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

CORRECTED VERSION

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 July 2015 (16.07.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/105928 A9

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

(21) International Application Number:
PCT/US2015/010550

(22) International Filing Date:
8 January 2015 (08.01.2015)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/924,735 8 January 2014 (08.01.2014) US
62/024,642 15 July 2014 (15.07.2014) US

(71) Applicant: **PRESIDENT AND FELLOWS OF HARVARD COLLEGE** [US/US]; 17 Quincy Street, Cambridge, MA 02138 (US).

(72) Inventors: **ESVELT, Kevin, M.**; 1946 Washington Street, #141, Auburndale, MA 02466 (US). **SMIDLER, Andrea, L.**; 170 Brookline Avenue, #813, Boston, MA 02215 (US).

(74) Agent: **IWANICKI, John, P.**; 28 State Street, Suite 1800, Boston, MA 02109 (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,

[Continued on next page]

(54) Title: RNA-GUIDED GENE DRIVES

(57) Abstract: RNA guided Cas9 gene drives and method for their use are disclosed. Embodiments of the present disclosure are based on the use of RNA guided DNA binding proteins to co-localize with guide RNA at a target DNA site and act as gene drives. DNA binding proteins included within the scope of the present disclosure include those which may be guided by RNA, referred to herein as guide RNA. DNA binding include naturally occurring DNA binding proteins having nuclease activity, such as Cas9 proteins. According to one aspect, the enzyme of the present disclosure, such as Cas9 unwinds the DNA duplex and searches for sequences matching the crRNA to cleave.

FIG. 1A

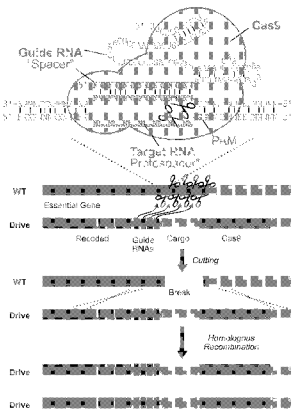


FIG. 1B

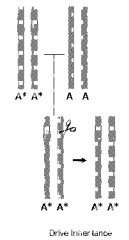


FIG. 1C

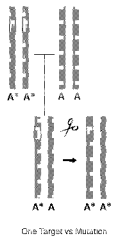


FIG. 1D

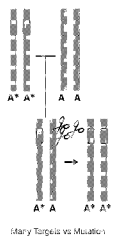


FIG. 1E

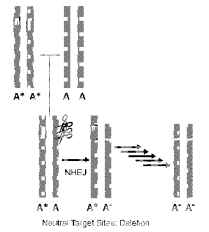
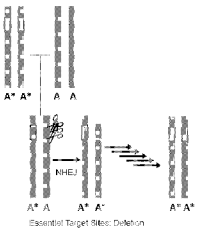


FIG. 1F



WO 2015/105928 A9

DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, 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, SA, 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, ST, 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, KM, ML, MR, NE, SN, TD, TG).

Published:

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

(48) Date of publication of this corrected version:
24 September 2015

(15) Information about Correction:
see Notice of 24 September 2015