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(54) Title: METHODS FOR DIAGNOSING AND TREATING HEMOSTATIC DISORDERS BY MODULATING P-SELECTIN ACTIVITY

(57) Abstract: The present invention identifies P-selectin as a modulator of hemostasis. Accordingly, the present invention relates to methods for the identification and use of modulators of P-selectin activity as modulators of hemostasis. The invention also relates to methods and compositions for the diagnosis and treatment of hemostatic disorders, including, but not limited to, hemorrhagic disorders and thrombotic disorders. The present invention describes methods for the diagnostic evaluation and prognosis of various hemostatic conditions, and for the identification of subjects exhibiting a predisposition to such conditions. In addition, the present invention provides methods for the diagnostic monitoring of patients undergoing clinical evaluation for the treatment of hemostatic or vascular disorders, and for monitoring the efficacy of compounds in clinical trials.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/16021

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/395 A61K48/00 A61K38/17 A61K35/14 A61P7/00
A61P9/00 A61P35/00 G01N33/50 G01N33/86 G01N33/68

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 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)
BIOSIS, EMBASE, WPI Data, PAJ, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M. SUBRAMANIAM ET AL.: "Defects in hemostasis in P-selectin-deficient mice." BLOOD, vol. 87, no. 4, 15 February 1996 (1996-02-15), pages 1238-1242, XP001064070 Philadelphia, PA, USA page 1241, right-hand column, line 12 - line 23 --- -/--	1,12-14, 37,38, 41,46, 48,49

[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

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
1 March 2002	14/03/2002

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	Nooij, F

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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	H. ZHANG ET AL.: "A recombinant soluble P-selectin glycoprotein ligand-1 chimera has a thrombolytic effect in a rat model of thrombosis." JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, vol. 35, no. 2 suppl. A, February 2000 (2000-02), page 280A XP001034262 USA abstract 1111-42 ---	24,25, 29, 31-40,49
X	E. PEERSCHKE ET AL.: "Platelet activation by C1q results in the induction of alpha-IIb/beta3 integrins (GPIIb/IIIa) and the expression of P-selectin and procoagulant activity." THE JOURNAL OF EXPERIMENTAL MEDICINE, vol. 178, no. 2, August 1993 (1993-08), pages 579-587, XP000655063 New York, NY, USA title abstract ---	1,4, 12-15, 37-39, 41,46-49
X	WO 94 11498 A (BOARD OF REGENTS OF THE UNIVERSITY OF OKLAHOMA) 26 May 1994 (1994-05-26) claims 16,18,19 ---	1,5-8, 12-15, 17,18, 24,29, 31-41, 46,48,49
X	WO 95 06118 A (STATE UNIVERSITY OF OKLAHOMA) 2 March 1995 (1995-03-02) claims ---	24,25, 27, 30-40, 42-45,49
X	J. STONE ET AL.: "P-selectin mediates adhesion of platelets to neuroblastoma and small cell lung cancer." JOURNAL OF CLINICAL INVESTIGATION, vol. 82, August 1993 (1993-08), pages 804-813, XP002927157 New York, NY, USA abstract page 810, right-hand column, line 35 -page 811, left-hand column, line 10 --- -/--	17,18, 22,23

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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	M. SHIMURA ET AL.: "Increased plasma soluble-adhesion molecules in thrombotic thrombocyopenic purpura and disseminated intravascular coagulation." CLINICAL AND APPLIED THROMBOSIS/HEMOSTASIS, vol. 4, no. 3, 1998, pages 196-200, XP001064068 New York, NY, USA abstract	42-45
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A	WO 92 12994 A (BRISTOL-MYERS SQUIBB COMPANY) 6 August 1992 (1992-08-06) page 12, line 20 - line 26 claims 1,5,14,24,29,31,34	20,21
P,X	P. ANDRÉ ET AL.: "Pro-coagulant state resulting from high levels of soluble P-selectin in blood." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE U.S.A., vol. 97, no. 25, 5 December 2000 (2000-12-05), pages 13835-13840, XP002191822 Washington, DC, USA the whole document	1-49

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 1-41 are directed to a method of treatment of the human/animal body, and although claims 46 and 47 (both partially, as far as an in vivo method is concerned) are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. Claims: 1-16, 41 (all completely) and 37-39, 48, 49 (partially)

   Method for inducing hemostasis using an inducer of P-selectin activity, and its use for treatment/prevention of a disorder associated with hypocoagulation.

2. Claims: 17-23

   Method for treating a vasculature-associated disease using an inducer of P-selectin

3. Claims: 24-36, 40 (all completely), 37-39, 48, 49 (all partially)

   Method for reducing hemostasis using an inhibitor of P-selectin, and method of treating/preventing thrombotic disorders.

4. Claims: 42-45

   Method for diagnosing a procoagulant state or a thrombotic disorder by determining a P-selectin activity.

5. Claims: 46, 47

   Method for identifying a compound capable of modulating hemostasis.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 01/16021

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