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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 September 2010 (02.09.2010)

PCT

(10) International Publication Number
WO 2010/098861 A1

(51) International Patent Classification:
*C12N 5/10* (2006.01) *C12P 21/00* (2006.01)

(21) International Application Number:
PCT/US2010/000567

(22) International Filing Date:
24 February 2010 (24.02.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/155,049 24 February 2009 (24.02.2009) US

(71) Applicant *(for all designated States except US)*: **THE SCRIPPS RESEARCH INSTITUTE** [US/US]; 10550 North Torrey Pines Road, La Jolla, CA 92037 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **MAURO, Vincent, P.** [CA/US]; 7311 Juncus Court, San Diego, CA 92121 (US). **CHAPPELL, Stephen, A.** [GB/US]; 3463 Jemez Drive, San Diego, CA 92117 (US). **ZHOU, Wei** [CN/US]; 9338 Babuata Road, #77, San Diego, CA 92129 (US). **EDELMAN, Gerald, M.** [US/US]; 7428 High Avenue, San Diego, CA 92037 (US).

(74) Agents: **ELRIFI, Ivor, R.** et al.; Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C., One Financial Center, Boston, MA 02111 (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, 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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, 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))*

(54) **Title**: REENGINEERING MRNA PRIMARY STRUCTURE FOR ENHANCED PROTEIN PRODUCTION

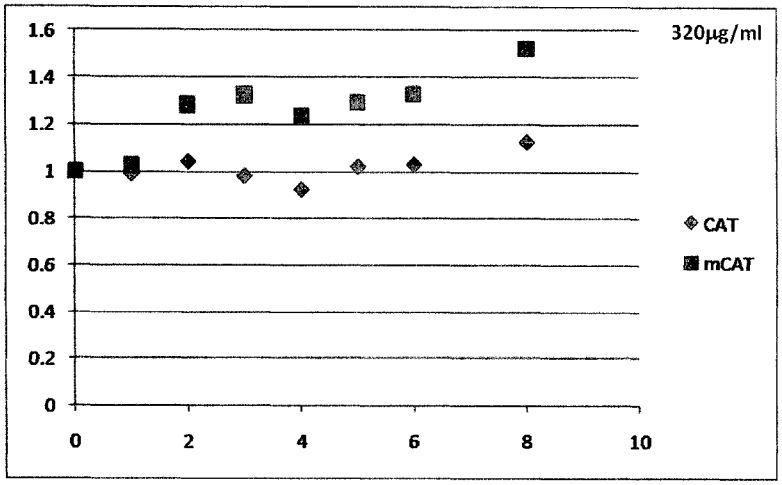



Figure 1A

(57) **Abstract**: Described herein are rules to modify natural mRNAs or to engineer synthetic mRNAs to increase their translation efficiencies. These rules describe modifications to mRNA coding and 3' UTR sequences intended to enhance protein synthesis by: 1) decreasing ribosomal diversion via AUG or non-canonical initiation codons in coding sequences, and/or 2) by evading miRNA-mediated down-regulation by eliminating one or more miRNA binding sites in coding sequences.

WO 2010/098861 A1