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(54) **Title:** THROMBIN SENSITIVE COAGULATION FACTOR X MOLECULES

(57) **Abstract:** The present invention relates to thrombin sensitive coagulation Factor X (FX), as well as use thereof in medicine. In particular the invention relates to FX molecules comprising 2 to 10 amino acid modifications in the activation peptide N-terminally of the FX "IVGG" motif as well as compositions comprising such molecules and use thereof. Such molecules may be useful in connection with convenient and patient friendly treatment regimens in treatment and prophylaxis of haemophilia.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/054841

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N9/64 A61K38/01 A61K38/48
ADD.
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)
A61K C12N

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)
EPO-Internal, WPI Data, BIOSIS, CHEM ABS Data, Sequence Search, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2010/070137 A1 (INST NAT SANTE RECH MED [FR]; CHRISTOPHE OLIVIER [FR]; DENIS CECILE [F] 24 June 2010 (2010-06-24) page 12, line 33 - page 16, line 18; claims -----	1,18,19
X	US 2006/148038 A1 (LOUVAIN VIRGINIE [FR] ET AL) 6 July 2006 (2006-07-06) paragraphs [0060] - [0061], [0133]; claims; table V -----	1,18,19
X	WO 98/38317 A1 (IMMUNO AG [AT]; HIMMELSPACH MICHELE [AT]; SCHLOKAT UWE [AT]; DORNER FR) 3 September 1998 (1998-09-03) page 22, last paragraph - page 23, paragraph 1; claims 1-4; example 11; sequence 2 -----	1,18,19
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Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search 16 June 2014	Date of mailing of the international search report 19/09/2014
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Huber, Angelika
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INTERNATIONAL SEARCH REPORT

International application No
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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 2007/096116 A1 (ZLB BEHRING GMBH [DE]; SCHULTE STEFAN [DE]; HAUSER HANS-PETER [DE]; KA) 30 August 2007 (2007-08-30) claims 9-11, 20; figure 1 -----	1,18,19

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2014/054841

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.:
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:

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 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.:

2(completely); 1, 18, 19(partially)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 2(completely); 1, 18, 19(partially)

A thrombin-sensitive Factor X molecule comprising 2-10 amino acid modifications N-terminally of the IVGG motif (aa 195-198 in SEQ ID NO: 1) in wild type factor X, said molecule having the sequence in position X10 to X1:
X10, X9, N, N, A ,T. [L, I, M, F, V, P, W], [Q, M, R, T, W, K, I, V], P, R

2. claims: 3, 9, 10, 12, 13(completely); 1, 18, 19(partially)

A thrombin-sensitive Factor X molecule comprising 2-10 amino acid modifications N-terminally of the IVGG motif (aa 195-198 in SEQ ID NO: 1) in wild type factor X, said molecule having the sequence in position X10 to X1:
X10, X9, R, G, D, N, [L, I, M, F, V, P, W], [T, S], P, R

3. claims: 4-8(completely); 1, 18, 19(partially)

A thrombin-sensitive Factor X molecule comprising 2-10 amino acid modifications N-terminally of the IVGG motif (aa 195-198 in SEQ ID NO: 1) in wild type factor X, said molecule having the sequence in position X10 to X1:
X10, A, T, N, A, T, [F, L, M, W, A, I, V, P], [T, K, Q, P, S, Y, R, A, V, W, I, H] ,P, R

4. claims: 11(completely); 1, 18, 19(partially)

A thrombin-sensitive Factor X molecule comprising 2-10 amino acid modifications N-terminally of the IVGG motif (aa 195-198 in SEQ ID NO: 1) in wild type factor X, said molecule having the sequence in position X10 to X1:
P, E, R, N, A, T, L, T, P, R

5. claims: 14(completely); 1, 18, 19(partially)

A thrombin-sensitive Factor X molecule comprising 2-10 amino acid modifications N-terminally of the IVGG motif (aa 195-198 in SEQ ID NO: 1) in wild type factor X, said molecule having the sequence in position X10 to X1:
S, T, P, S, I, L, L, K, P, R

6. claims: 15(completely); 1, 18, 19(partially)

A thrombin-sensitive Factor X molecule comprising 2-10 amino acid modifications N-terminally of the IVGG motif (aa 195-198 in SEQ ID NO: 1) in wild type factor X, said

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

molecule having the sequence in position X10 to X1:
T, R, P, S, I, L, F, T, P, R

7. claims: 16(completely); 1, 18, 19(partially)

A thrombin-sensitive Factor X molecule comprising 2-10 amino acid modifications N-terminally of the IVGG motif (aa 195-198 in SEQ ID NO: 1) in wild type factor X, said molecule having the sequence in position X10 to X1:
D, F, L ,A, E, G, G, G, P, R

8. claims: 17(completely); 1, 18, 19(partially)

A thrombin-sensitive Factor X molecule comprising 2-10 amino acid modifications N-terminally of the IVGG motif (aa 195-198 in SEQ ID NO: 1) in wild type factor X, said molecule having the sequence in position X10 to X1:
N, E, S, T, T, K, I, K, P, R

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/054841

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