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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 March 2006 (16.03.2006)

PCT

(10) International Publication Number
WO 2006/028889 A3

(51) International Patent Classification:
C12N 15/82 (2006.01) *C12N 15/63* (2006.01)
C12N 15/85 (2006.01)

(21) International Application Number:
PCT/US2005/031081

(22) International Filing Date:
1 September 2005 (01.09.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/606,439 2 September 2004 (02.09.2004) US

(71) Applicant *(for all designated States except US)*: **WYETH** [US/US]; 5 Giralda Farms, Madison, NJ 07940 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **GAO, Yijie** [US/US]; 173 Bonad Road, Brookline, MA 02467 (US). **PICHE, Nicole, M.** [US/US]; 56 Caldwell Road, Waltham, MA 02453 (US). **GENG, Mei** [CA/US]; 11 Hemlock Land, Bedford, MA 01730 (US). **HERRMANN, Stephen, H.** [US/US]; 61 Wheeler Road, Stowe, MA 01775 (US). **ZHONG, Xiaotian**; 18 Oak Street, Wayland, MA 01778 (US). **KRIZ, Ronald** [US/US]; 84 Little Pond Road, Northborough, MA 01532 (US). **LU, Zhijian** [US/US]; 120 Old Burlington Road, Bedford, MA 01730 (US).

(74) Agent: **FAIRCHILD, Brian, A.**; Kirkpatrick and Lockhart Nicholson Graham LLP, State Street Financial Center, One Lincoln Street, Boston, MA 02111-2950 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
5 October 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SYSTEMS AND METHODS FOR PROTEIN PRODUCTION

(57) Abstract: The invention relates to systems and methods for producing proteins of interest. The invention employs genetically-engineered animal or plant cells that have modified protein folding or processing capacities. In one aspect, the invention features genetically-engineered cells comprising one or more recombinant expression cassettes which encode (1) a protein of interest and (2) a polypeptide that is functional in the unfolded protein response (UPR) pathway of the cells. Co-expression of the polypeptide significantly increases the yield of the protein of interest in the genetically-engineered cells. In one example, the genetically-engineered cells aare animal cells, and the co-expressed polypeptide is a component or modulator of an XBP1- or ATF6-mediated UPR pathway.

WO 2006/028889 A3