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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 August 2013 (08.08.2013)

WIPO | PCT

(10) International Publication Number
WO 2013/116771 A1

(51) International Patent Classification:
C12P 19/34 (2006.01)

(21) International Application Number:
PCT/US2013/024496

(22) International Filing Date:
1 February 2013 (01.02.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/593,813 1 February 2012 (01.02.2012) US

(71) Applicant: **SYNTHETIC GENOMICS, INC.** [US/US]; 11149 North Torrey Pines Road, Suite 100, La Jolla, CA 92037 (US).

(72) Inventors: **GIBSON, Daniel**; 1623 Dryden Way, Crofton, MD 21114 (US). **CAIAZZA, Nicky**; 16426 La Gracia, Rancho Santa Fe, CA 92067 (US). **RICHARDSON, Toby**; 11646 Candy Rose Way, San Diego, CA 92131 (US).

(74) Agent: **HAILE, Lisa, A.**; DLA Piper LLP (US), 4365 Executive Drive, Suite 1100, San Diego, CA 92121-2133 (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, 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, 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, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

WO 2013/116771 A1

(54) Title: MATERIALS AND METHODS FOR THE SYNTHESIS OF ERROR-MINIMIZED NUCLEIC ACID MOLECULES

(57) Abstract: Materials and methods useful for error correction of nucleic acid molecules are provided. A first plurality of double stranded nucleic acid molecules having a nucleotide mismatch are fragmented by exposure to a molecule having unidirectional mismatch endonuclease activity leaving a double-stranded nucleic acid molecule having a mismatch at the end or near end of the molecule. The nucleic acid molecule is then exposed to a molecule having unidirectional exonuclease activity to remove the mismatched nucleotide. The missing nucleotides can then be filled in by the action of, e.g., a molecule having DNA polymerase activity. The result is double-stranded nucleic acid molecules with a decreased frequency of nucleotide mismatches. Also provided are novel nucleic acid sequences encoding mismatch endonucleases, polypeptides encoded thereby, as well as nucleic acid constructs, transgenic cells, and various compositions thereof.