



- (51) **International Patent Classification:**
C12N 15/86 (2006.01) *A61K 48/00* (2006.01)
- (21) **International Application Number:**
PCT/US2014/042129
- (22) **International Filing Date:**
12 June 2014 (12.06.2014)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
61/834,512 13 June 2013 (13.06.2013) 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, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,

KZ, LA, LC, LK, LR, LS, LT, 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, 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).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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:**
12 March 2015

(54) **Title:** MESSENGER RNA BASED VIRAL PRODUCTION

(57) **Abstract:** The present invention provides methods for producing recombinant viral particles based on the use of exogenous mRNAs to supply various helper factors for assembly of viral particles, purified recombinant viral particles produced using such methods, and methods of using such viral particles.



INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/042129A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/86 A61K48/00
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 A61K

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.
Y	WALTHER W ET AL: "VIRAL VECTORS FOR GENE TRANSFER A REVIEW OF THEIR USE IN THE TREATMENT OF HUMAN DISEASES", DRUGS, ADIS INTERNATIONAL LTD, NZ, vol. 60, no. 2, 1 August 2000 (2000-08-01), pages 249-271, XP000979501, ISSN: 0012-6667, DOI: 10.2165/00003495-200060020-00002 page 254; figure 2 page 258; figure 4 ----- -/--	1-76, 80-89



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

7 October 2014

Date of mailing of the international search report

20/01/2015

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2014/042129

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	STONE D ET AL: "Viral vectors for gene delivery and gene therapy within the endocrine system.", THE JOURNAL OF ENDOCRINOLOGY FEB 2000, vol. 164, no. 2, February 2000 (2000-02), pages 103-118, XP002730679, ISSN: 0022-0795 page 110; figure 3 -----	1-76, 80-89
Y	YAMAMOTO A ET AL: "Current prospects for mRNA gene delivery", EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS, vol. 71, no. 3, 1 March 2009 (2009-03-01), pages 484-489, XP025992169, ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, NL ISSN: 0939-6411, DOI: 10.1016/J.EJPB.2008.09.016 [retrieved on 2008-10-10] page 484 abstract -----	1-76, 80-89
A	Anonymous: "RNA Transfection vs Plasmid DNA transfection", Protocol Online 24 December 2006 (2006-12-24), XP002730680, Retrieved from the Internet: URL: http://www.protocol-online.org/biology-forums/posts/23298.html [retrieved on 2014-10-02] the whole document -----	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/042129

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.:

1-76, 80-89

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-76, 80-89

A method for producing a viral particle by introducing an mRNA encoding required 'helper factors' into a packaging cell, and culturing the cell such that a gene of interest is packaged, related packaging cells per se comprising an mRNA encoding a helper factor, systems for producing the virus comprising at least reagents for in vitro transcription of mRNA from a construct encoding a helper factor, and a virus population produced by the method claims.

2. claims: 77-79

A viral particle (lentiviral or AAV) encoding a lysosomal enzyme for the treatment of a subject having or at risk of a lysosomal storage disease.
