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(54) Title: MONOVALENT CD27 ANTIBODIES

(57) Abstract: The present invention relates to a monovalent antibody, such as a Fab fragment, which is capable of specifically binding CD27 and reducing CD27 induced signalling. The present invention also relates to a fusion protein or conjugate comprising the monovalent antibody of the invention and a half-life extending moiety. The monovalent antibody, fusion protein or conjugate of the invention may be suitable for use as a medicament, such as in the treatment of autoimmune diseases in which suppression of CD27 signaling is desirable.



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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28
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 practicable, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011/130434 A2 (CELLEX THERAPEUTICS INC [US]; KELER TIBOR [US]; MARSH HENRY C [US]; H) 20 October 2011 (2011-10-20) cited in the application	1,2,4-7, 11-13, 15,18
Y	page 1, line 12 - line 14 page 2, line 12 - line 14 page 2, line 20 - line 23 page 4, line 9 - line 15 page 15, line 19 - page 16, line 12; claims; figures; examples ----- -/--	17



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

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"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

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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/055331

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JEVSEVAR SIMONA ET AL: "PEGylation of antibody fragments for half-life extension", METHODS IN MOLECULAR BIOLOGY, vol. 901, 1 January 2012 (2012-01-01), pages 233-246, XP009169915, (CLIFTON, N.J.) UNITED STATES ISSN: 1940-6029 abstract	17
A	----- WO 2012/004367 A1 (ORGANON NV [NL]; STICHTING HET NL KANKER INST [NL]; VAN EENENNAAM HANS) 12 January 2012 (2012-01-12) claims; examples	1-18
A	----- AGEMATSU K ET AL: "B CELL SUBPOPULATIONS SEPARATED BY CD27 AND CRUCIAL COLLABORATION OF CD27+ B CELLS AND HELPER T CELLS IN IMMUNOGLOBULIN PRODUCTION", EUROPEAN JOURNAL OF IMMUNOLOGY, vol. 27, no. 8, 1 January 1997 (1997-01-01), pages 2073-2079, XP001031448, WILEY - V C H VERLAG GMBH & CO. KGAA, DE ISSN: 0014-2980, DOI: 10.1002/EJI.1830270835 abstract	1-18
A	----- KOBATA T ET AL: "CD27-CD70 interactions regulate B-cell activation by T cells", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 92, no. 24, 21 November 1995 (1995-11-21), pages 11249-11253, XP002582843, NATIONAL ACADEMY OF SCIENCES, US ISSN: 0027-8424, DOI: 10.1073/PNAS.92.24.11249 abstract page 11250, paragraph 2	1-18
A	----- NAKAJIMA A ET AL: "Involvement of CD70-CD27 interactions in the induction of experimental autoimmune encephalomyelitis", JOURNAL OF NEUROIMMUNOLOGY, vol. 109, no. 2, 22 September 2000 (2000-09-22), pages 188-196, XP002423716, ELSEVIER SCIENCE PUBLISHERS BV ISSN: 0165-5728, DOI: 10.1016/S0165-5728(00)00324-6 abstract	1-18
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/055331

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MATTHIAS MATTER ET AL: "Elimination of chronic viral infection by blocking CD27 signaling", THE JOURNAL OF EXPERIMENTAL MEDICINE, vol. 203, no. 9, 21 August 2006 (2006-08-21), pages 2145-2155, XP007906013, ROCKEFELLER UNIVERSITY PRESS, US ISSN: 0022-1007, DOI: 10.1084/JEM.20060651 abstract	1-18
A	----- GREENALL SAMEER A ET AL: "Non-agonistic bivalent antibodies that promote c-MET degradation and inhibit tumor growth and others specific for tumor related c-MET.", PLOS ONE, vol. 7, no. 4, E34658, April 2012 (2012-04), pages 1-10, XP002697775, ISSN: 1932-6203 abstract page 2, right-hand column, paragraph 1 page 6, right-hand column, paragraph 3	1-18
X,P	----- WO 2013/138586 A1 (JANSSEN BIOTECH INC [US]) 19 September 2013 (2013-09-19)	1-4, 8-10, 14-16,18
Y,P	claims; examples 3-9	17
A	----- MAGE R G ET AL: "B cell and antibody repertoire development in rabbits: The requirement of gut-associated lymphoid tissues", DEVELOPMENTAL AND COMPARATIVE IMMUNOLOGY, PERGAMON PRESS, US, vol. 30, no. 1-2, 1 January 2006 (2006-01-01), pages 137-153, XP027942078, ISSN: 0145-305X [retrieved on 2006-01-01] page 150, left-hand column, last paragraph - right-hand column, last paragraph	11-13,15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2014/055331

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.:
3, 5-14, 16(completely); 1, 2, 4, 15, 17, 18(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: 3, 8-10, 14, 16(completely); 1, 2, 4, 15, 17, 18(partially)

Subject-matter of claims 1 to 4, 8 to 10 and 14 to 18 as far as the antibody does not compete with CD70 for binding to CD27 (including the Fab 5F24 and the derivatives thereof, in particular the humanized versions thereof)

2. claims: 5-7(completely); 1, 2, 4, 15, 17, 18(partially)

Subject-matter of claims 1, 2, 4 to 7, 15, 17 and 18 as far as the antibody comprises the CDRs of the antibody 2F2

3. claims: 11-13(completely); 1, 2, 4, 15, 17, 18(partially)

Subject-matter of claims 1, 2, 4, 11 to 13, 15, 17 and 18 as far as the antibody comprises the CDRs of Fab 0151

- 4-11. claims: 1, 2, 4, 15, 17, 18(all partially)

Subject-matter of claims 1, 2, 4, 15, 17 and 18 as far as it is related to the antibodies 5F32, 10F13, 10F31, 11F26, Fab 0152, Fab 0153, Fab 0154 or Fab 0155. Each of the antibodies corresponds to a different invention

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011130434 A2	20-10-2011	AU 2011239706 A1 CA 2796571 A1 CN 103154034 A EA 201291039 A1 EP 2558498 A2 JP 2013531970 A KR 20130066605 A SG 184310 A1 US 2011274685 A1 WO 2011130434 A2	01-11-2012 20-10-2011 12-06-2013 30-04-2013 20-02-2013 15-08-2013 20-06-2013 30-10-2012 10-11-2011 20-10-2011
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WO 2013138586 A1	19-09-2013	TW 201345922 A US 2013243795 A1 UY 34680 A WO 2013138586 A1	16-11-2013 19-09-2013 30-09-2013 19-09-2013