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- (71) **Applicant:** AMPLIMUNE, INC. [US/US]; 45 W. Watkins Mill Road, Gaithersburg, MD 20878 (US).
- (72) **Inventors:** LANGERMAN, Solomon; 6606 Cross Country Blvd., Baltimore, MD 21215 (US). YAO, Sheng; 11748 Bryce Overlook Ct., Columbia, MD 21004 (US). OVERSTREET, Michael, Glen; 1500 Brewster Gate Road, Crownsville, MD 21032 (US). LIU, Linda; 6512 Tipperary Court, Clarksville, MD 21029 (US).
- (74) **Agents:** PABST, Patrea L. et al.; Pabst Patent Group LLP, 1545 Peachtree Street, N.E., Suite 320, Atlanta, GA 30309 (US).
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25 September 2014

(54) **Title:** B7-H4 SPECIFIC ANTIBODIES, AND COMPOSITIONS AND METHODS OF USE THEREOF

(57) **Abstract:** B7-H4 specific antibodies and compositions and methods of use thereof are disclosed. The antibodies can be specific for endogenous B7-H4 polypeptides, recombinant B7-H4 proteins and fusions thereof, or combinations thereof. Methods of using B7-H4 specific antibodies to reduce an inflammatory response, or to treat an inflammatory or autoimmune disease/disorders are also disclosed. The antibodies can be administered to a subject to reduce the levels of cell-free B7-H4 in the subject, or reduce cell-free B7-H4 blockage of B7-H4-mediated signal transduction. In some embodiments the antibodies are administered in combination with a B7-H4-Ig fusion protein that mimics transmembrane B7-H4. Preferably, the antibody binds cell-free B7-H4, without binding to the co-administered B7-H4-Ig fusion protein. Methods of diagnosis, determining therapeutic efficacy, and selecting patients for treatment are also disclosed.



WO 2014/100439 A3

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/00 G01N33/68
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 G01N

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, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2009/011444 A1 (CHEN LIEPING [US]) 8 January 2009 (2009-01-08) claims 1-2; example; par. 32-33; SEQ. 1-4 -----	1-40
A	US 2008/160036 A1 (CHEN LIEPING [US]) 3 July 2008 (2008-07-03) claims 1-3, 16, examples 5, 9-10, par. 191 -----	1-40
A	WO 2011/026122 A2 (AMPLIMMUNE INC [US]; LANGERMANN SOLOMON [US]; LIU LINDA [US]; PODOJIL) 3 March 2011 (2011-03-03) examples; claims 1-6 -----	1-40
X,P	WO 2013/025779 A1 (AMPLIMMUNE INC [US]; LIU LINDA [US]; MARSHALL SHANNON [US]; LANGERMANN) 21 February 2013 (2013-02-21) par 197-200; SEQ 38, 40; claims 9,11,16 ----- -/-	1-40



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 application or patent 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

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European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Hohwy, Morten

INTERNATIONAL SEARCH REPORT

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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.
A	US 2009/041783 A1 (TAKAYAMA HIROSHI [JP] ET AL) 12 February 2009 (2009-02-12) SEQ 114 -----	1-40
A	WO 2012/145493 A1 (AMPLIMMUNE INC [US]; LANGERMANN SOLOMON [US]; LIU LINDA [US]; MARSHALL) 26 October 2012 (2012-10-26) Table 22; Figs 1-2 -----	1-40
A	WO 2006/074418 A2 (DIADEXUS INC [US]; PAPKOFF JACKIE [US]; SHROYER KENNETH R [US]) 13 July 2006 (2006-07-13) p. 27; claim 1 -----	1-40

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/076619

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.:
1-40(partially)
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: 1-40(partially)

A method for measuring the level of a B7-H4 polypeptide in a biological sample and the use of said measurement for diagnosis and monitoring of immune/inflammatory diseases, wherein said methods comprise the use of an anti-B7-H4 antibody, wherein said antibody is 2H9.

2. claims: 1-40(partially)

A method for measuring the level of a B7-H4 polypeptide in a biological sample and the use of said measurement for diagnosis and monitoring of immune/inflammatory diseases, wherein said methods comprise the use of an anti-B7-H4 antibody, wherein said antibody is hB7-H4.m1.

3. claims: 1-40(partially)

A method for measuring the level of a B7-H4 polypeptide in a biological sample and the use of said measurement for diagnosis and monitoring of immune/inflammatory diseases, wherein said methods comprise the use of an anti-B7-H4 antibody, wherein said antibody is 2D1.

4. claims: 1-40(partially)

A method for measuring the level of a B7-H4 polypeptide in a biological sample and the use of said measurement for diagnosis and monitoring of immune/inflammatory diseases, wherein said methods comprise the use of an anti-B7-H4 antibody, wherein said antibody is 6H3.

5. claims: 1-40(partially)

A method for measuring the level of a B7-H4 polypeptide in a biological sample and the use of said measurement for diagnosis and monitoring of immune/inflammatory diseases, wherein said methods comprise the use of an anti-B7-H4 antibody, wherein said antibody is 8E11.

6. claims: 1-40(partially)

A method for measuring the level of a B7-H4 polypeptide in a biological sample and the use of said measurement for diagnosis and monitoring of immune/inflammatory diseases, wherein said methods comprise the use of an anti-B7-H4 antibody, wherein said antibody is H74.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

7. claims: 1-40(partially)

A method for measuring the level of a B7-H4 polypeptide in a biological sample and the use of said measurement for diagnosis and monitoring of immune/inflammatory diseases, wherein said methods comprise the use of an anti-B7-H4 antibody, wherein said antibody is HMH4-5G1.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2013/076619

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