



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/57, A61K 48/00, 38/48, 38/20, 38/19, 38/21	A3	(11) International Publication Number: WO 99/47152 (43) International Publication Date: 23 September 1999 (23.09.99)
(21) International Application Number: PCT/US99/05918 (22) International Filing Date: 19 March 1999 (19.03.99) (30) Priority Data: 60/078,806 20 March 1998 (20.03.98) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 60/078,806 (CON) Filed on 20 March 1998 (20.03.98) (71) Applicant (for all designated States except US): SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH [US/US]; 1275 York Avenue, New York, NY 10021 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): HOUGHTON, Alan, N. [US/US]; 1233 York Avenue, Apartment 23B, New York, NY 10021 (US). WESLEY, Umadevi, V. [IN/US]; 500 East 63rd Street, Apartment 22F, New York, NY 10021 (US). WOLCHOK, Jedd, D. [US/US]; 333 East 30th Street, Apartment #17C, New York, NY 10016 (US).		(74) Agents: COHEN, Mark et al.; Klauber & Jackson, 411 Hackensack Avenue, Hackensack, NJ 07601 (US). (81) Designated States: AU, CA, JP, MX, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). 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> (88) Date of publication of the international search report: 27 January 2000 (27.01.00)
(54) Title: USE OF DIPEPTIDYL PEPTIDASE (DPP4) OF FIBROBLAST ACTIVATING PROTEIN ALPHA FOR SUPPRESSING THE MALIGNANT PHENOTYPE OF CANCER CELLS (57) Abstract This invention provides a method of suppressing the malignant phenotype or inducing apoptosis of cancer cells in a subject, comprising introducing into the cancer cell an amount of a nucleic acid encoding a dipeptidyl peptidase IV protein or fibroblast activating protein-α, thereby suppressing the malignant phenotype of the cancer. This invention provides a method of treating a subject with cancer which comprises administering to the subject a pharmaceutical composition comprising a therapeutically effective amount of a purified dipeptidyl peptidase IV protein or fibroblast activating protein-α and a pharmaceutical acceptable carrier or diluent. This invention provides a method of inducing expression of dipeptidyl peptidase IV or fibroblast activating protein-α in cancer cells of a subject, comprising administering to the subject a pharmaceutical composition comprising a therapeutically effective amount of an agent capable of activating transcription of the dipeptidyl peptidase IV gene or fibroblast activating protein-α and a pharmaceutical acceptable carrier or diluent.		

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INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 99/05918

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/57 A61K48/00 A61K38/48 A61K38/20 A61K38/19
A61K38/21

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 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	MORRISON M E ET AL: "A marker for neoplastic progression of human melanocytes is a cell surface ectopeptidase." JOURNAL OF EXPERIMENTAL MEDICINE, (1993 APR 1) 177 (4) 1135-43. , XP002124289 the whole document --- -/--	1,2,5-22

☒ Further documents are listed in the continuation of box C.

☐ 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

"E" earlier document 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

30 November 1999

Date of mailing of the international search report

15/12/1999

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/05918

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WESLEY, U. ET AL: "Implicating a cell surface peptidase, adenosine deaminase binding protein (ADAbp) in growth and survival of melanocytes and melanoma." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, (1997) VOL. 38, NO. 0, PP. 626. MEETING INFO.: EIGHTY-EIGHTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH SAN DIEGO, CALIFORNIA, USA APRIL 12-16, 1997 , XP002124290 abstract #4201 ---	1-22
X	BÖHM ET AL: "HUMAN DIPEPTIDYL PEPTIDASE IV GENE PROMOTER: TISSUE-SPECIFIC REGULATION FROM A TATA-LESS GC-RICH SEQUENCE CHARACTERISTIC OF A HOUSEKEEPING GENE PROMOTER" BIOCHEMICAL JOURNAL, vol. 311, 1995, pages 835-843, XP002124291 cited in the application page 842 -page 843 ---	9-13
A	PINEIRO-SANCHEZ, MAYRA L. ET AL: "Identification of the 170-kDa melanoma membrane-bound gelatinase (seprase) as a serine integral membrane protease." JOURNAL OF BIOLOGICAL CHEMISTRY, (1997) VOL. 272, NO. 12, PP. 7595-7601. , XP002124292 the whole document -----	23-42

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/05918

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 claims 1-42 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:

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.