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8 March 2012

(54) Title: ANTIBODIES THAT BIND HUMAN CD27 AND USES THEREOF

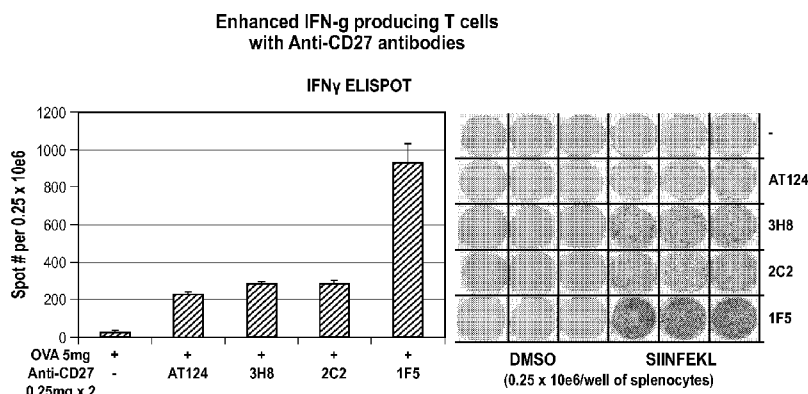


Fig. 20

(57) Abstract: Isolated monoclonal antibodies which bind to human CD27 and related antibody-based compositions and molecules are disclosed. Also disclosed are therapeutic and diagnostic methods for using the antibodies.

WO 2011/130434 A3

INTERNATIONAL SEARCH REPORT

International application No  
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A. CLASSIFICATION OF SUBJECT MATTER  
 INV. C07K16/28 A61K39/395 A61P35/00 A61P37/02 C07K14/705  
 A01K67/027  
 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)  
 C07K

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, 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.
X	SAKANISHI T ET AL: "Anti-tumor effects of depleting and non-depleting anti-CD27 monoclonal antibodies in immune-competent mice", BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 393, no. 4, 19 March 2010 (2010-03-19), pages 829-835, XP026970765, ISSN: 0006-291X, DOI: 10.1016/J.BBRC.2010.02.092 [retrieved on 2010-02-18] the whole document ----- -/--	1-37, 41-116

Further documents are listed in the continuation of Box C.

See patent family annex.

\* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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.</p> <p>"&amp;" document member of the same patent family</p>
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Date of the actual completion of the international search  9 January 2012	Date of mailing of the international search report  17/01/2012
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  Chapman, Rob
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2011/032355

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>VENKY RAMAKRISHNA ET AL: "In vitro characterization of novel anti-human CD27 mAbs",            JOURNAL OF IMMUNOLOGY, AMERICAN ASSOCIATION OF IMMUNOLOGISTS, US,            vol. 184, 1 January 2010 (2010-01-01),            page 87.23, XP009140789,            ISSN: 0022-1767            the whole document</p> <p style="text-align: center;">-----</p>	1-37, 41-116
X	<p>EP 2 090 320 A1 (HELMHOLTZ INFEKTIONSFORSCHUNG [DE])            19 August 2009 (2009-08-19)            the whole document</p> <p style="text-align: center;">-----</p>	1-37, 41-116
X	<p>FRENCH RUTH R ET AL: "Eradication of lymphoma by CD8 T cells following anti-CD40 monoclonal antibody therapy is critically dependent on CD27 costimulation",            BLOOD, AMERICAN SOCIETY OF HEMATOLOGY, US,            vol. 109, no. 11, 1 June 2007 (2007-06-01)            , pages 4810-4815, XP002582844,            ISSN: 0006-4971, DOI:            10.1182/BLOOD-2006-11-057216            [retrieved on 2007-02-20]            the whole document</p> <p style="text-align: center;">-----</p>	1-37, 41-116
X	<p>TAKEDA K ET AL: "CD27-mediated activation of murine NK cells",            JOURNAL OF IMMUNOLOGY, AMERICAN ASSOCIATION OF IMMUNOLOGISTS, US,            vol. 164, no. 4,            15 February 2000 (2000-02-15), pages            1741-1745, XP002401131,            ISSN: 0022-1767            the whole document</p> <p style="text-align: center;">-----</p>	1-37, 41-116
X	<p>YANG F C ET AL: "CD27/CD70 INTERACTION DIRECTLY INDUCES NATURAL KILLER CELL KILLING ACTIVITY",            IMMUNOLOGY, BLACKWELL PUBLISHING, OXFORD, GB,            vol. 88, no. 2,            1 January 1996 (1996-01-01), pages            289-293, XP000886773,            ISSN: 0019-2805, DOI:            10.1046/J.1365-2567.1996.D01-682.X            the whole document</p> <p style="text-align: center;">-----</p>	1-37, 41-116
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2011/032355

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GRAVESTAIN L A ET AL: "Novel mAbs reveal potent co-stimulatory activity of murine CD27", INTERNATIONAL IMMUNOLOGY, OXFORD UNIVERSITY PRESS, GB, vol. 7, no. 4, 1 January 1995 (1995-01-01), pages 551-557, XP008122319, ISSN: 0953-8178 the whole document	1-37, 41-116
X	SUGITA K ET AL: "The 1A4 molecule (CD27) is involved in T cell activation", JOURNAL OF IMMUNOLOGY, AMERICAN ASSOCIATION OF IMMUNOLOGISTS, US, vol. 147, no. 5, 1 September 1991 (1991-09-01), pages 1477-1483, XP002582841, ISSN: 0022-1767 the whole document	1-37, 41-116
X	VAN LIER R A W ET AL: "TISSUE DISTRIBUTION AND BIOCHEMICAL AND FUNCTIONAL PROPERTIES OF TP55 CD27 A NOVEL T CELL DIFFERENTIATION ANTIGEN", JOURNAL OF IMMUNOLOGY, AMERICAN ASSOCIATION OF IMMUNOLOGISTS, US, vol. 139, no. 5, 1 September 1987 (1987-09-01), pages 1589-1596, XP002467371, ISSN: 0022-1767 the whole document	1-37, 41-116
X	KOBATA T ET AL: "CD27-CD70 interactions regulate B-cell activation by T cells", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, NATIONAL ACADEMY OF SCIENCES, WASHINGTON, DC; US, vol. 92, no. 24, 21 November 1995 (1995-11-21), pages 11249-11253, XP002582843, ISSN: 0027-8424, DOI: 10.1073/PNAS.92.24.11249 the whole document	1-37, 41-116
X	WO 2008/051424 A2 (UNIV SOUTHAMPTON [GB]; TESKIN ROBIN L [US]; GLENNIE MARTIN JOHN [GB];) 2 May 2008 (2008-05-02) cited in the application the whole document	1-37, 41-116
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2011/032355

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	<p>HE LI-ZHEN ET AL: "Development of novel anti-CD27 human antibodies with therapeutic potential", PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 51, 17 May 2010 (2010-05-17), - 23 April 2010 (2010-04-23), page 1295, XP007919464, &amp; 101ST ANNUAL MEETING OF THE AMERICAN-ASSOCIATION-FOR-CANCER-RESEARCH; WASHINGTON, DC, USA; APRIL 17 -21, 2010 ISSN: 0197-016X the whole document</p>	1-37, 41-116
A	<p>MATTER MATTHIAS ET AL: "Elimination of chronic viral infection by blocking CD27 signaling", THE JOURNAL OF EXPERIMENTAL MEDICINE, ROCKEFELLER UNIVERSITY PRESS, US, vol. 203, no. 9, 4 September 2006 (2006-09-04), pages 2145-2155, XP002499867, ISSN: 0022-1007, DOI: 10.1084/JEM.20060651 the whole document</p>	1-37, 41-116
A	<p>RUDIKOFF S ET AL: "Single amino acid substitution altering antigen-binding specificity", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, NATIONAL ACADEMY OF SCIENCES, WASHINGTON, DC; US, vol. 79, 1 March 1982 (1982-03-01), pages 1979-1983, XP007901436, ISSN: 0027-8424, DOI: 10.1073/PNAS.79.6.1979 the whole document</p>	1-37, 41-116

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2011/032355

## 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.:  
  
1-37, 41-116(all 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.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2011/032355

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 2090320	A1	19-08-2009	EP 2090320 A1
			EP 2244736 A1
			US 2011052579 A1
			WO 2009100942 A1
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WO 2008051424	A2	02-05-2008	CA 2667020 A1
			EP 2083858 A2
			JP 2010506925 A
			US 2011033449 A1
			WO 2008051424 A2
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**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

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

1. claims: 1-37, 41-116(all partially)

An antibody which binds to human CD27 wherein the antibody comprises HC and LC CDRs 1-3 comprising SEQ ID NO:38-40 and 44-46, respectively; and related subject-matter.

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2. claims: 1-37, 41-116(all partially)

An antibody which binds to human CD27 wherein the antibody comprises HC and LC CDRs 1-3 comprising SEQ ID NO:50-52 and 56-58, respectively; and related subject-matter.

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3-14. claims: 1-37, 41-116(all partially)

An antibody which binds to human CD27 wherein the antibody comprises HC and LC CDRs 1-3 comprising SEQ ID NO: 86-88 and 92 or 99, 93 or 99, 94 or 100, respectively; and related subject-matter.

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15. claims: 1-37, 41-116(all partially)

An antibody which binds to human CD27 wherein the antibody comprises HC and LC CDRs 1-3 comprising SEQ ID NO:26-28 and 32-34, respectively; and related subject-matter.

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16. claims: 1-37, 41-116(all partially)

An antibody which binds to human CD27 wherein the antibody comprises HC and LC CDRs 1-3 comprising SEQ ID NO:104-106 and 110-112, respectively; and related subject-matter.

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17. claims: 1-37, 41-116(all partially)

An antibody which binds to human CD27 wherein the antibody comprises HC and LC CDRs 1-3 comprising SEQ ID NO:74-76 and 80-82, respectively; and related subject-matter.

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18-29. claims: 1-37, 41-116(all partially)

An antibody which binds to human CD27 wherein the antibody comprises HC and LC CDRs 1-3 comprising SEQ ID NO:8-10 and 14 or 20, 15 or 21, 16 or 22, respectively; and related subject-matter.

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30. claims: 1-37, 41-116(all partially)



**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

An antibody which binds to human CD27 wherein the antibody comprises HC and LC CDRs 1-3 comprising SEQ ID NO:62-64, and 68-70, respectively; and related subject-matter.

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31. claims: 38, 40(all partially)

An anti-CD27 antibody derived from a human germline VH 3-7

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32. claims: 38, 40(all partially)

An anti-CD27 antibody derived from a human germline VH 3-33

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33. claims: 39, 40(partially)

An anti-CD27 antibody derived from a human germline Vk3-20

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34. claims: 39, 40(partially)

An anti-CD27 antibody derived from a human germline Vk3-11

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35. claims: 39, 40(partially)

An anti-CD27 antibody derived from a human germline Vk1D-16

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36. claims: 39, 40(partially)

An anti-CD27 antibody derived from a human germline Vk1-13

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