



## (51) International Patent Classification:

A61K 9/127 (2006.01) C12N 15/113 (2010.01)  
A61K 48/00 (2006.01) C12N 15/86 (2006.01)

## (21) International Application Number:

PCT/US20 18/027793

## (22) International Filing Date:

16 April 2018 (16.04.2018)

## (25) Filing Language:

English

## (26) Publication Language:

English

## (30) Priority Data:

62/485,625 14 April 2017 (14.04.2017) US

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(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, 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, SM, ST, SV, SY, TH, TJ, TM, TN,  
TR, TT, TZ, UA, UG, US, UZ, VC, VN, 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))

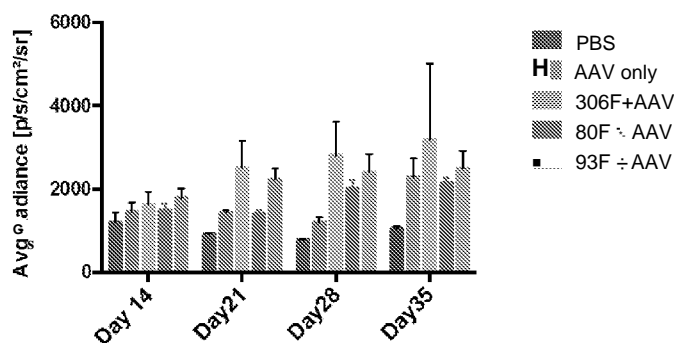
## (88) Date of publication of the international search report:

29 November 2018 (29.11.2018)

(54) Title: NOVEL DELIVERY OF LARGE PAYLOADS

**D.**

Luciferase intensity



(57) Abstract: The disclosure includes non-naturally occurring or engineered CRISPR systems and proteins, associated with a delivery system comprising a virus component and a lipid component. The disclosure includes CRISPR proteins associated with capsid proteins, e.g., AAV VP1, VP2, and/or VP3, on the surface of or internal to the AAV, along with compositions, systems and complexes involving the AAV-CRISPR protein, nucleic acid molecules and vectors encoding the same, deliver} - systems, and uses therefor.



## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2018/027793

A. CLASSIFICATION OF SUBJECT MATTER  
INV. A61K9/127 A61K48/00 C12N15/113 C12N15/86  
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)

A61K 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, EMBASE, INSPEC, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LUYAO WANG ET AL: "In Vivo Delivery Systems for Therapeutic Genome Editing", INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES, vol. 17, no. 5, 27 April 2016 (2016-04-27), page 626, XP055499285, DOI: 10.3390/ijms17050626	1,2,4,5
Y	the whole document In particular: Section 4.3 on page 10. ----- -/-	3,5



Further documents are listed in the continuation of Box C.



See patent family annex.

\* Special categories of cited documents:

"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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

15 August 2018

Date of mailing of the international search report

31/10/2018

Name and mailing address of the ISA/

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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2018/027793

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HAO YIN ET AL: "Therapeutic genome editing by combined viral and non-viral delivery of CRISPR system components in vivo", NATURE BIOTECHNOLOGY, vol . 34, no. 3, 1 February 2016 (2016-02-01) , pages 328-333 , XP055382113 , ISSN: 1087-0156, DOI: 10. 1038/nbt.3471	1, 2, 4, 5
Y	the whole document In particular: Title; Abstract; Page 329, first column, second paragraph ; Figure 2.	3, 5
X	DAVID E FEIN ET AL: "Cationic Lipid Formulations Alter the In Vivo Tropism of AAV2/9 Vector in Lung", MOLECULAR THERAPY, vol . 17, no. 12, 28 December 2009 (2009-12-28) , pages 2078-2087 , XP055068573 , ISSN: 1525-0016, DOI: 10. 1038/mt.2009 .173	1-4
Y	the whole document In particular: Title; Abstract; Figures 1-6; Materials and Methods section.	3, 5
L	W0 2018/035387 AI (BROAD INST INC [US] ; MASSACHUSETTS INSTITUTE OF TECH [US] ) 22 February 2018 (2018-02-22) the whole document For novelty see in particular: Paragraphs 637-639 and claims 91-95 .	
L	w0 2018/035388 AI (BROAD INST INC [US] ; MASSACHUSETTS INSTITUTE OF TECH [US] ) 22 February 2018 (2018-02-22) the whole document For novelty see in particular: Paragraphs 752-754 and claims 118-122 .	

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: Incompletely) ; 12, 13, 16-41, 44, 45, 86, 91-98(partially)

The particle delivery system of claim 1 and related uses/methods.

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2. claims: 6-9 (completely) ; 12, 13, 16-45, 49-56, 86, 91-98(partially)

A delivery system as defined in claim 6 and related uses/methods.

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3. claims: 10, 11, 14, 15, 46-48(completely) ; 12, 13, 16-45, 49-56, 86, 91-98(partially)

A delivery system as defined in claim 10 and related uses/methods.

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4. claims: 57-84(completely) ; 86, 91-98(partially)

A particle delivery system as defined in claim 57 and related uses/methods.

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5. claims: 85, 87-90(completely) ; 91-98(partially)

A virus particle as defined in claim 85 and related uses/methods.

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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2018/027793

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos. :
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos. :

Incompletely) ; 12 , 13 , 16-41 , 44 , 45 , 86 , 91-98(partially)

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☒ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2018/027793

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2018035387	A1	22-02-2018	NONE
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WO 2018035388	A1	22-02-2018	NONE
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