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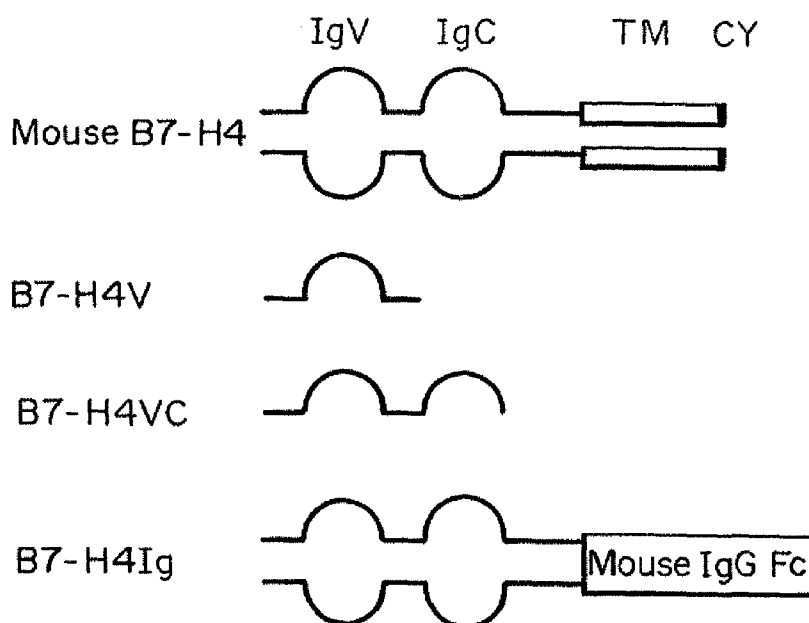
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR TREATING INFLAMMATION AND AUTO-IMMUNE DISEASES



(57) Abstract: Compositions containing soluble B7-H4 (sH4) antagonists in an amount effective to reduce, inhibit, or mitigate an inflammatory response in an individual and methods for the treatment or prophylaxis of inflammatory disorders and autoimmune diseases or disorders are provided. Soluble H4 has been discovered to interfere with B7-H4 activity including B7-H4's activity as an inhibitor of T cell immunity. Thus, interference of sH4 biological activity is an effective method to restore B7-H4 activity and thereby provide an effective method for treating inflammatory diseases or disorders including autoimmune diseases or disorders.

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— *with sequence listing part of description published separately in electronic form and available upon request from the International Bureau*

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INTERNATIONAL SEARCH REPORT

International application No

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A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K38/17 A61K38/55 A61P37/00

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)

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, EMBASE, MEDLINE, BIOSIS, COMPENDEX, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/000221 A (UNIV CALIFORNIA [US]; UNIV WASHINGTON [US]; ALLISON JAMES P [US]; MURP) 31 December 2003 (2003-12-31) page 6, lines 11-19; claims 4,8,10; figure 1 page 54, line 21 - line 23	1-7, 16, 17
X	US 2004/152105 A1 (VOGT LORENZ [CH] ET AL) 5 August 2004 (2004-08-05) paragraphs [0076], [0089], [0103]; claims 5,13,23,21; examples 3,18	1-15
X	US 2002/168762 A1 (CHEN LIEPING [US]) 14 November 2002 (2002-11-14) paragraphs [0095], [0104]	1-7
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☒ Further documents are listed in the continuation of Box C.☒ See patent family 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

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22/09/2008

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/088960

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	OU DAWEI ET AL: "B7-H4.Ig inhibits human beta-cell destruction mediated by beta cell-specific cytotoxic T cells derived from patients with type 1 diabetes" DIABETES, NEW YORK, NY, US, vol. 54, no. Suppl. 1, 14 June 2005 (2005-06-14), page A311, XP009101950 ISSN: 0012-1797 abstract	1-15
X	US 6 537 968 B1 (LEZDEY DARREN [US] ET AL). 25 March 2003 (2003-03-25) claim 1	1,4-10
X	US 2004/229795 A1 (ROEMISCH JUERGEN [DE] ET AL) 18 November 2004 (2004-11-18) paragraphs [0011], [0016] - [0034]	1,4-10
X	MEDINA C ET AL: "THERAPEUTIC EFFECT OF PHENANTROLINE IN TWO RAT MODELS OF INFLAMMATORY BOWEL DISEASE" SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY, XX, XX, vol. 36, no. 12, 1 January 2001 (2001-01-01), pages 1314-1319, XP008067562 ISSN: 0036-5521 page 1316 - page 1317	1,4-10
X	US 3 840 513 A (UMEZAWA H ET AL) 8 October 1974 (1974-10-08) column 2, lines 10-12	1,4-10
X	SICA GABRIEL L ET AL: "B7-H4, a molecule of the B7 family, negatively regulates T cell immunity." IMMUNITY, vol. 18, no. 6, June 2003 (2003-06), pages 849-861, XP002485368 ISSN: 1074-7613 page 853 - page 856	1-15
X	US 2004/175380 A1 (ALLISON JAMES P [US] ET AL MURPHY KENNETH P [US] ET AL) 9 September 2004 (2004-09-09) paragraph [0318]	16,17
X	US 2005/163772 A1 (DONG CHEN [US] ET AL) 28 July 2005 (2005-07-28) paragraph [0149]	16,17

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/088960

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DAU P C: "The fundamental basis for therapeutic plasmapheresis in autoimmune diseases" TRANSFUSION SCIENCE, PERGAMON PRESS, OXFORD, GB, vol. 17, no. 2, 1 June 1996 (1996-06-01), pages 235-244, XP004568785 ISSN: 0955-3886 the whole document	18-21
A	"Plasmapheresis in severe autoimmune hepatitis - N Zakaria, P Harrison, I McFarlane, J Devlin, King's College Hospital, London United Kingdom" HEPATOLOGY, WILLIAMS AND WILKINS, BALTIMORE, MD, US, vol. 34, no. 4, 1 October 2001 (2001-10-01), page A529, XP004716960 ISSN: 0270-9139 the whole document	18-21
A	MALCHESKY P S ET AL: "ARE SELECTIVE MACROMOLECULE REMOVAL PLASMAPHERESIS SYSTEMS USEFUL FOR AUTOIMMUNE DISEASES OR HYPERLIPIDEMIA?" ASAIO JOURNAL, LIPPINCOTT WILLIAMS & WILKINS / ASAIO, HAGERSTOWN, MD, US, vol. 39, no. 4, 1 October 1993 (1993-10-01), pages 868-872, XP000423348 ISSN: 1058-2916 the whole document	18-21

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: -

The present claims 1 and 8 relate to an extremely large number of possible compounds. Support and disclosure in the sense of Article 6 and 5 PCT is to be found however for only a very small proportion of the compounds, see claims 2-3, 11-15 and page 14 lines 1-7. The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of claims 1 and 8 (PCT Guidelines 9.19 and 9.23).

The search of claims 1-8 was restricted to those claimed compounds which appear to be supported by claims 2-3, 11-15 and page 14 lines 1-7. Furthermore, in the description protease inhibitors are defined as falling in the scope of the feature "B7-H4 antagonist" (see page 14 line 4 and page 15 lines 4-10). The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claims 1 and 8 may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). The documents cited with regard to protease inhibitors are merely a selection amongst the prior art documents dealing with protease inhibitors and inflammatory conditions.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2)PCT declaration be overcome.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/088960

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:
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 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 allsearchable 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.:

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: 1-15

pharmaceutical composition comprising a soluble B7-H4 antagonist and method for treating an inflammatory response with an antagonist of a soluble B7-H4

2. claims: 16-17

method for assessing the severity or risk of developing an autoimmune disease by determining the levels of soluble B7-H4

3. claims: 18-21

method for treating an inflammatory response by removing soluble B7-H4 from a biological fluid

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/088960

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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US 3840513	A	08-10-1974	BE 731760 A CH 523318 A DE 1919837 A1 DK 134705 B FR 2007478 A5 GB 1268212 A NL 6906010 A SE 375546 B	01-10-1969 31-05-1972 06-11-1969 27-12-1976 09-01-1970 22-03-1972 21-10-1969 21-04-1975
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