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*A61K 39/395* (2006.01) *A61P 31/18* (2006.01)  
*C07K 16/10* (2006.01)
- (21) **International Application Number:**  
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- (71) **Applicant: BETH ISRAEL DEACONESS MEDICAL CENTER, INC.** [US/US]; 330 Brookline Avenue, BR-2, Boston, MA 02215 (US).
- (72) **Inventors: CAVACINI, Lisa;** 5 Perry Road, Natick, MA 01760 (US). **POSNER, Marshall;** 31 Laporte Avenue, Mount Vernon, NY 10552 (US). **YU, Xiacong;** 130 Linden Street, Needham, MA 02492 (US).
- (74) **Agent: BIEKER-BRADY, Kristina;** Clark & Elbing LLP, 101 Federal Street, 15th Floor, Boston, MA 02110 (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, IS, JP, KE, KG, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, 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, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, 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:**

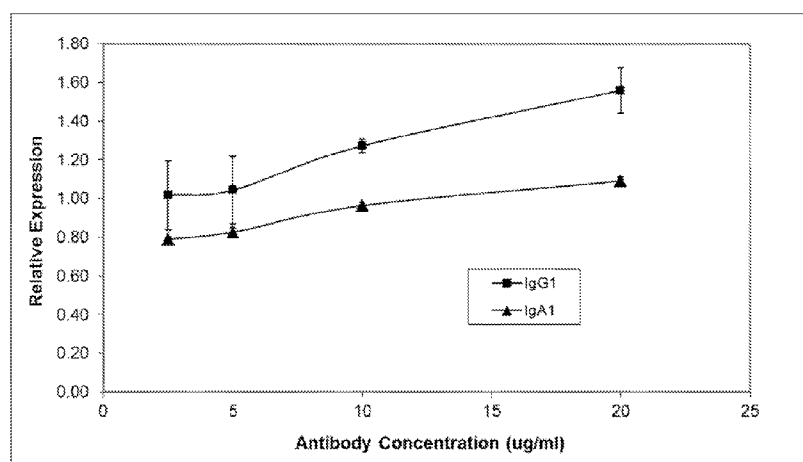
- with international search report (Art. 21(3))
- with sequence listing part of description (Rule 5.2(a))

- (88) **Date of publication of the international search report:**  
27 February 2014

(54) **Title:** IgA CD4i ANTIBODIES AND METHODS OF TREATMENT USING SAME

FIGURE 7

F425-A1g8A1g8 IgG1 and IgA1 Variants immunoreactivity with HIV-infected cells



(57) **Abstract:** The present invention relates to isolated IgA antibodies, or fragments thereof, which have variable domains derived from an antibody that specifically binds to a CD4-induced (CD4i) epitope. In particular, the isolated IgA antibodies display enhanced neutralization activity relative to their IgG, non-chimeric counterparts. The invention also provides methods for therapy with the isolated IgA antibodies for the treatment of a subject having a viral infection or having an increased risk of a viral infection.

INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US13/46124

<p><b>A. CLASSIFICATION OF SUBJECT MATTER</b>                  IPC(8) - A61K 39/395; C07K 16/10; A61P 31/18 (2013.01)                  USPC - 424/160.1, 159.1; 530/388.35                  According to International Patent Classification (IPC) or to both national classification and IPC</p>																													
<p><b>B. FIELDS SEARCHED</b></p> <p>Minimum documentation searched (classification system followed by classification symbols)                  IPC(8): A61K 39/395; C07K 16/10, 16/08, 16/00, 16/46; A61P 31/18, 31/14, 31/12, 31/00 (2013.01)                  USPC: 424/160.1, 159.1, 130.1; 530/388.35, 388.3, 388.1, 389.4, 389.1, 387.3, 387.1; 435/339.1, 339, 326</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)                  MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Proquest Dialog (Pharmaceutical &amp; Biomedical); Google/Google Scholar; Pubmed/Pubmed central; IgA, antibody, immunoglobulin, heavy chain, light chain, constant region, constant domain, CH3, CH2, CH1, CD4, induced, fragment, epitope, variable, Fab, Fv</p>																													
<p><b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b></p> <table border="1"> <thead> <tr> <th>Category*</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X --- Y</td> <td>US 6030772 A (DEVICO, AL et al.) February 29, 2000; abstract; column 9, lines 36-48; column 12, line 13; Claim 1</td> <td>1 ----- 2-5, 6/1-5, 7/6/1-5</td> </tr> <tr> <td>Y</td> <td>US 2005/0106722 A1 (JONES, D et al.) May 19, 2005; paragraphs [0032]-[0036]; pages 7-10; Claim 8</td> <td>2-5, 6/1-5, 7/6/1-5</td> </tr> <tr> <td>A</td> <td>CN 1435433 A (GONG, J) August 13, 2003; page 29</td> <td>7/6/1-5</td> </tr> <tr> <td>A</td> <td>US 2007/0196274 A1 (SUN, L) August 23, 2007; English machine translation; abstract; paragraphs [0004], [0024]-[0026]; Claims 1, 16-18</td> <td>1-5, 6/1-5, 7/6/1-5</td> </tr> <tr> <td>A</td> <td>CAVACINI, L et al. Conformational Changes In Env Oligomer Induced By An Antibody Dependent On The V3 Loop Base. AIDS. 28 March 2003, Vol. 17, pp 685-689; entire document.</td> <td>1-5, 6/1-5, 7/6/1-5</td> </tr> <tr> <td>A</td> <td>US 7566451 B2 (DIMITROV, DS et al.) July 28, 2009; entire document</td> <td>1-5, 6/1-5, 7/6/1-5</td> </tr> <tr> <td>A</td> <td>WO 1996/02273 A1 (BURTON, DR et al.) February 1, 1996; entire document</td> <td>1-5, 6/1-5, 7/6/1-5</td> </tr> <tr> <td>A</td> <td>PLANQUE, S et al. Neutralization Of Genetically Diverse HIV-1 Strains By IgA Antibodies To The gp120 CD4 Binding Site From Long-term Survivors Of HIV Infection. AIDS. 27 March 2010, Vol. 24, No. 6, pp. 875-884; entire document; DOI: 10.1097/QAD.0b013e3283376e88.</td> <td>1-5, 6/1-5, 7/6/1-5</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X --- Y	US 6030772 A (DEVICO, AL et al.) February 29, 2000; abstract; column 9, lines 36-48; column 12, line 13; Claim 1	1 ----- 2-5, 6/1-5, 7/6/1-5	Y	US 2005/0106722 A1 (JONES, D et al.) May 19, 2005; paragraphs [0032]-[0036]; pages 7-10; Claim 8	2-5, 6/1-5, 7/6/1-5	A	CN 1435433 A (GONG, J) August 13, 2003; page 29	7/6/1-5	A	US 2007/0196274 A1 (SUN, L) August 23, 2007; English machine translation; abstract; paragraphs [0004], [0024]-[0026]; Claims 1, 16-18	1-5, 6/1-5, 7/6/1-5	A	CAVACINI, L et al. Conformational Changes In Env Oligomer Induced By An Antibody Dependent On The V3 Loop Base. AIDS. 28 March 2003, Vol. 17, pp 685-689; entire document.	1-5, 6/1-5, 7/6/1-5	A	US 7566451 B2 (DIMITROV, DS et al.) July 28, 2009; entire document	1-5, 6/1-5, 7/6/1-5	A	WO 1996/02273 A1 (BURTON, DR et al.) February 1, 1996; entire document	1-5, 6/1-5, 7/6/1-5	A	PLANQUE, S et al. Neutralization Of Genetically Diverse HIV-1 Strains By IgA Antibodies To The gp120 CD4 Binding Site From Long-term Survivors Of HIV Infection. AIDS. 27 March 2010, Vol. 24, No. 6, pp. 875-884; entire document; DOI: 10.1097/QAD.0b013e3283376e88.	1-5, 6/1-5, 7/6/1-5
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<p><input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/></p>																													
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td style="vertical-align: top;"> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </td> <td style="vertical-align: top;"> <p>"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</p> <p>"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</p> <p>"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</p> <p>"&amp;" document member of the same patent family</p> </td> </tr> </table>			<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"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</p> <p>"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</p> <p>"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</p> <p>"&amp;" document member of the same patent family</p>																									
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<p>Date of the actual completion of the international search 19 November 2013 (19.11.2013)</p>		<p>Date of mailing of the international search report <b>02 DEC 2013</b></p>																											
<p>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</p>		<p>Authorized officer: Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774</p>																											

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US13/46124

**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.: 8-41  
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.