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DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
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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,
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ZA, ZM, ZW.

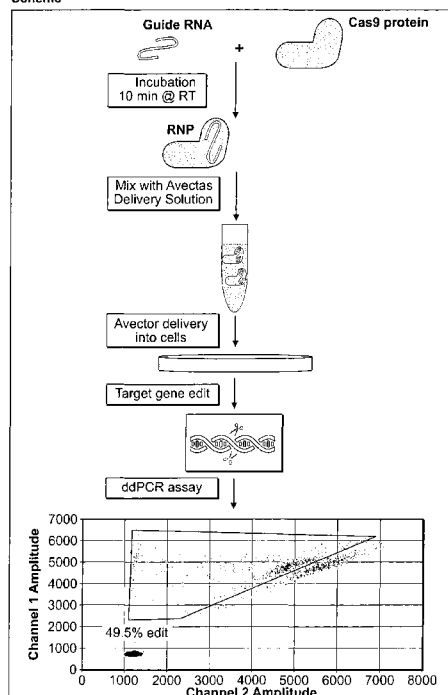
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DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
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[Continued on next page]

(54) Title: VECTOR-FREE DELIVERY OF GENE EDITING PROTEINS AND COMPOSITIONS TO CELLS AND TISSUES

FIG. 1
Scheme

(57) Abstract: The present subject matter provides a method for delivering a gene editing composition across a plasma membrane of a cell. Related apparatus, systems, techniques, compositions, and articles are also described.



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- *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:**
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/001895

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N9/22 C12N15/10 C12N15/113
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	X. HAN ET AL: "CRISPR-Cas9 delivery to hard-to-transfect cells via membrane deformation", SCIENCE ADVANCES, vol. 1, no. 7, E1500454, 14 August 2015 (2015-08-14), pages 1-8, XP055339291, DOI: 10.1126/sciadv.1500454 the whole document ----- -/--	1-61

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

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Date of the actual completion of the international search

17 May 2017

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Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/001895

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	O'DEA SHIRLEY ET AL: "Transfection of 'Hard To Transfect' Cells Using Electrospray: 'Sprayfection'", MOLECULAR THERAPY, vol. 20, no. Suppl. 1, May 2012 (2012-05), page S241, XP002770127, & 15TH ANNUAL MEETING OF THE AMERICAN-SOCIETY-OF-GENE-AND-CELL-THERAPY (ASGCT); PHILADELPHIA, PA, USA; MAY 16 -19, 2012 the whole document	1-61
A	----- LING LI ET AL: "Challenges in CRISPR/CAS9 Delivery: Potential Roles of Nonviral Vectors", HUMAN GENE THERAPY, vol. 26, no. 7, 1 July 2015 (2015-07-01), pages 452-462, XP055263140, US ISSN: 1043-0342, DOI: 10.1089/hum.2015.069 the whole document	1-61
A	----- XIQUN LIANG ET AL: "Rapid and highly efficient mammalian cell engineering via Cas9 protein transfection", JOURNAL OF BIOTECHNOLOGY, vol. 208, 21 May 2015 (2015-05-21), pages 44-53, XP055196365, ISSN: 0168-1656, DOI: 10.1016/j.jbiotec.2015.04.024 cited in the application the whole document	1-61
X,P	----- WO 2016/065341 A1 (AVECTAS LTD [US]) 28 April 2016 (2016-04-28) page 41; claim 53	52
T	----- O'DEA SHIRLEY ET AL: "Vector-free intracellular delivery by reversible permeabilization.", PLOS ONE, vol. 12, no. 3, E0174779, 30 March 2017 (2017-03-30), pages 1-23, XP002770129, ISSN: 1932-6203, DOI: 10.1371/journal.pone.0174779 the whole document	
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INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	DARREN MARTIN, VALERIA ANNIBALDI, JOANNE MASTERSON, LOUISE GALLAGHER, SHIRLEY O'DEA: "LB50 -Efficient vector-free engineering of MSC with retention of cell viability and differentiation potential", CYTOTHERAPY, vol. 19, no. 5 Suppl, 1 May 2017 (2017-05-01), page e23, XP002770130, DOI: 10.1016/j.jcyt.2017.03.061 the whole document -----	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2016/001895

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
 - a. ☒ forming part of the international application as filed:
 - ☒ in the form of an Annex C/ST.25 text file.
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 - b. ☐ furnished together with the international application under PCT Rule 13~~ter~~.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
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 - ☐ on paper or in the form of an image file (Rule 13~~ter~~.1(b) and Administrative Instructions, Section 713).
2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2016/001895

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2016065341 A1	28-04-2016	AU 2015335618 A1	18-05-2017
		CA 2965509 A1	28-04-2016
		WO 2016065341 A1	28-04-2016
