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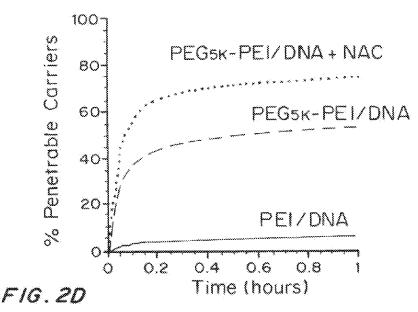
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- with international search report (Art. 21(3))
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- (88) Date of publication of the international search report:

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(54) Title: MUCUS PENETRATING GENE CARRIERS



(57) Abstract: Nanoparticles gene carriers, particularly nanoparticle gene carriers which exhibit increased rates of diffusion through cystic fibrosis (CF) mucus, as well as methods of making and using thereof, are described herein. The nanoparticle gene carriers are formed from a nucleic acid complexed to one or more biocompatible, polycationic polymers. The nanoparticle gene carriers also contain one or more mucus resistant polymers. In a particularly preferred embodiment, the nanoparticle gene carrier is a nanoparticle formed from one or more nucleic acids, PEI, and a mucus-resistant/diffusive graft copolymer composed of a PEI backbone function alized by one or more PEG side chains. The nanoparticle gene carriers can efficiently diffuse through CF mucus, and can effectively serve as a vehicle to administer one or more nucleic acids to a patient suffering from CF.



International application No PCT/US2012/024344

A. CLASSIFICATION OF SUBJECT MATTER INV. A61K47/48 A61P11/00 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)

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, EMBASE, CHEM ABS Data, DISSERTATION ABS, PASCAL, WPI Data, FSTA, INSPEC

C. DOCUM	ENTS CONSIDERED TO BE RELEVANT	
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	Treniece La'Shay Terry: "Ternary particles for effective vaccine delivery to the pulmonary system (Ph. D. thesis", 2008, UMI, ProQuest LLC, Ann Arbor, XP008155164, ISBN: 978-1-109-02396-1 page 115 - page 157	1-18
X	WO 02/060412 A2 (BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM, USA) 8 August 2002 (2002-08-08) examples	1-18

Further documents are listed in the continuation of Box C.	X 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	<ul> <li>"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</li> <li>"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</li> <li>"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</li> </ul>
the priority date claimed  Date of the actual completion of the international search	"&" document member of the same patent family  Date of mailing of the international search report
24 August 2012	10/01/2013
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk	Authorized officer
Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Dullaart, Anwyn

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C(Continua	tion). DOCUMENTS CONSIDERED TO BE RELEVANT	PC1/US2012/024344
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KICHLER A ET AL: "Intranasal gene delivery with a polyethylenimine-PEG conjugate", JOURNAL OF CONTROLLED RELEASE, vol. 81, no. 3, 17 June 2002 (2002-06-17), pages 379-388, XP004358078, ISSN: 0168-3659, DOI: 10.1016/S0168-3659(02)00080-9 abstract page 382, paragraph 3.1 - page 387, paragraph 4.	1-18
X	WO 2007/133812 A2 (PHILADELPHIA HEALTH & EDUCATIO [US]; LUTZ GORDON JOHN [US]; WHEATLEY M) 22 November 2007 (2007-11-22) paragraph [0182] examples	1-18
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Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	SANDERS N ET AL: "Extracellular barriers in respiratory gene therapy", ADVANCED DRUG DELIVERY REVIEWS, vol. 61, no. 2, 27 February 2009 (2009-02-27), pages 115-127, XP025950269, ISSN: 0169-409X, DOI: 10.1016/J.ADDR.2008.09.011 [retrieved on 2009-02-20] abstract page 122, left-hand column page 124, right-hand column, paragraph 5.2.3	1-18
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Υ	WO 2010/086406 A1 (UNIV MARBURG PHILIPPS [DE]; WENDORFF JOACHIM H [DE]; AIGNER ACHIM [DE]) 5 August 2010 (2010-08-05) figures 3,6a	1-18
Υ	WO 2009/151539 A1 (SIRNAOMICS INC [US]; UNIV DUKE [US]; YAN HAI [US]; LU PATRICK Y [US];) 17 December 2009 (2009-12-17) page 30 - page 31	1-18
Y	WO 02/24232 A2 (UNIV TEXAS [US]; CRISTIANO RICHARD J [US]; YAMASHITA MOTOYUKI [JP]) 28 March 2002 (2002-03-28) examples 4,6,10,13	1-18

C(Continua	ation). DOCUMENTS CONSIDERED TO BE RELEVANT	
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Υ	KLEEMANN E ET AL: "Modified polyethylenimines as non-viral gene delivery systems for aerosol gene therapy: investigations of the complex structure and stability during air-jet and ultrasonic nebulization", JOURNAL OF CONTROLLED RELEASE, vol. 100, no. 3, 10 December 2004 (2004-12-10), pages 437-450, XP004656464, ISSN: 0168-3659, DOI: 10.1016/J.JCONREL.2004.09.005 page 445 page 449	1-18
Υ	WO 98/59064 A1 (BOEHRINGER INGELHEIM INT [DE]; WAGNER ERNST [AT]; OGRIS MANFRED [AT];) 30 December 1998 (1998-12-30) figures 2a-2c figures 2,14	1-18
Υ	WO 2005/012407 A2 (CANJI INC [US]; SCHLUEP THOMAS [US]) 10 February 2005 (2005-02-10) examples 3-4	1-18
Υ	US 2007/111959 A1 (YOCKMAN JAMES [US] ET AL) 17 May 2007 (2007-05-17) example 9	1-18
Α	US 2003/118550 A1 (KABANOV ALEXANDER V [US] ET AL) 26 June 2003 (2003-06-26) example 42	1-18
X,P	SUK ET AL: "Overcoming the cystic fibrosis sputum barrier to nanoparticle-based gene carriers",  10 February 2011 (2011-02-10), OVERCOMING THE CYSTIC FIBROSIS SPUTUM BARRIER TO NANOPARTICLE-BASED GENE CARRIERS (Ph. D. thesis), JOHN HOPSKINS, BALTIMORE, MARYLAND,, XP008155162, ISBN: 978-1-124-76016-2 page 93, paragraph 6.3.1 - page 94, paragraph 6.3.2	1-18

International application No. PCT/US2012/024344

# **INTERNATIONAL SEARCH REPORT**

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:
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
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.:  See annex
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: 1-18(partially)

Composition for delivery of nucleic acid, or method as defined in these claims, in which the polycationic polymer is polyethyleneimine.

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2. claims: 1-18(partially)

Composition for delivery of nucleic acid, or method as defined in these claims, in which the polycationic polymer is polyarginine.

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3. claims: 1-18(partially)

Composition for delivery of nucleic acid, or method as defined in these claims, in which the polycationic polymer is polylysine.

\_\_\_

4. claims: 1-18(partially)

Composition for delivery of nucleic acid, or method as defined in these claims, in which the polycationic polymer is polyhistidine.

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5. claims: 1-18(partially)

Composition for delivery of nucleic acid, or method as defined in these claims, in which the polycationic polymer is copolymer of the above-mentioned polycationic polymers.

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Information on patent family members

	atent document d in search report		Publication date		Patent family member(s)		Publication date
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