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[Continued on next page]

(54) Title: ANTI-IL-6/IL-6R ANTIBODIES AND METHODS OF USE THEREOF

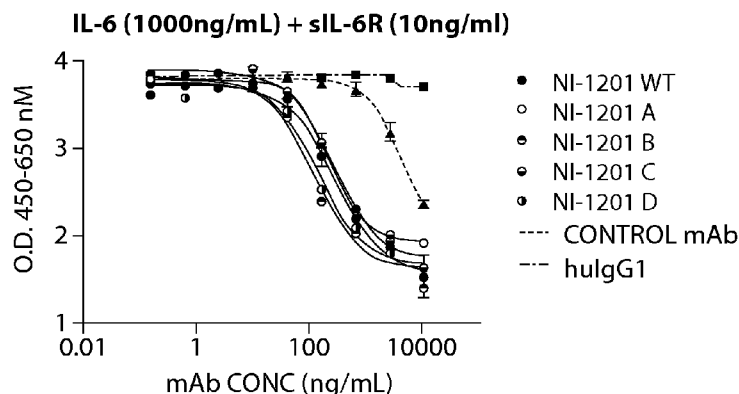


Fig. 1D

(57) Abstract: Fully human monoclonal antibodies that recognize the IL6/ IL-6R complex and methods of using such monoclonal antibodies as a therapeutic, diagnostic, and prophylactic are disclosed.



Published:

(88) Date of publication of the international search report:

— *with international search report (Art. 21(3))*

7 January 2010

— *with sequence listing part of description (Rule 5.2(a))*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 09/43734

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07K 16/24; C12P 21/08 (2009.01)

USPC - 530/388.22, 388.23

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)

IPC(8) - C07K 16/24; C12P 21/08 (2009.01)

USPC - 530/388.22, 388.23

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

USPC - 530/387.1, 388.1, 388.22, 388.23

(Text Search)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST (PGPB, USPT, USOC, EPAB, JPAB); DialogPRO (Engineering); PubMed and Google Scholar.

Search Terms: antibody, gp130, IL-6R, IL6R, IL-6/IL-6R, IL-6Rc, IL6/IL6R, sIL-6/sIL-6R, sIL-6Rc, sIL6/sIL6R, huIL-6/huIL-6R, huIL-6Rc, huIL6/huIL6R, hIL-6/hIL-6R, hIL-6Rc, hIL6/hIL6R, antisera, antiserum, anti-, receptor, complex, blocking, IL-6 receptor

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GAILLARD, J. P. et al. Identification of a Novel Antigenic Structure of the Human Receptor for Interleukin-6 Involved in the Interaction with the Glycoprotein 130 Chain. Immunology. September 1996, Vol 89(1), pages 135-141: abstract; pg 138, right col, para 1; pg 140, left col, para 1.	1, 3-7, 18, 23 and 24
Y	US 2007/0280945 A1 (STEVENS et al.) 06 December 2007 (06.12.2007) claim 20; para [0003], [0005], [0036], [0037], [0051], [0054]-[0057], [0068], [0071], [0072].	1, 3-7, 18, 23 and 24
Y	GRUBE, B. J. et al. Identification of a Regulatory Domain of the Interleukin-6 Receptor. The Journal of Biological Chemistry. August 1994, Vol 269(32), pages 20791-20797: abstract; pg 20792, left col, para 3; pg 20796, right col, para 2.	5
A	US 2005/0074821 A1 (WILD et al.) 07 April 2005 (07.04.2005) SEQ ID NO: 20, 24, 44; claim 78; para [0069], [0325].	2 and 8-17

☐ Further documents are listed in the continuation of Box C.

* 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

22 September 2009 (22.09.2009)

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 09/43734

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

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing filed or furnished:

a. (means)

☐

on paper

☒

in electronic form

b. (time)

☐

in the international application as filed

☒

together with the international application in electronic form

☐

subsequently to this Authority for the purposes of search

2. ☒ In addition, in the case that more than one version or copy of a sequence listing 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/US 09/43734

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:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I+: Claims 1-18, 23 and 24, directed to a human antibody that binds to IL-6/IL6R complex and prevents the complex from binding to gp130, limited to an antibody comprising a heavy chain sequence comprising SEQ ID NO: 2 and a light chain sequence comprising SEQ ID NO: 4, or, correspondingly, a heavy chain comprising CDR1, CDR2 and CDR3 comprising SEQ ID NO: 15, 16 and 17, respectively and a light chain comprising CDR1, CDR2 and CDR3 comprising SEQ ID NO: 24, 25 and 26, respectively, which contain the sequence options listed in claim 2 option (iii). (applicants may elect to pay for additional heavy chain sequences SEQ ID NO: 8 or 12, and light chain sequences 6, 10 or 14 with the payment of an additional invention fee for each specified sequence. The corresponding CDR's for each sequence will also be searched with election of these sequences. Should the applicant wish to select further combinations of CDR's not contained within any of the above specified sequences, the applicant must fully specify the combination of light chain or heavy chain CDR's and include an additional invention payment for the search of said sequence combinations).

- Please see extra sheet for continuation -

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. ☒ 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.: 1-18, 23 and 24; limited to SEQ ID NO: 2, 4, 15-17 and 24-26

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.

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Continuation of Box III: Lack of Unity of Invention

Group II: claims 19-21, directed to a method of alleviating a symptom of a clinical indication associated with rheumatoid arthritis, Crohn's disease or multiple sclerosis in a subject, comprising administering an antagonist of IL-6Rc to a subject.

The inventions listed as Groups I+ and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of the Group I+ claims is a human antibody that binds to IL-6/IL6R complex and prevents the complex from binding to gp130, wherein the antibody comprises a particular light chain and heavy chain sequence - not required by the claims of Group II. The special technical feature of the Group II claims is a method of alleviating a symptom of a clinical indication associated with rheumatoid arthritis, Crohn's disease or multiple sclerosis in a subject, comprising administering an antagonist of IL-6Rc to a subject - not required by the claims of Group I+. Neither of these special technical features is common to the other group, nor do they correspond to a special technical feature in the other group.

The only common technical element shared by the above groups is that they are related to inhibition of the activity of the IL-6R complex. While it may be possible to use the invention of the claims of Group I+ to provide the inhibitor for the invention of the claims of Group II, the claims of Group II are not so limited. The common technical element does not represent an improvement over the prior art of US 2007/0280945 A1 to Stevens et al. (see abstract, para [0005], [0037]). Further, Stevens discloses wherein the entity that inhibits the activity of the IL-6R complex is an antibody (abstract). Therefore, the inventions of Group I+ and Group II lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.