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Published:

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

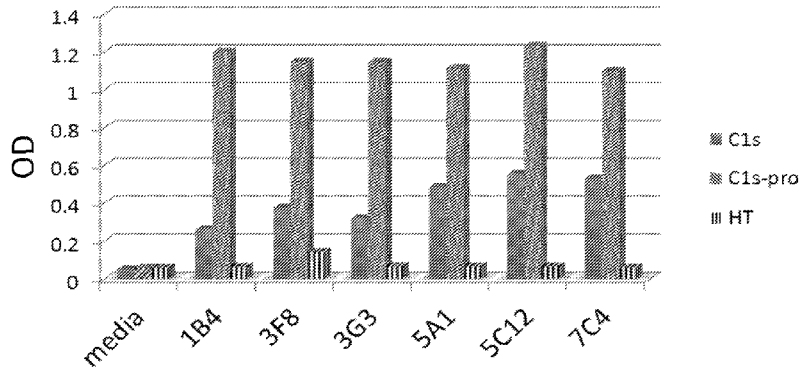
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

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

(88) Date of publication of the international search report:
4 June 2015

(54) Title: ANTI-COMPLEMENT FACTOR C1S ANTIBODIES AND USES THEREOF

FIG 1



(57) Abstract: The present invention relates generally to the generation and characterization of neutralizing anti-C1s monoclonal antibodies. The invention further relates to the use of such anti-C1s antibodies in the detection of complement factors of the classical complement activation pathway, such as C1s. Additionally, the antibodies of this disclosure are useful for the diagnosis and treatment of disorders associated with an increased activation of the classical complement pathway, in particular autoimmune disorders and neurodegenerative diseases, including neurodegenerative diseases with synapse loss, such as Alzheimer's Disease. Methods of treatment of autoimmune and neurodegenerative diseases are also provided.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C07K 16/40 (2014.01)
CPC - C07K 16/40 (2014.09)
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) - A61K 39/395; C07K 16/18, 16/40; C12Q 1/00 (2014.01)
USPC - 424/9.1, 9.34, 9.4, 133.1, 135.1, 139.1, 172.1, 450; 435/1.2, 7.4, 320.1, 331; 530/387.3, 387.9, 389.1, 391.1; 536/23.53

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - A61K 39/3955, 2039/505; C07K 16/18, 16/40, 2317/24, 2317/35, 2317/54, 2317/55, 2317/76, 2317/92; C12Q 1/005 (2014.09)

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CARROLL et al. "Antibody-mediates inhibition of human C1s and the classical complement pathway," Immunobiology, 10 January 2013 (10.01.2013), Vol. 218, Pgs. 1041-1048. entire document	1-7, 14-19, 32
A	"Complement C1s Antibody (49)," Product Data Sheet. ThermoScientific. Pierce Antibody Products. 1995. Pgs. 1-2. Retrieved from the Internet:<http://www.pierce-antibodies.com/Complement-C1s-antibody-clone-49-Monoclonal--ABS0024902.html#> on 23 September 2014 (23.09.2014). entire document	1-7, 14-19, 32
A	US 2002/0160433 A1 (WELCH et al) 31 October 2002 (31.10.2002) entire document	1-7, 14-19, 32
P, Y	WO 2014/066744 A2 (VAN VLASSELAER et al) 01 May 2014 (01.05.2014) entire document	1-7, 14-19, 32
T, Y	US 2014/0140933 A1 (VAN VLASSELAER et al) 22 May 2014 (22.05.2014) entire document	1-7, 14-19, 32

☐ 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	Date of mailing of the international search report
23 September 2014	02 APR 2015

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

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PCT/US2014/038239

Box No. I 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.
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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.: 8-13, 20-31, 33-51
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:

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.:

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.