

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
28 April 2022 (28.04.2022)



(10) International Publication Number
WO 2022/087235 A1

(51) International Patent Classification:

C12N 15/113 (2010.01) C12N 9/22 (2006.01)
C12N 15/90 (2006.01) A61K 31/7088 (2006.01)
C12N 9/12 (2006.01)

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))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

(21) International Application Number:

PCT/US2021/056006

(22) International Filing Date:

21 October 2021 (21.10.2021)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/094,803 21 October 2020 (21.10.2020) US
63/222,550 16 July 2021 (16.07.2021) US

(71) Applicant: MASSACHUSETTS INSTITUTE OF
TECHNOLOGY [US/US]; 77 Massachusetts Avenue,
Cambridge, MA 02139 (US).

(72) Inventors: ABUDAYYEH, Omar; 49 Bristol Street, Cam-
bridge, MA 02141 (US). GOOTENBERG, Jonathan; 300
Third Street, Apt. 510, Cambridge, MA 02142 (US).

(74) Agent: LABEOTS, Laura, A. et al.; Lathrop GPM
LLP, 155 North Wacker Drive, Suite 3000, Chicago, IL
60606-1787 (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, DJ, DK, DM, DO,
DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,
HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN,
KP, KR, KW, 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, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, 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,

(54) Title: SYSTEMS, METHODS, AND COMPOSITIONS FOR SITE-SPECIFIC GENETIC ENGINEERING USING PROGRAM-
MABLE ADDITION VIA SITE-SPECIFIC TARGETING ELEMENTS (PASTE)

(57) Abstract: This disclosure provides systems, methods, and compositions for site-specific genetic engineering using Programmable Addition via Site-Specific Targeting Elements (PASTE). PASTE comprises the addition of an integration site into a target genome followed by the insertion of one or more genes of interest or one or more nucleic acid sequences of interest at the site. PASTE combines gene editing technologies and integrase technologies to achieve unidirectional incorporation of genes in a genome for the treatment of diseases and diagnosis of disease.



WO 2022/087235 A1