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(88) Date of publication of the international search report:
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(54) Title: LIPID-NUCLEIC ACID PARTICLES PREPARED VIA A HYDROPHOBIC LIPID-NUCLEIC ACID COMPLEX INTERMEDIATE AND USE FOR GENE TRANSFER

(57) Abstract

Novel lipid-nucleic acid particulate complexes which are useful for *in vitro* or *in vivo* gene transfer are described. The particles can be formed using either detergent dialysis methods or methods which utilize organic solvents. Upon removal of a solubilizing component (i.e, detergent or an organic solvent) the lipid-nucleic acid complexes form particles wherein the nucleic acid is serum-stable and is protected from degradation. The particles thus formed have access to extravascular sites and target cell populations and are suitable for the therapeutic delivery of nucleic acids.

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INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/US 96/09949

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/87 C12N15/88 A61K48/00 A61K9/127

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)
IPC 6 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 practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 12756 A (UNIV CALIFORNIA) 8 July 1993	1,2,12, 14-17, 19-24, 26,27, 34,35,38
Y	see the whole document	29-31, 33,39

X	US 5 279 833 A (ROSE JOHN K) 18 January 1994 cited in the application	1,2,4,5, 7,10,18
Y	see the whole document	29-31, 33,39

X	WO 95 02698 A (LIFE TECHNOLOGIES INC) 26 January 1995 see the whole document	1,2

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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

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"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

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Date of the actual completion of the international search	Date of mailing of the international search report
7 November 1996	21.03.97
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Authorized officer Hix, R

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/US 96/09949

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 96 10390 A (INEX PHARMACEUTICALS CORP) 11 April 1996 see the whole document -----	1-3

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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

ternational application No.
PCT/US 96/09949

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

see continuation-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 searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

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.:

1-7,10,12-27,29-35,38,39(partially) and 8,9,11,28,36,37, 40,41(completely)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 96/ 09949

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

1.} Claims 1-7, 10, 12 to 27, 29 to 35, 38 and 39 (partially) and Claims 8, 9, 11, 28, 36, 37, 40 and 41 (completely) : Lipid-nucleic acid complexes comprising DODAC as the cationic lipid and methods of preparation using a detergent or organic solvent based system.

2.} Claims 1-7, 10, 12 to 27, 29 to 35, 38 and 39 (partially) : Lipid-nucleic acid complexes comprising DDAB as the cationic lipid and methods of preparation using a detergent or organic solvent based system.

3.} Claims 1-7, 10, 12 to 27, 29 to 35, 38 and 39 (partially) : Lipid-nucleic acid complexes comprising DOTMA as the cationic lipid and methods of preparation using a detergent or organic solvent based system.

4.} Claims 1-7, 10, 12 to 27, 29 to 35, 38 and 39 (partially) : Lipid-nucleic acid complexes comprising DOSPA as the cationic lipid and methods of preparation using a detergent or organic solvent based system.

5.} Claims 1-7, 10, 12 to 27, 29 to 35, 38 and 39 (partially) : Lipid-nucleic acid complexes comprising DMRIE as the cationic lipid and methods of preparation using a detergent or organic solvent based system.

6.} Claims 1-7, 10, 12 to 27, 29 to 35, 38 and 39 (partially) : 6.} Lipid-nucleic acid complexes comprising DOGS as the cationic lipid and methods of preparation using a detergent or organic solvent based system.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int ional Application No
PCT/US 96/09949

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9312756 A	08-07-93	AU 3329193 A	28-07-93
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