(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 September 2016 (22.09.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/149698 A3

(51) International Patent Classification:
A61K 39/42 (2006.01) *C07K 14/155* (2006.01)
A61K 49/16 (2006.01) *C07K 14/16* (2006.01)
A61K 39/12 (2006.01) *C07K 16/08* (2006.01)
A61P 31/18 (2006.01) *C12P 21/08* (2006.01)

(21) International Application Number:
PCT/US2016/023380

(22) International Filing Date:
21 March 2016 (21.03.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

62/135,309	19 March 2015 (19.03.2015)	US
62/191,054	10 July 2015 (10.07.2015)	US
62/222,175	22 September 2015 (22.09.2015)	US
62/260,100	25 November 2015 (25.11.2015)	US
62/261,233	30 November 2015 (30.11.2015)	US

(71) Applicant: **DUKE UNIVERSITY** [US/US]; 2812 Erwin Road, Suite 306, Durham, NC 27705 (US).

(72) Inventors: **HAYNES, Barton, F.**; c/o Duke University, 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). **MEYERHOFF, Ryan**; c/o Duke University, 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). **MOODY, M., Anthony**; c/o Duke University, 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). **LIAO, Hua-Xin**; c/o Duke University, 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). **BRADLEY, Todd**; c/o Duke University, 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). **BONSIGNORI, Mattia**; c/o Duke University, 2812 Erwin Road, Suite 306, Durham, NC 27705 (US).

(74) Agents: **KIM, William, W.** et al.; Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, MA 02109 (US).

(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, 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, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,

[Continued on next page]

(54) Title: HIV-1 NEUTRALIZING ANTIBODIES AND USES THEREOF (V3 ANTIBODIES)

Figure 1A

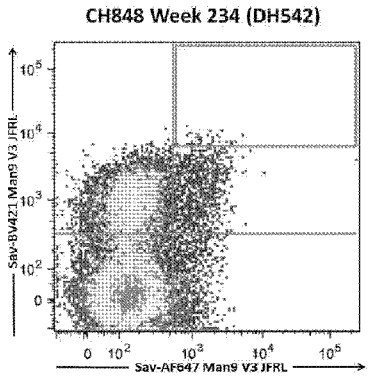
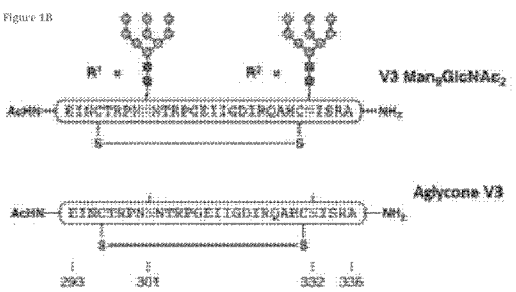


Figure 1B



(57) Abstract: The invention is directed to HIV-1 neutralizing antibodies, CD4 binding site and V3 glycan antibodies, and methods for their uses.

WO 2016/149698 A3

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))*

(88) Date of publication of the international search report:
3 November 2016

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/23380

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/42, 49/16, 39/12; A61P 31/18; C07K 14/155, 14/16, 16/08; C12P 21/08 (2016.01)
CPC - A61K 39/42, 49/16, 39/12; C07K 14/155, 14/162, 16/1045, 16/1063
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 39/42, 49/16, 39/12, 39/00; A61P 31/18, 31/12; C07K 14/155, 14/16, 16/08, 16/10; C12P 21/08, 21/04 (2016.01)
CPC: A61K 39/42, 49/16, 39/12, 39/295, 39/21; C07K 14/155, 14/162, 16/1045, 16/1063; C12N 5/166, 2740/16011

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)
PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); Google Scholar; Pubmed; EBSCO
Keywords: antibody, fragment, HIV, V3, glycan, glycopeptide, specificity, light chain, heavy chain, fusion

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2014/172366 A1 (DUKE UNIVERSITY, et al.) 23 October, 2014; paragraph [16]	1-12, 13/1-12, 14/1-12, 15/1-2, 16/15/1-12, 17/1-12, 18/17/1-12, 19/17/1-12
A	US 2012/0237523 A1 (MASCOLA, JR et al.) 20 September, 2012; SEQ ID NO. 1420; page 65	1-12, 13/1-12, 14/1-12, 15/1-2, 16/15/1-12, 17/1-12, 18/17/1-12, 19/17/1-12
A	(ZHU, D et al.) Biased Immunoglobulin Light Chain Use in the Chlamydophila psittaci Negative Ocular Adnexal Marginal Zone Lymphomas. American Journal of Hematology. 28 March 2013; Vol. 88, No. 5; pages 1-15; abstract; page 3, paragraph 2; supplemental document: immunoglobulin lambda light chain variable region, partial [Homo sapiens]. National Center for Biotechnology Information. Genbank Entry Accession AGG22572. 13 August, 2012 [retrieved on 30 August 2016]. Retrieved from the Internet: <URL: http://www.ncbi.nlm.nih.gov/protein/453071254/>; page 1	1-12, 13/1-12, 14/1-12, 15/1-2, 16/15/1-12, 17/1-12, 18/17/1-12, 19/17/1-12
A	US 2014/0314784 A1 (BEDIAN, V et al.) 23 October, 2014; paragraph [0041]; claim 27; SEQ ID NO.s 16, 36	1-12, 13/1-12, 14/1-12, 15/1-2, 16/15/1-12, 17/1-12, 18/17/1-12, 19/17/1-12

☐ 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	Date of mailing of the international search report
31 August 2016 (31.08.2016)	16 SEP 2016
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/23380

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:
-Please See Supplemental Page-*-

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.:
Groups I+, Claims 1-19 and SEQ ID NOs: 3, 4, 51, 116

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.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US16/23380

-***-Continued from Box No. III: Observations where unity of invention is lacking-***-

Groups I+, Claims 1-19 and SEQ ID NOs: 3, 4, 51, 116 are directed toward a recombinant antibody or fragment thereof with the binding specificity of the V3 glycan binding antibody DH542, DH542_L4 or DH5422_QSA; and compositions and methods relating thereto.

The recombinant antibodies, compositions and methods will be searched to the extent they encompass an antibody comprising a heavy chain encompassing SEQ ID NO: 3 (first exemplary heavy chain sequence) and a light chain encompassing SEQ ID NO: 4 (first exemplary light chain sequence), SEQ ID NO: 51 (second exemplary light chain sequence), or SEQ ID NO: 116 (third exemplary light chain sequence). Applicant is invited to elect additional antibodie(s), with paired heavy and light chain sequence(s) for each, to be searched. Additional pair(s) of antibody heavy and light chain sequence(s) will be searched upon the payment of additional fees. It is believed that claims 1, 2, 4-12, 13 (in-part), 14 (in-part), 15 (in-part), 16 (in-part), 17 (in-part), 18 (in-part) and 19 (in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass SEQ ID NO: 3 (heavy chain sequence), SEQ ID NO: 4 (light chain sequence), SEQ ID NO: 51 (light chain sequence) and SEQ ID NO: 116 (light chain sequence). Applicants must specify the claims that encompass any additionally elected paired antibody heavy and light chain sequence(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be an antibody encompassing a heavy chain encompassing SEQ ID NO: 28 (first exemplary elected heavy chain sequence) and a light chain encompassing SEQ ID NO: 52 (first exemplary elected light chain sequence).

No technical features are shared between the antibody sequences of Groups I+ and, accordingly, these groups lack unity a priori.

Groups I+ share the technical features including: a recombinant antibody or fragment thereof with the binding specificity of the V3 glycan binding antibody DH542, DH542_L4 or DH5422_QSA; a pharmaceutical composition comprising any one of the antibodies or fragments and another HIV-1 broad neutralizing antibody; a composition comprising a vector comprising a nucleic acid encoding the antibody or fragment thereof; a method to treat or prevent HIV -1 infection in a subject comprising administering to the subject a composition comprising an antibody or fragment thereof in a therapeutically effective amount.

However, these shared technical features are previously disclosed by WO 2014/063059 A1 to Rockefeller University (hereinafter 'Rockefeller').

Rockefeller discloses a recombinant antibody or fragment thereof (a recombinant antibody or fragment thereof; page 9, lines 22-24; page 11, lines 23-26) with the binding specificity of the V3 glycan binding antibody DH542, DH542_L4 or DH5422_QSA (that binds specifically to the V3 loop (with the binding specificity of the V3 glycan binding antibody DH542, DH542_L4 or DH5422_QSA); page 18, lines 27-29; page 45, lines 21-24; wherein the antibodies disclosed, absent evidence to the contrary, share the binding specificity of antibodies DH542, DH542_L4 or DH5422_QSA); a pharmaceutical composition comprising any one of the antibodies or fragments (a pharmaceutical composition comprising any one of the antibodies or fragments; page 4, lines 21-23) and another HIV-1 broad neutralizing antibody (and another HIV-1 broad neutralizing antibody; page 19, lines 15-17); a composition comprising a vector comprising a nucleic acid encoding the antibody or fragment thereof (a composition comprising a vector comprising a nucleic acid encoding the antibody or fragment thereof; page 4, lines 12-15; page 19, lines 27-30); a method to treat or prevent HIV -1 infection in a subject (a method to treat or prevent HIV -1 infection in a subject; page 4, lines 24-29) comprising administering to the subject a composition comprising an antibody or fragment thereof in a therapeutically effective amount (comprising administering to the subject a composition comprising an antibody or fragment thereof in a therapeutically effective amount; page 4, lines 24-29).

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Rockefeller reference, unity of invention is lacking.