

CORRECTED VERSION

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
29 November 2012 (29.11.2012)



(10) International Publication Number
WO 2012/161956 A9

(51) International Patent Classification:

C12N 1/19 (2006.01) *C12N 1/38* (2006.01)
C12P 21/08 (2006.01) *C12N 15/12* (2006.01)

(21) International Application Number:

PCT/US2012/036953

(22) International Filing Date:

8 May 2012 (08.05.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/488,660	20 May 2011 (20.05.2011)	US
61/496,873	14 June 2011 (14.06.2011)	US
61/496,860	14 June 2011 (14.06.2011)	US
61/525,307	19 August 2011 (19.08.2011)	US

(71) Applicants (for all designated States except US): **ALDER BIOPHARMACEUTICALS, INC.** [US/US]; 11804 North Creek Parkway South, Bothel, WA 98011 (US). **ALDERBIO HOLDINGS LLC** [US/US]; 101 Convention Center Dr., Ste. 850, Las Vegas, NV 89109 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **MCNEILL, Patricia, Dianne** [US/US]; 1333 South 290th Place, Federal Way,

WA 98003 (US). **JANSON, Nicole** [US/US]; 8005 Talbot Road, Edmonds, WA 98026 (US). **LESNICKI, Gary, L.** [CA/US]; 14625 NE 145th St., Apt. 204, Woodinville, WA 98072 (US). **QL, Pei** [CA/US]; 2121 227th St. SE D305, Bothell, WA 98021 (US). **LATHAM, John, A.** [US/US]; 2409 10th Ave. NW, Seattle, WA 98119 (US). **GARCIA-MARTINEZ, Leon, F.** [US/US]; 4926 214th St. SE, Woodinville, WA 98072 (US).

(74) Agent: **TESKIN, Robin, L.**; Hunton & Williams LLP, IP Department, 2200 Pennsylvania Ave. NW, Washington, DC 20037-1701 (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, 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,

[Continued on next page]

(54) Title: HIGH-PURITY PRODUCTION OF MULTI-SUBUNIT PROTEINS SUCH AS ANTIBODIES IN TRANSFORMED MICROBES SUCH AS *PICHTIA PASTORIS*

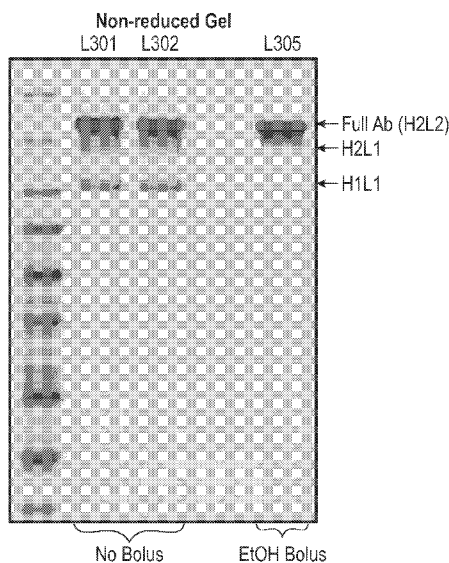


FIG. 1A

(57) Abstract: Methods for producing heterologous multi-subunit proteins in transformed cells are disclosed. In particular, the present disclosure provides improved methods of producing multi-subunit proteins, including antibodies and other multi-subunit proteins, which may or may not be secreted, with a higher yield and decreased production of undesired side-products. In exemplary embodiments, the transformed cells are a yeast, e.g., methylotrophic yeast such as *Pichia pastoris*.



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, 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:

17 January 2013

(48) Date of publication of this corrected version:

6 September 2013

Declarations under Rule 4.17:

- as to the identity of the inventor (Rule 4.17(i))
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

(15) Information about Correction:

see Notice of 6 September 2013