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CA, CH, 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, IS, JP, KE, KG, KM, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG,
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ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI
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NE, SN, TD, TG).

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(88) Date of publication of the international search report:
13 August 2009

(54) Title: METHODS AND COMPOSITIONS FOR ANTIBODY OR VACCINE THERAPY

(57) Abstract: Methods and materials are provided for determining the responsiveness of a subject to a therapy, such as an antibody therapy or vaccine therapy and for selecting and/or for treating a subject based on a FcγRIIA polymorphism, or a FcγRIIIA polymorphism, or both an FcγRIIA polymorphism and a FcγRIIIA polymorphism, including where the treatment is an therapy, such as rituximab. Methods and materials are also provided for designing, making, screening, testing and/or administering antibodies or vaccines as well as for optimizing antibody therapies or vaccine therapies based upon a subject's FcγRIIA polymorphism, or FcγRIIIA polymorphism, or both the FcγRIIA polymorphism and the FcγRIIIA polymorphism.



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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/082864

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12Q1/68 C07K16/28

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)
C12Q 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	WENG WEN-KAI ET AL: "Genetic polymorphism of the inhibitory IgG Fc receptor Fc gamma RIIB is not associated with clinical outcome of rituximab treated follicular lymphoma patients." BLOOD, vol. 106, no. 11, Part 1, November 2005 (2005-11), page 683A, XP009113247 & 47TH ANNUAL MEETING OF THE AMERICAN-SOCIETY-OF-HEMATOLOGY; ATLANTA, GA, USA; DECEMBER 10 -13, 2005 ISSN: 0006-4971 the whole document ----- -/--	1-14, 39-48, 56,57, 65-151

☒ 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.
- *Z* document member of the same patent family

Date of the actual completion of the international search

24 April 2009

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Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
- a. type of material
- ☒ a sequence listing
- ☐ table(s) related to the sequence listing
- b. format of material
- ☒ on paper
- ☒ in electronic form
- c. time of filing/furnishing
- ☒ contained in the international application as filed
- ☒ filed together with the international application in electronic form
- ☐ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/082864

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2006/008825 A1 (LEVY RONALD [US] ET AL) 12 January 2006 (2006-01-12) the whole document	1-14, 39-48, 56,57, 65-151
X	LIN THOMAS S ET AL: "FCGR3A and FCGR2A polymorphisms may not correlate with response to alemtuzumab in chronic lymphocytic leukemia" BLOOD, vol. 105, no. 1, 1 January 2005 (2005-01-01), pages 289-291, XP002516947 ISSN: 0006-4971 the whole document	1-14, 39-48, 56,57, 65-151
X	KIM DONG HWAN ET AL: "FCGR3A gene polymorphisms may correlate with response to frontline R-CHOP therapy for diffuse large B-cell lymphoma" BLOOD, vol. 108, no. 8, October 2006 (2006-10), pages 2720-2725, XP002516948 ISSN: 0006-4971 the whole document	1-14, 39-48, 56,57, 65-151
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X	CAMILLERI-BROET S ET AL: "Fc[gamma]RIIB expression in diffuse large B-cell lymphomas does not alter the response to CHOP + rituximab (R-CHOP) [3]" LEUKEMIA 200412 GB, vol. 18, no. 12, December 2004 (2004-12), pages 2038-2040, XP002523994 ISSN: 0887-6924 the whole document	1-14, 39-48, 56,57, 65-151
X	EP 1 801 234 A (SANQUIN BLOEDVOORZIENING [NL]) 27 June 2007 (2007-06-27) example 4	39-48, 142-153
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/082864

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FORTHAL DONALD N ET AL: "Recombinant gp120 vaccine-induced antibodies inhibit clinical strains of HIV-1 in the presence of Fc receptor-bearing effector cells and correlate inversely with HIV infection rate" JOURNAL OF IMMUNOLOGY, vol. 178, no. 10, May 2007 (2007-05), pages 6596-6603, XP002525292 ISSN: 0022-1767 cited in the application the whole document	1-3, 7-10,56, 57,81-89
X	WENG WEN-KAI ET AL: "Clinical outcome of lymphoma patients after idiotype vaccination is correlated with humoral immune response and immunoglobulin G Fc receptor genotype." JOURNAL OF CLINICAL ONCOLOGY : OFFICIAL JOURNAL OF THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY 1 DEC 2004, vol. 22, no. 23, 1 December 2004 (2004-12-01), pages 4717-4724, XP002525293 ISSN: 0732-183X the whole document	1-3, 7-10,56, 57,81-92
A	WO 2005/062929 A (CHIRON COPORATION [US]; WILSON SUSAN E [US]) 14 July 2005 (2005-07-14) example 3 example 4 the whole document	
A	SU KAIHONG ET AL: "A promoter haplotype of the immunoreceptor tyrosine-based inhibitory motif-bearing FcγRIIb alters receptor expression and associates with autoimmunity. I. Regulatory FCGR2B polymorphisms and their association with systemic lupus erythematosus" JOURNAL OF IMMUNOLOGY, vol. 172, no. 11, 1 June 2004 (2004-06-01), pages 7186-7191, XP002518094 ISSN: 0022-1767 cited in the application the whole document	1-14, 39-48, 56,57, 65-151
A	WO 2005/113815 A (UAB RESEARCH FOUNDATION [US]; KIMBERLY ROBERT P [US]; EDBERG JEFFREY []) 1 December 2005 (2005-12-01) cited in the application the whole document	1-14, 39-48, 56,57, 65-151
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2008/082864

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CARTRON G ET AL: "THERAPEUTIC ACTIVITY OF HUMANIZED ANTI-CD20 MONOCLONAL ANTIBODY AND POLYMORPHISM IN IGG FC RECEPTOR FCGAMMARIIA GENE" BLOOD, AMERICAN SOCIETY OF HEMATOLOGY, US, vol. 99, no. 3, 1 February 2002 (2002-02-01), pages 754-758, XP001193741 ISSN: 0006-4971 the whole document	1-14, 39-48, 56,57, 65-151
A	SHIELDS R L ET AL: "High resolution mapping of the binding site on human IgG1 for Fc gamma RI, Fc gamma RII, Fc gamma RIII and FcRn and design of IgG1 variants with improved binding to the Fc gamma R" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BIRMINGHAM,; US, vol. 276, no. 9, 2 March 2001 (2001-03-02), pages 6591-6604, XP002971008 ISSN: 0021-9258 the whole document	1-14, 39-48, 56,57, 65-151
A	VAN SORGE N M ET AL: "Fc(gamma)R polymorphisms: Implications for function, disease susceptibility and immunotherapy" TISSUE ANTIGENS, MUNKSGAARD, COPENHAGEN, DK, vol. 61, 1 January 2003 (2003-01-01), pages 189-202, XP007905614 ISSN: 0001-2815 the whole document	1-14, 39-48, 56,57, 65-151
A	WO 2007/044616 A (XENCOR INC [US]; LAZAR GREGORY ALAN [US]; DESJARLAIS JOHN R [US]; HAMM) 19 April 2007 (2007-04-19) the whole document	1-14, 39-48, 56,57, 65-151
A	WIERTSEMA S ET AL: "Fc Receptor Polymorphism determines the efficacy of pneumococcal vaccines for mucosal infections" IMMUNOBIOLOGY, URBAN UND FISCHER VERLAG, DE, vol. 209, no. 4-6, 14 October 2004 (2004-10-14), pages 476-477, XP009115508 ISSN: 0171-2985 the whole document	1-14, 39-48, 56,57, 65-151

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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 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 reportcovers 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.:

1-14, 39-48, 56-57, 65-153

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: 1-14, 39-48, 56-57, 65-153

Methods of determining the responsiveness to a given antibody or vaccine therapy of a subject having an ADCC-treatable disorder (claims 1-14, 56-57, 112-126, 127-141); methods of treating a subject having an ADCC-treatable disorder with a given antibody or vaccine for said disorder (81-96); methods of selecting or classifying subjects having an ADCC-treatable disorder (claims 65-80, 97-111); and kits suitable for use in said methods (claims 39-48, 142-153). All of said methods are based on genotyping the subject's Fc gamma receptor II A (FcγRIIA) and Fc gamma receptor III A (FcγRIIIA).

2. claims: 15-38, 49-55, 58-65, 154-227

Methods of selecting a specific vaccine or (Fc) variant antibody therapy from a set of two or more vaccine or (Fc) variant antibody therapies for a subject having an ADCC-treatable disorder (claims 16-27, 154-167, 200-227); methods of treating a subject having an ADCC-treatable disorder involving selection of the therapeutic agent from a set of Fc-variant antibodies (claims 49-55, 168-179) Methods of generating variant antibodies by modifying the Fc region of a parent antibody (claims 15, 28-38, 58-64, 180-199, 219-227). Most of said methods are based on genotyping the subject's Fc gamma receptor II A (FcγRIIA) and Fc gamma receptor III A (FcγRIIIA).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2008/082864

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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