Abstract: The present invention provides anti-human ICOS antibodies with increased effector function. The invention further relates to pharmaceutical compositions, immunotherapeutic compositions, and methods using therapeutic antibodies that bind to the human ICOS antigen and that may mediate ADCC, CDC, and/or antibody-dependent phagocytosis (opsonisation) for the treatment and prevention of T cell-mediated diseases and disorders, such as, but not limited to, chronic infection, autoimmune disease or disorder, inflammatory disease or disorder, graft-versus-host disease (GVHD), transplant rejection, and T cell proliferative disorder.
(88) Date of publication of the international search report:
8 January 2009
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/395 (2008.04)
USPC - 530/387.1, 44/130.1
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)
USPC -- 530/387.1, 424/130.1, 424/133.1, 424/139.1, 424/142.1, 424/143.1, 424/144.1, 435/69.6, 435/70.2, 435/70.21, 530/387.3, 530/387.8, 530/388.1, 530/388.15, 530/388.2, 530/388.22, 530/388.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of database and where practicable, search terms used)
WEST -- PGPB USPTO USOC EPAB JPAB; Dialog Classic Files 854, 692, 351, 349, 315, 6, 153, 35, 65; USPTO Web Page; Google Scholar; Search terms -- anti-ICOS, variant Fc, glycosidic carbohydrate chain, enhanced ADCC activity, assay, Fcgammah1A, amino acid substitution, IgG1, primata, human, carrier, B-cell depletion

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>Y</td>
<td>US 20060024826 A1 (CARRERNO et al.) 16 February 2006 (16.02.2006) para [0074], [0076], [0104], [0165], [0211], [0257]</td>
<td>1-11, 13, 15-17, 19-63</td>
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<td>Y</td>
<td>US 20070036799 A1 (STAVENHAGEN et al.) 15 February 2007 (15.02.2007) para [0002], [0007], [0027], [0039], [0084], [0086], [0072], [0073], [0075], [0080], [0089], [0154], [0202], [0216], [0228], [0295], [0322], [0456], [0477], [0652], Fig 29</td>
<td>1-11, 13, 15-17, 19-63</td>
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<tr>
<td>Y</td>
<td>US 200501276803 A1 (CHAN et al.) 15 December 2005 (15.12.2003) para [0004], [0014], [0016], [0019], [0026], [0272]</td>
<td>35-63</td>
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</table>

[ ] Further documents are listed in the continuation of Box C.

Date of the actual completion of the international search
02 October 2008 (02.10.2008)

Date of mailing of the international search report
24 OCT 2008

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-3201

Authorized officer: Lee W. Young

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>Y</td>
<td>US 2002/0102658 A1 (TSUJI et al) 01 August 2002 (01.08.2002) para [0002], [0066]-[0067], [0080]-[0081], SEQ ID NOS: 28 and 30</td>
<td>10-11, 13, 15-17, 23, 24-45</td>
</tr>
</tbody>
</table>
INTERNATIONAL SEARCH REPORT

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 CONTINUATION 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 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. [x] 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.: 1-11, 13, 15-17, 19-63, limited to SEQ ID NO:2 and SEQ ID NO:7

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.

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2007)
Continuation of Box No III (Lack of Unity):

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

The species are the polypeptide sequences of SEQ ID NO:2 and SEQ ID NO:7, and the nucleotide sequences of SEQ ID NO:28-31.

The claims are deemed to correspond to the species listed above in the following manner:

Group 1: Claims 1-11, 13, 15-17, 19-63, directed to an isolated anti-ICOS antibody, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:7, and the VK domain comprises the amino acid sequence of SEQ ID NO:2, as well as nucleic acids encoding the antibody and methods of using thereof.

Group 2: Claims 1-63, directed to an isolated anti-ICOS antibody, as well as nucleic acids encoding the antibody and methods of using thereof, wherein the nucleic acid sequence comprises SEQ ID NO:28.

Group 3: Claims 1-63, directed to an isolated anti-ICOS antibody, as well as nucleic acids encoding the antibody and methods of using thereof, wherein the nucleic acid sequence comprises SEQ ID NO:29.

Group 4: Claims 1-63, directed to an isolated anti-ICOS antibody, as well as nucleic acids encoding the antibody and methods of using thereof, wherein the nucleic acid sequence comprises SEQ ID NO:30.

Group 5: Claims 1-63, directed to an isolated anti-ICOS antibody, as well as nucleic acids encoding the antibody and methods of using thereof, wherein the nucleic acid sequence comprises SEQ ID NO:31.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The different polynucleotide sequences represented by the nucleic acid content and the different polypeptide sequences represented by the amino acid content of the species are different structures that are not common to one another but are different because they are composed of unique nucleic acid and amino acid sequences. Thus, the various species within claims 1-63 lack unity of invention because they do not share a same or corresponding special technical feature.