

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

(19) World Intellectual Property
Organization
International Bureau



(10) International Publication Number
WO 2021/221508 A1

(43) International Publication Date
04 November 2021 (04.11.2021)

(51) International Patent Classification:

C12N 15/11 (2006.01) C12N 15/67 (2006.01)
C12N 15/52 (2006.01) C12P 19/34 (2006.01)
C12N 15/10 (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))
- with sequence listing part of description (Rule 5.2(a))

(21) International Application Number:

PCT/NL2021/050284

(22) International Filing Date:

30 April 2021 (30.04.2021)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

2025475 30 April 2020 (30.04.2020) NL

(71) Applicant: **RIBOPRO B.V.** [NL/NL]; Morsestraat 23,
4004 JP Tiel (NL).

(72) Inventors: **BARON VAN ASBECK, Alexander Henrik**;
Hertogplein 24, 6511 SK Nijmegen (NL). **DIEKER, Jürgen**
Wilhelmus Carolus; Freulepark 6, 7207 KD Zutphen
(NL).

(74) Agent: **VAN SOMEREN, Petronella Francisca Hendrika**
Maria; Arnold & Siedsma, Bezuidenhoutseweg 57,
2594 AC THE HAGUE (NL).

(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: METHODS FOR REDUCING RNA IMMUNOGENICITY AND RNA MOLECULES WITH DECREASED IMMUNOGENICITY

(57) Abstract: The present invention relates to a method for decreasing the immunogenicity of an RNA molecule and/or at least maintaining the translation efficacy thereof. The present invention further relates to an RNA molecule, which is modified as compared to a corresponding wildtype RNA molecule, wherein the exchange of codons results in the total cytidine content of the modified RNA molecule being at least 10% less than the total cytidine content of the corresponding RNA molecule transcribed from said wildtype DNA sequence. The present invention also relates to an RNA molecule, wherein the exchange of codons results in the total uridine content of the modified RNA molecule being at least 10% less than the total uridine content of the corresponding RNA molecule transcribed from said wild-type DNA sequence. Finally, the present invention relates to the use of an RNA molecule of this invention in genome editing.



WO 2021/221508 A1