

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
15 December 2022 (15.12.2022)



(10) International Publication Number
WO 2022/261475 A1

(51) International Patent Classification:

A61K 38/44 (2006.01) C12N 9/02 (2006.01)
A61K 38/52 (2006.01) C12N 9/90 (2006.01)
C12N 7/02 (2006.01) C12N 15/864 (2006.01)
C12N 7/04 (2006.01) A61K 38/16 (2006.01)

(21) International Application Number:

PCT/US2022/033071

(22) International Filing Date:

10 June 2022 (10.06.2022)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/209,735 11 June 2021 (11.06.2021) US
63/350,849 09 June 2022 (09.06.2022) US

(71) Applicant: **SPARK THERAPEUTICS, INC.** [US/US];
3737 Marke Street, Ste 1300, Philadelphia, PA 19104 (US).

(72) Inventors: **YAZICIOGLU, Mustafa**; 2787 Highland Avenue,
Broomall, PA 19008 (US). **OZDEMIR, Ahmet, Yunus**; 64 Peregrine Dr, Voorhees, NJ 08043 (US).

(74) Agent: **LENDARIS, Steven, P.**; Baker Botts L.L.P., 30
Rockefeller Plaza, New York, NY 10112-4498 (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, IQ, IR, IS, IT, JM, 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: METHODS OF REGULATING ADENO-ASSOCIATED VIRUS PRODUCTION

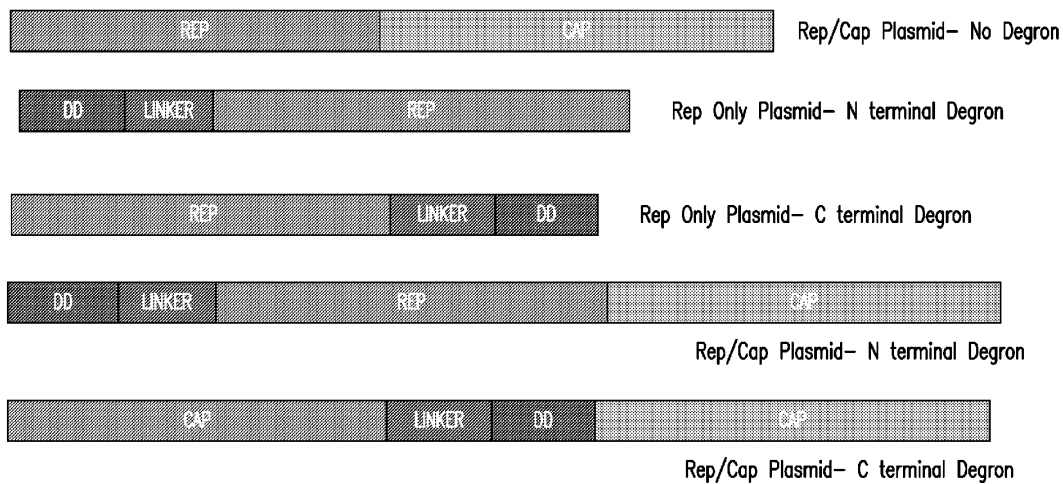


FIG. 1

(57) Abstract: The presently disclosed subject matter relates to compositions and methods for regulating recombinant adeno-associated virus (rAAV) production in cell culture. In particular, the presently disclosed subject matter relates to strategies to overcome AAV Rep protein-mediated cytotoxicity by reversible post-translational regulation of the expression of AAV Rep and helper proteins, resulting in regulated rAAV production.

[Continued on next page]

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))*