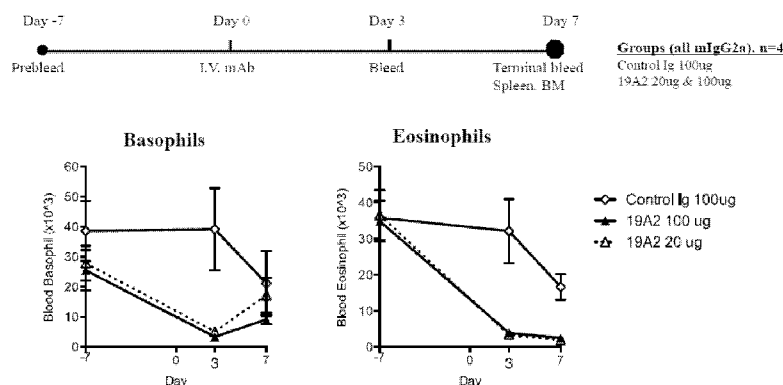


- (51) **International Patent Classification:**
C07K 16/28 (2006.01) A61K 39/395 (2006.01)
- (21) **International Application Number:**
PCT/US2014/029455
- (22) **International Filing Date:**
14 March 2014 (14.03.2014)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
61/786,370 15 March 2013 (15.03.2013) US
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- (81) **Designated States (unless otherwise indicated, for every kind of national protection available):** AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) **Designated States (unless otherwise indicated, for every kind of regional protection available):** ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).
- Published:**
- with international search report (Art. 21(3))
 - before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
 - with sequence listing part of description (Rule 5.2(a))
- (88) **Date of publication of the international search report:**
20 November 2014

(54) Title: ANTI-CRTH2 ANTIBODIES AND THEIR USE

FIG. 18A



(57) Abstract: The invention provides anti-CRTH2 antibodies and methods of using the same.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/029455A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28 A61K39/395
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 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 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.
X	NAGATA ET AL: "Selective expression of a novel surface molecule by human Th2 cells in vivo.", THE JOURNAL OF IMMUNOLOGY, vol. 162, no. 3, 1 February 1999 (1999-02-01), pages 1278-1286, XP055121136, ISSN: 0022-1767	1
Y	The whole document, in particular section entitled 'Production of rat anti-CRTH2 antibodies', p.1280, col.2 ----- -/--	1-28, 46-72



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

Date of the actual completion of the international search

3 June 2014

Date of mailing of the international search report

18/09/2014

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2014/029455

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ULVEN TROND ET AL: "Novel CRTH2 antagonists: a review of patents from 2006 to 2009", EXPERT OPINION ON THERAPEUTIC PATENTS, INFORMA HEALTHCARE, GB, vol. 20, no. 11, 1 November 2010 (2010-11-01), pages 1505-1530, XP009142666, ISSN: 1354-3776 the whole document	1-28, 46-72
A	MICHAEL R CLARK: "IgG Effector Mechanisms", CHEMICAL IMMUNOLOGY, vol. 65, 1 January 1997 (1997-01-01), pages 88-110, XP055121316, ISSN: 1015-0145 The whole document, in particular p.7 - 8 regarding the isotype of antibodies and their ADCC activity	1
A	OKAZAKI A ET AL: "Fucose Depletion from Human IgG1 Oligosaccharide Enhances Binding Enthalpy and Association Rate Between IgG1 and FcγRIIIa", JOURNAL OF MOLECULAR BIOLOGY, ACADEMIC PRESS, UNITED KINGDOM, vol. 336, no. 5, 5 March 2004 (2004-03-05), pages 1239-1249, XP004490178, ISSN: 0022-2836, DOI: 10.1016/J.JMB.2004.01.007 The whole document; see Abstract for summary of features which also appear in the present claims.	3-10
X	HIRAI H ET AL: "PROSTAGLANDIN D2 SELECTIVELY INDUCES CHEMOTAXIS IN T HELPER TYPE 2 CELLS, EOSINOPHILS, AND BASOPHILS VIA SEVEN-TRANSMEMBRANE RECEPTOR CRTH2", THE JOURNAL OF EXPERIMENTAL MEDICINE, ROCKEFELLER UNIVERSITY PRESS, US, vol. 193, no. 2, 15 January 2001 (2001-01-15), pages 255-261, XP008050257, ISSN: 0022-1007, DOI: 10.1084/JEM.193.2.255	1
Y	The whole docuemnt, in particular Fig.3	1-28, 46-72
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/029455

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	A. CASADEVALL ET AL: "Immunoglobulin isotype influences affinity and specificity", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 109, no. 31, 31 July 2012 (2012-07-31), pages 12272-12273, XP055047920, ISSN: 0027-8424, DOI: 10.1073/pnas.1209750109 the whole document	1
A	----- K. MUTALITHAS ET AL: "CRTH2 expression on T cells in asthma", CLINICAL & EXPERIMENTAL IMMUNOLOGY, 1 June 2010 (2010-06-01), pages no-no, XP055121166, ISSN: 0009-9104, DOI: 10.1111/j.1365-2249.2010.04161.x the whole document	1
A	----- RUDIKOFF S ET AL: "Single amino acid substitution altering antigen-binding specificity", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, NATIONAL ACADEMY OF SCIENCES, 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 -----	27,28

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/029455

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.:
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.:

1-28(completely); 46-72(partially)

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: 1-28(completely); 46-72(partially)

An isolated antibody that binds human CRTh2 and can deplete CRTh2 expressing cells, and related subject-matter

2. claims: 29-72(partially)

An anti-CRTh2 antibody, wherein the antibody comprises:(i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:9;(ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 10;(iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3;(iv) HVR-H1 comprising the amino acid sequence of SEQ ID NO:15;(v) HVR-H2 comprising the amino acid sequence of SEQ ID NO:20; and(vi) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6.

3. claims: 29-72(partially)

An anti-CRTh2 antibody,wherein the antibody comprises:(i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:8;(ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 10;(iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3;(iv) HVR-H1 comprising the amino acid sequence of SEQ ID NO:13;(v) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 19; and(vi) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6.

4. claims: 29-72(partially)

An anti-CRTh2 antibody, wherein the antibody comprises:(i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:9;(ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11;(iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3;(iv) HVR-H1 comprising the amino acid sequence of SEQ ID NO:15;(v) HVR-H2 comprising the amino acid sequence of SEQ ID NO:20; and(vi) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6.
