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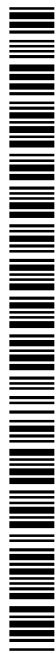
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(54) Title: METHOD AND COMPOSITION FOR INHIBITION OF TUMOR GROWTH AND ENHANCING AN IMMUNE RESPONSE

(57) Abstract: Provided is a method and composition for enhancing an immune response in a subject by administering to the subject an inhibitor of IL-13 or an inhibitor of an NK-T cell to the subject. The method can be used to prevent growth of a tumor in the subject, e.g., to inhibit tumor recurrence or metastasis. The method can also be used to enhance a response to a vaccine in a subject.

INTERNATIONAL SEARCH REPORT

International Application No

PC/US 01/51339

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/00

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 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)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 94 04680 A (SCHERING CORP) 3 March 1994 (1994-03-03)</p> <p>claims 4,5,11 page 21, line 33 -page 22, line 2 page 22, line 21 - line 27</p>	<p>1-4,14, 16-24, 27-32, 34, 37-44,59</p>
E	<p>EP 1 176 140 A (MITSUBISHI PHARMA CORP) 30 January 2002 (2002-01-30)</p> <p>claim 14 page 36, line 27,53 page 37, line 6,12</p>	<p>1-4, 19-24, 27-32, 34,37, 38,49-53</p>

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

27 June 2002

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International Application No

P US 01/51339

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 6 143 871 A (GAUCHAT JEAN-FRANCOIS ET AL) 7 November 2000 (2000-11-07) claims 1,3,16 column 4, line 1 - line 4 ---	1-4,13, 19-24, 27-32, 34,37, 38, 49-53,59
P,X	WO 01 77332 A (HESKA CORP ;TANG LIANG (US); MCCALL CATHERINE A (US)) 18 October 2001 (2001-10-18) claim 44 page 53, line 26 - line 28 ---	59
X	WO 00 36103 A (GENETICS INST ;UNIV JOHNS HOPKINS (US)) 22 June 2000 (2000-06-22) claims 21,30,45,46 page 14, line 25 -page 15, line 6 page 15, line 25 -page 16, line 8 ---	1-4, 13-30, 34-44, 49-53,59
X	WO 00 40264 A (DEBINSKI WALDEMAR ;CONNOR JAMES R (US); PENN STATE RES FOUND (US)) 13 July 2000 (2000-07-13) claims 1,4,5 page 7, line 21 - line 25 -----	1-4, 8-24,27, 29,34-44

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/51339**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:
Although claims 1 - 44, 49 - 53, 59 - 73 and 85 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.
2. Claims Nos.: 1, 2, 19, 38, 49, 59
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:
see FURTHER INFORMATION sheet PCT/ISA/210
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:

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 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.:
1-44, 49-53, 59-73

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 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: 1 - 44, 49 - 53, 59 - 73

1.1. Claims: 1 - 44

Method of inhibiting the growth of tumor comprising administering an IL-13 inhibitor

1.2. Claims: 49 - 53

Method of inhibiting the growth of a virus comprising administering an IL-13 inhibitor

1.3. Claims: 59 - 73

Method of enhancing an immune response comprising administering an IL-13 inhibitor

2. Claims: 45 - 48, 54 - 58, 74 - 84

Invention 2:

Method of inhibiting the growth of a tumor, of inhibiting the growth of a virus or of enhancing an immune response comprising administering a NK-T cell inhibitor

3. Claim : 85

Invention 3:

Method of inhibiting the growth of a tumor comprising administering a nucleic acid encoding an IL-13 ligand

Please note that all inventions mentioned under item 1, although not necessarily linked by a common inventive concept, could be searched without effort justifying an additional fee.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1, 2, 19, 38, 49, 59

Present claims 1, 2, 19, 38, 49, 59 and 85 relate to a method defined by reference to a desirable characteristic or property, namely "IL-13 inhibitor". The claims cover all methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such methods. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the method by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been limited to a key word search relating to those parts of the claims which appear to be clear, supported and disclosed, namely an IL-13 inhibitor comprising an IL-13 binding region of an IL-13 receptor, an IL-13 inhibitor comprising an immunoglobulin polypeptide and a fusion protein comprising an IL-13 polypeptide and an Fc region of a IgG polypeptide (claims 13 - 18).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/51339

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9404680	A	03-03-1994	US 5596072	A 21-01-1997
			AU 5010793	A 15-03-1994
			CA 2142860	A1 03-03-1994
			EP 0656947	A1 14-06-1995
			JP 7508179	T 14-09-1995
			WO 9404680	A1 03-03-1994
			CN 1085953	A 27-04-1994
			ZA 9306097	A 21-02-1994

EP 1176140	A	30-01-2002	AU 2460600	A 29-08-2000
			BR 0008173	A 22-10-2002
			EP 1176140	A1 30-01-2002
			CN 1346348	T 24-04-2002
			WO 0047558	A1 17-08-2000
			NZ 514095	A 28-09-2001

US 6143871	A	07-11-2000	NONE	

WO 0177332	A	18-10-2001	AU 5328201	A 23-10-2001
			WO 0177332	A2 18-10-2001

WO 0036103	A	22-06-2000	AU 2177500	A 03-07-2000
			BR 9916209	A 26-12-2001
			CN 1352686	T 05-06-2002
			EP 1141286	A1 10-10-2001
			WO 0036103	A1 22-06-2000

WO 0040264	A	13-07-2000	US 2001053371	A1 20-12-2001
			AU 2223800	A 24-07-2000
			EP 1140167	A1 10-10-2001
			JP 2002534395	T 15-10-2002
			WO 0040264	A1 13-07-2000
			US 2002031492	A1 14-03-2002
