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(54) Title: VIRION-LIKE DELIVERY PARTICLES FOR SELF-REPLICATING RNA MOLECULES

(57) Abstract: Nucleic acid immunisation is achieved by delivering a self-replicating RNA encapsulated within a small particle. The RNA encodes an immunogen of interest, and the particle may deliver this RNA by mimicking the delivery function of a natural RNA virus. Thus the invention provides a non-virion particle for in vivo delivery of RNA to a vertebrate cell, wherein the particle comprises a delivery material encapsulating a self-replicating RNA molecule which encodes an immunogen. These particles are useful as components in pharmaceutical compositions for immunising subjects against various diseases.



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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER INV. A61K39/155 A61K39/245 C12N15/86 C12N15/88 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 practical, search terms used) EPO-Internal , BIOSIS, EMBASE, 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	ZHOU W Z ET AL: "RNA melanoma vacci ne: inducti on of anti tumor immunity by human glycoprotei n 100 mRNA immuni zati on.", HUMAN GENE THERAPY 1 NOV 1999 LNKD- PUBMED: 10566900, vol . 10, no. 16, 1 November 1999 (1999-11-01) , pages 2719-2724, XP002660042 , ISSN: 1043-0342 abstract page 2720 page 2722 - page 2723 Reference: Saeki et al . 1997 ----- -/- .	1, 2, 5-7 , 10-16
☒ 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 document 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	Date of mailing of the international search report	
10 October 2011	25/01/2012	
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Brero, Al essandro	

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2011/043103

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EL OUAHABI A ET AL: "Double long-chain amidine liposome-mediated self replication RNA transfection.", FEBS LETTERS 12 FEB 1996 LNKD-PUBMED:8603716, vol . 380, no. 1-2 , 12 February 1996 (1996-02-12) , pages 108-112 , XP002660043 , ISSN: 0014-5793 cited in the application abstract page 111 - page 112 -----	1, 2, 5, 10-13, 15
X, P	Wo 2011/008974 A2 (NOVARTIS AG [CH] ; SWANSON KURT [US] ; DORMITZER PHILIP R [US]) 20 January 2011 (2011-01-20) page 49, line 25 - page 52, line 22 page 54, line 6 - page 56, line 2 -----	1, 2, 5-7 , 10-16
A	LEVINE MYRON M ET AL: "Vaccine development strategies for improving immunization: the role of modern immunology. ", NATURE IMMUNOLOGY MAY 2004 LNKD-PUBMED: 15116108, vol . 5, no. 5, May 2004 (2004-05) , pages 460-464, XP002660044, ISSN: 1529-2908 page 462 Box 2 -----	1, 2, 5-7 , 10-16
A	M MCKEY ET AL: "mRNA-based cancer vaccine: prevention of B16 melanoma progression and metastasis by systemic injection of MART1 mRNA histidylated lipopolyplexes" , CANCER GENE THERAPY, vol . 14, no. 9, 1 September 2007 (2007-09-01) , pages 802-814, XP055007324, ISSN: 0929-1903 , DOI : 10.1038/sj.cgt.7701072 the whole document -----	1, 2, 5-7 , 10-16
A	MARTINON F ET AL: "Induction of virus-specific cytotoxic T lymphocytes in vivo by liposome-entrapped mRNA. ", EUROPEAN JOURNAL OF IMMUNOLOGY JUL 1993 LNKD- PUBMED:8325342 , vol . 23, no. 7, July 1993 (1993-07) , pages 1719-1722 , XP002660045 , ISSN: 0014-2980 cited in the application the whole document -----	1, 2, 5-7 , 10-16
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2011/043103

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CANNON GEORGETTA ET AL: "RNA based vaccines .", DNA AND CELL BIOLOGY DEC 2002 LNKD-PUBMED: 12573052 , vol . 21, no. 12, December 2002 (2002-12) , pages 953-961 , XP002660046, ISSN : 1044-5498 the whole document -----	1, 2, 5-7 , 10-16
A	SAEKI Y ET AL: "DEVELOPMENT AND CHARACTERIZATION OF CATIONIC LIPOSOMES CONJUGATED WITH HVJ (SENDAI VIRUS) : RECIPROCAL EFFECT OF CATIONIC LIPID FOR IN VITRO AND IN VIVO GENE TRANSFER", HUMAN GENE THERAPY, MARY ANN LIEBERT, NEW YORK ,NY, US, vol . 8, no. 17, 20 November 1997 (1997-11-20) , pages 2133-2141 , XP000992958, ISSN : 1043-0342 abstract page 2134 - page 2135 table 3 page 2140 -----	5-7

INTERNATIONAL SEARCH REPORT

International application No.
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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.:

2, 5-7(completely) ; 1, 10-16 (partial ly)

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: 2, 5-7 (completely) ; 1, 10-16(parti al ly)

A non-vi rion parti cle for in vivo delivery of RNA to a vertebrate cell, wherein (a) the parti cle comprises a delivery materi al encapsulati ng a self-repl icati ng RNA molecule which encodes an immunogen and (b) the RNA incl udes no modified nucl eoti des.

2. claims: 3, 4, 8, incompl etely) ; 1, 10-16(parti al ly)

A non-vi rion parti cle for in vivo delivery of RNA to a vertebrate cell, wherein (a) the parti cle comprises a delivery materi al on which a self-repl i eati ng RNA molecule which encodes an immunogen is adsorbed and (b) the RNA incl udes no modified nucl eoti des.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2011/043103

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011008974 A2	20-01-2011	AR 077757 A1	21-09-2011
		TW 201116294 A	16-05-2011
		US 2011305727 A1	15-12-2011
		WO 2011008974 A2	20-01-2011
