008 (03.08.2008) para [0076]	95-96
X	Erhardtson et al. Blocking of tissue factor pathway inhibitor (TFPI) shortens the bleeding time in rabbits with antibody induced haemophilia A. Blood Coagul Fibrinolysis 1995, 6(5):388-394;Abstract	95-96
A	Hedner, et al. Tissue Factor and Factor VIIa as Therapeutic Targets in Disorders of Hemostasis. Annu. Rev. Med. E-Pub September 2007, 59:29-41	95-96
A	Lean, et al. The effects of tissue factor pathway inhibitor and anti-b-2-glycoprotein-I IgG on thrombin generation. Haematologica 2006, 91:1360-1366	95-96
A	Yun, et al. Proteolytic inactivation of tissue factor pathway inhibitor by bacterial omlptins. Blood E-Pub 06 November 2008, 113(5):1139-1148	95-96, 98
A	WO 1992/07584 A1 (HEDNER, et al.) 14 May 1992 (14.05.1992)	95-96
A	Liu, et al. Improved coagulation in bleeding disorders by Non-Anticoagulant Sulfated Polysaccharides (NASP). Thromb Haemost 2006; 95:68-76	95-96
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* 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 application or patent 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 28 July 2010 (28.07.2010)		Date of mailing of the international search report 18 AUG 2010
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. 571-273-3201		Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/69060

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 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.: 4-9, 13-28, 31, 36-40, 44-51, 54, 59-62, 66-82, 85, 88-94, 97, 99-133
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Group I: claims 1-3, 10-12, 29-30, 32-35, 41-43, 52-53, 55-58, 63-65, 83-84, 86-87, drawn to a peptide that binds TFPI.
Group II, claims 95-96, 98, drawn to administering to the subject a peptide that inhibits TFPI activity.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:
The inventions of Group II do not include the inventive concept of a peptide of specific structure, wherein said peptide binds TFPI, as required by Group I. The inventions of Groups I-II share the technical feature of a peptide that binds TFPI. However, this shared technical feature does not represent a contribution over prior art. Specifically, a paper titled "Sepsis-Induced Coagulation in the Baboon Lung Is Associated with Decreased Tissue Factor Pathway Inhibitor" by Tang, et al. (Am J Pathol 2007, 171:1066?1077) discloses Blocking antibodies against TFPI (Abstract). As said peptide that binds TFPI was known at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

Groups I-II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

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 additional fees, this Authority did not invite payment of additional fees.
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 and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.