

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
9 September 2011 (09.09.2011)

(10) International Publication Number
WO 2011/109726 A3

(51) International Patent Classification:

G01N 33/53 (2006.01) *C40B 40/10* (2006.01)
C07K 16/18 (2006.01) *C40B 30/04* (2006.01)

(21) International Application Number:

PCT/US2011/027222

(22) International Filing Date:

4 March 2011 (04.03.2011)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/339,533 5 March 2010 (05.03.2010) US

(71) Applicant (for all designated States except US): **BIOAT-LA LLC** [US/US]; 10190 Teiesis Court, San Diego, CA 92121-2719 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SHORT, Jay, M.** [US/US]; 12985 Via Esperia, Del Mar, CA 92014 (US). **CHANG, Hwai, Wen** [US/US]; 1318 Shadow Hills Drive, San Marcos, CA 92069 (US). **FREY, Gerhard** [DE/US]; 13768 Cima Bella, San Diego, CA 92129 (US).

(74) Agent: **DUNLEAVY, Kevin, J.**; Knoble Yoshida & Dunleavy, LLC, 1628 John F. Kennedy Boulevard, Eight Penn Center, Suite 1350, Philadelphia, PA 19103 (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, 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, KM, 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, PE, PG, PH, PL, PT, RO, RS, RU, 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, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, 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, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- of inventorship (Rule 4.17(iv))

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:

26 January 2012

(54) Title: HOMOLOGOUS MULTI-SPECIFIC ANTIBODIES

(57) Abstract: The present invention is relevant to the generation and optimization of homologous multi-specific antibodies, antibodies that are distinguished by their ability to bind to multiple antigens with high specificity and with high affinity. The invention is also relevant to other multi-specific proteins that bind more than one target.



WO 2011/109726 A3

A. CLASSIFICATION OF SUBJECT MATTER*G01N 33/53(2006.01)i, C07K 16/18(2006.01)i, C40B 40/10(2006.01)i, C40B 30/04(2006.01)i*

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)

G01N ; C07K

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

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & Keywords: multispecific antibody, display, evolv*, library, mutant, etc.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y A	US 2005-0266425 A1 (ZAUDERER, M., et al.) 01 December 2005 See the whole document, especially abstract, claim 1, [0004], [0143], [0233], [0236].	1, 12, 19, 20, 37-41 ,45-48 35-36 2, 3, 11, 13-18, 21-34 ,42
Y A	US 2007-0111260 A1 (GAO, C., et al.) 17 May 2007 See the whole document, especially abstract, claims.	35-36 1-3, 11-34, 37-42 ,45-48
PA	WO 2011-009058 A2 (BIOATLA, LLC et al.) 20 January 2011 See the whole document, especially abstract, claims.	1-3, 11-42, 45-48
A	US 6171820 B1 (SHORT, J. M.) 09 January 2001 See the whole document.	1-3, 11-42, 45-48
A	US 7647184 B2 (VEGA, M., et al.) 12 January 2010 See the whole document.	1-3, 11-42, 45-48

 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 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

29 NOVEMBER 2011 (29.11.2011)

Date of mailing of the international search report

30 NOVEMBER 2011 (30.11.2011)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
Government Complex-Daejeon, 189 Cheongsa-ro,
Seo-gu, Daejeon 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

AHN, Kyu Jeong

Telephone No. 82-42-481-5975



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.: 8, 10
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:

Claims 8, 10 refer to claims 7, 9 respectively, which are unsearchable. Thus, it is not possible to make meaningful search regarding claims 8, 10.

3. Claims Nos.: 4-7, 9, 43, 44
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 an additional fee, this Authority did not invite payment of any additional fee.

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2011/027222

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2005-0266425 A1	01.12.2005	WO 2005-072112 A2 WO 2005-072112 A3	11.08.2005 30.03.2006
US 2007-0111260 A1	17.05.2007	AU 2006-304387 A1 CA 2625619 A1 CN 101331223 A EP 1943332 A2 JP 2009-511067 A KR 10-2008-0073293 A US 2010-0331208 A1 US 7790655 B2 WO 2007-047578 A2 WO 2007-047578 A3	26.04.2007 26.04.2007 24.12.2008 16.07.2008 19.03.2009 08.08.2008 30.12.2010 07.09.2010 26.04.2007 26.04.2007
WO 2011-009058 A2	20.01.2011	WO 2011-009058 A3 WO 2011-009058 A3	14.04.2011 20.01.2011
US 6171820 B1	09.01.2001	AU 1997-11489 B2 AU 1997-36626 B2 AU 1998-81502 B2 AU 1998-89231 B2 AU 1999-12765 A1 AU 2000-34839 A1 AU 2000-38793 A1 AU 2000-40394 A1 AU 2000-56246 A1 AU 2001-17961 A1 AU 2001-63148 A1 AU 2001-63148 B2 AU 2001-63148 C AU 2001-66978 A1 AU 2001-91208 A1 AU 2002-11402 A1 AU 2002-11642 A1 AU 2003-217678 A1 AU 2003-220235 A1 AU 2003-287386 A1 AU 2003-287386 A8 AU 782529 C CA 2227342 A1 CA 2227342 C CA 2294380 A1 CA 2301601 A1 CA 2308292 A1 CA 2325351 A1 CA 2325351 C CA 2329122 A1 CA 2360750 A1 CA 2361927 A1	25.05.2000 21.09.2000 27.06.2002 22.11.2001 24.05.1999 25.08.2000 28.09.2000 16.10.2000 02.01.2001 04.06.2001 26.11.2001 04.08.2005 26.11.2001 24.12.2001 26.03.2002 15.04.2002 22.04.2002 09.09.2003 29.09.2003 07.06.2004 07.06.2004 23.02.2006 06.02.1997 29.03.2011 23.12.1998 04.03.1999 14.05.1999 10.08.2000 01.02.2005 05.10.2000 31.05.2001 14.09.2000

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2011/027222

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		CA 2374667 A1	21. 12. 2000
		CA 2374667 C	26. 08. 2008
		CA 2375082 A1	22. 11. 2001
		CA 2391626 A1	21. 03. 2002
		CA 2393374 A1	18. 04. 2002
		CA 2413022 A1	20. 12. 2001
		CA 2424178 A1	11. 04. 2002
		CA 2477317 A1	04. 09. 2003
		CA 2478334 A1	25. 09. 2003
		CA 2492661 A1	10. 08. 2000
		EP 0839185 A1	13. 04. 2005
		EP 0839185 B1	22. 11. 2006
		EP 0866853 A1	16. 04. 2003
		EP 0866853 B1	03. 03. 2004
		EP 1007727 A1	14. 06. 2000
		EP 1007727 A4	23. 08. 2000
		EP 1009858 A1	21. 06. 2000
		EP 1009858 A4	07. 03. 2001
		EP 1025262 A1	09. 08. 2000
		EP 1027450 A1	16. 08. 2000
		EP 1027450 A4	05. 03. 2003
		EP 1061416 A1	20. 12. 2000
		EP 1073710 A2	07. 02. 2001
		EP 1073710 A3	07. 03. 2001
		EP 1073710 A4	19. 12. 2007
		EP 1092041 A1	18. 04. 2001
		EP 1092041 A4	19. 09. 2001
		EP 1130090 A2	05. 09. 2001
		EP 1130090 A3	26. 11. 2003
		EP 1144679 A2	17. 10. 2001
		EP 1144679 A3	06. 02. 2002
		EP 1161529 A2	12. 12. 2001
		EP 1192280 A1	03. 04. 2002
		EP 1192280 A4	05. 04. 2006
		EP 1294869 A2	26. 03. 2003
		EP 1319068 A2	18. 06. 2003
		EP 1356090 A2	29. 10. 2003
		EP 1364052 A2	26. 11. 2003
		EP 1415160 A2	06. 05. 2004
		EP 1480748 A1	01. 12. 2004
		EP 1483590 A1	08. 12. 2004
		EP 1696025 A2	30. 08. 2006
		EP 1696025 A3	13. 09. 2006
		EP 1696025 B1	21. 04. 2010
		JP 04-298155 B2	24. 04. 2009
		JP 04-699662 B2	11. 03. 2011
		JP 2000-501606 A	15. 02. 2000
		JP 2000-514651 A	07. 11. 2000
		JP 2001-078786 A	27. 03. 2001
		JP 2001-514017 A	11. 09. 2001

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2011/027222

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		JP 2002-156209 A	31.05.2002
		JP 2002-505590 A	19.02.2002
		JP 2002-505845 A	26.02.2002
		JP 2002-514894 A	21.05.2002
		JP 2002-537836 A	12.11.2002
		JP 2003-245073 A	02.09.2003
		JP 2003-515150 A	22.04.2003
		JP 2003-524392 A	19.08.2003
		JP 2004-500019 A	08.01.2004
		JP 2004-500027 A	08.01.2004
		JP 2004-504014 A	12.02.2004
		JP 2004-524811 A	19.08.2004
		JP 2004-536553 A	09.12.2004
		JP 2005-095192 A	14.04.2005
		JP 2005-245453 A	15.09.2005
		JP 2005-501217 A	13.01.2005
		JP 2005-518533 A	23.06.2005
		JP 2005-520157 A	07.07.2005
		JP 4298155 B2	15.07.2009
		JP 4699662 B2	15.06.2011
		US 05830696A A	03.11.1998
		US 05939250A A	17.08.1999
		US 05958672A A	28.09.1999
		US 05965408A A	12.10.1999
		US 06004788A A	21.12.1999
		US 06030779A A	29.02.2000
		US 06054267A A	25.04.2000
		US 06057103A A	02.05.2000
		US 2001-0034031 A1	25.10.2001
		US 2001-0034040 A1	25.10.2001
		US 2001-0036605 A1	01.11.2001
		US 2001-0041333 A1	15.11.2001
		US 2002-0001809 A1	03.01.2002
		US 2002-0015997 A1	07.02.2002
		US 2002-028443 A1	07.03.2002
		US 2002-031771 A1	14.03.2002
		US 2002-037505 A1	28.03.2002
		US 2002-048809 A1	25.04.2002
		US 2002-051987 A1	02.05.2002
		US 2002-058254 A1	16.05.2002
		US 2002-060783 A1	23.05.2002
		US 2002-080350 A1	27.06.2002
		US 2002-086279 A1	04.07.2002
		US 2002-102598 A1	01.08.2002
		US 2002-119457 A1	29.08.2002
		US 2002-127560 A1	12.09.2002
		US 2002-142394 A1	03.10.2002
		US 2002-146762 A1	10.10.2002
		US 2002-150949 A1	17.10.2002
		US 2002-155489 A1	24.10.2002

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2011/027222

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		US 2002-164580 A1	07.11.2002
		US 2002-172944 A1	21.11.2002
		US 2002-187489 A1	12.12.2002
		US 2003-003500 A1	02.01.2003
		US 2003-008319 A1	09.01.2003
		US 2003-013115 A1	16.01.2003
		US 2003-036116 A1	20.02.2003
		US 2003-044968 A1	06.03.2003
		US 2003-049841 A1	13.03.2003
		US 2003-054543 A1	20.03.2003
		US 2003-073165 A1	17.04.2003
		US 2003-077620 A1	24.04.2003
		US 2003-077677 A1	24.04.2003
		US 2003-083575 A1	01.05.2003
		US 2003-092022 A1	15.05.2003
		US 2003-096220 A1	22.05.2003
		US 2003-113759 A1	19.06.2003
		US 2003-119052 A1	26.06.2003
		US 2003-175887 A1	18.09.2003
		US 2003-194763 A1	16.10.2003
		US 2003-207287 A1	06.11.2003
		US 2003-211543 A1	13.11.2003
		US 2003-215798 A1	20.11.2003
		US 2003-219752 A1	27.11.2003
		US 2004-002103 A1	01.01.2004
		US 2004-005587 A1	08.01.2004
		US 2004-023327 A1	05.02.2004
		US 2004-029173 A1	12.02.2004
		US 2004-029174 A1	12.02.2004
		US 2004-077090 A1	22.04.2004
		US 2004-152077 A1	05.08.2004
		US 2004-241759 A1	02.12.2004
		US 2004-248143 A1	09.12.2004
		US 2005-009080 A1	13.01.2005
		US 2005-032054 A1	10.02.2005
		US 2005-040550 A1	24.02.2005
		US 2005-046833 A1	03.03.2005
		US 2005-064498 A1	24.03.2005
		US 2005-069917 A1	31.03.2005
		US 2005-070005 A1	31.03.2005
		US 2005-100985 A1	12.05.2005
		US 2005-208515 A1	22.09.2005
		US 2006-068493 A1	30.03.2006
		US 2008-248464 A1	09.10.2008
		US 2009-130718 A1	21.05.2009
		US 2011-165627 A1	07.07.2011
		US 6168919 B1	02.01.2001
		US 6174673 B1	16.01.2001
		US 6238884 B1	29.05.2001
		US 6280926 B1	28.08.2001

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2011/027222

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		US 6335179 B1	01.01.2002
		US 6344328 B1	05.02.2002
		US 6352842 B1	05.03.2002
		US 6358709 B1	19.03.2002
		US 6361974 B1	26.03.2002
		US 6368798 B1	09.04.2002
		US 6440668 B1	27.08.2002
		US 6455254 B1	24.09.2002
		US 6468724 B2	22.10.2002
		US 6483536 B2	19.11.2002
		US 6489145 B1	03.12.2002
		US 6528249 B1	04.03.2003
		US 6537776 B1	25.03.2003
		US 6555315 B1	29.04.2003
		US 6562594 B1	13.05.2003
		US 6566050 B2	20.05.2003
		US 6602675 B2	05.08.2003
		US 6605449 B1	12.08.2003
		US 6632600 B1	14.10.2003
		US 6635449 B2	21.10.2003
		US 6656677 B2	02.12.2003
		US 6677115 B2	13.01.2004
		US 6696275 B2	24.02.2004
		US 6709841 B2	23.03.2004
		US 6713279 B1	30.03.2004
		US 6713281 B2	30.03.2004
		US 6713282 B2	30.03.2004
		US 6740506 B2	25.05.2004
		US 6764835 B2	20.07.2004
		US 6773900 B2	10.08.2004
		US 6790605 B1	14.09.2004
		US 6794127 B1	21.09.2004
		US 6806048 B2	19.10.2004
		US 6849395 B2	01.02.2005
		US 6866824 B2	15.03.2005
		US 6872526 B2	29.03.2005
		US 6939689 B2	06.09.2005
		US 6972183 B1	06.12.2005
		US 7018793 B1	28.03.2006
		US 7019827 B2	28.03.2006
		US 7033781 B1	25.04.2006
US 7647184 B2	12.01.2010	AU 2002-328128 A8	10.03.2003
		EP 1427823 A2	16.06.2004
		US 2003-0129203 A1	10.07.2003
		US 2003-0134351 A1	17.07.2003
		WO 03-018820 A2	06.03.2003
		WO 03-018820 A3	06.03.2003
		WO 03-023032 A2	20.03.2003
		WO 03-023032 A3	20.03.2003

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2011/027222

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		WO 0302-3032A3	23.10.2003