



(51) International Patent Classification:

CI2N 15/11 (2006.01) A61K 31/713 (2006.01)
CI2N 15/113 (2010.01)

(21) International Application Number:

PCT/US2022/034756

(22) International Filing Date:

23 June 2022 (23.06.2022)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/215,102	25 June 2021 (25.06.2021)	US
63/232,324	12 August 2021 (12.08.2021)	US
63/320,954	17 March 2022 (17.03.2022)	US
63/353,109	17 June 2022 (17.06.2022)	US

(71) Applicant: **THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY** [US/US];
Office of the General Counsel, Building 170, 3rd
Floor, Main Quad, P.O. Box 20386, Stanford, California
94305-2038 (US).

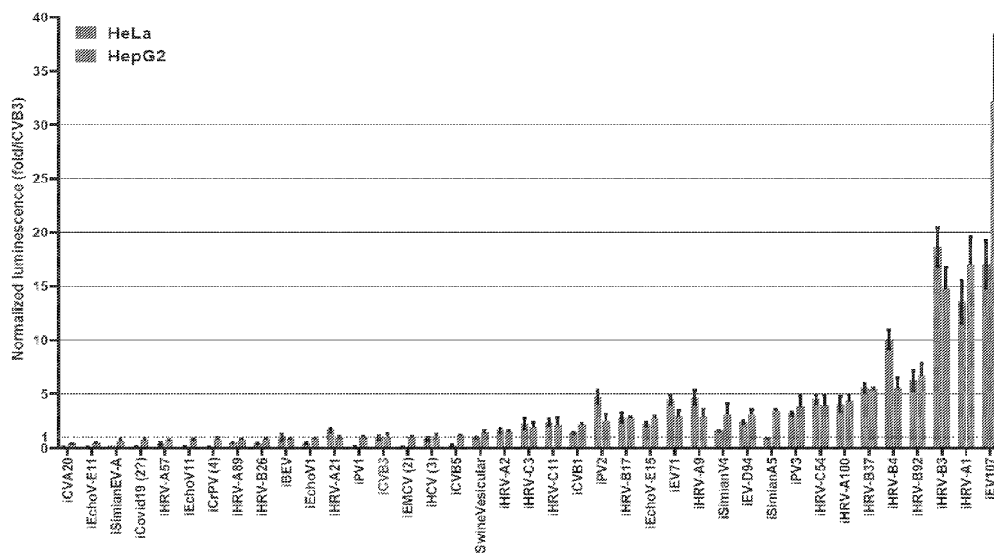
(72) Inventors: **CHEN, Robert**; c/o Office of the General
Counsel, Building 170, 3rd Floor, Main Quad, P.O. Box
20386, Stanford, California 94305-2038 (US). **CHANG,
Howard Y.**; c/o Office of the General Counsel, Building
170, 3rd Floor, Main Quad, P.O. Box 20386, Stanford, Cal-
ifornia 94305-2038 (US). **CHEN, Chun-Kan**; c/o Office of
the General Counsel, Building 170, 3rd Floor, Main Quad,
P.O. Box 20386, Stanford, California 94305-2038 (US).

(74) Agent: **ARENSEN, Tanya A.**; c/o Casimir Jones, S.C.,
2275 Deming Way, Ste 310, Middleton, Wisconsin 53562
(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,

(54) Title: COMPOSITIONS AND METHODS FOR IMPROVED PROTEIN TRANSLATION FROM RECOMBINANT CIRCULAR RNAS

FIG. 1



(57) Abstract: Provided herein are recombinant circular RNA (circRNA) molecules comprising an internal ribosome entry site (IRES) operably linked to a protein-coding nucleic acid sequence. The IRES may be, for example, a Type I IRES, such as a viral IRES. In some embodiments, the IRES is a synthetic IRES, such as an IRES comprising an aptamer. Methods of producing a protein *in vitro* or *in vivo* using the recombinant circRNA molecules are also provided.

[Continued on next page]

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, 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))*

(88) Date of publication of the international search report:

23 February 2023 (23.02.2023)