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0015624.0 26 June 2000 (26.06.2000) GB(71) Applicant (for all designated States except US): **NCC TECHNOLOGY PTE LTD.** [SG/SG]; 11 Hospital Drive, Singapore 169610 (SG).(71) Applicant (for MN only): **STUART, Ian** [GB/GB]; c/o Mewburn Ellis, No. 1 Redcliff Street, Bristol, Avon BS1 6NP (GB).

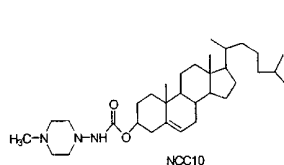
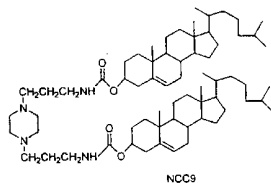
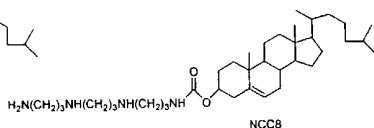
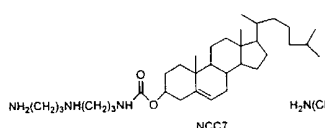
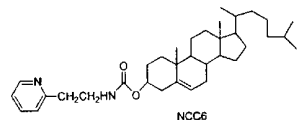
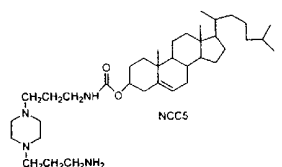
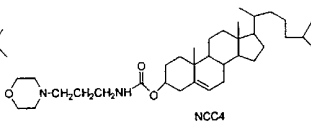
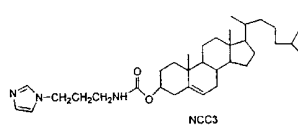
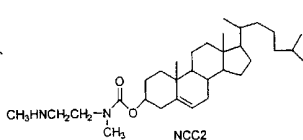
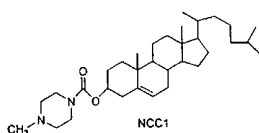
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(75) Inventors/Applicants (for US only): **HUI, Kam, Man** [SG/SG]; Gene Vector Laboratory, Division of Cellular and Molecular Research, National Cancer Center, 11 Hospital Drive, Singapore 169610 (SG). **GAO, Hui** [CN/SG]; Gene Vector Laboratory, Division of Cellular and Molecular Research, National Cancer Center, 11 Hospital Drive, Singapore 169610 (SG).(74) Agents: **STUART, Ian** et al.; Mewburn Ellis, York House, 23 Kingsway, London, Greater London WC2B 6HP (GB).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

[Continued on next page]

(54) Title: CATIONIC STEROID DERIVATIVES FOR GENE DELIVERY



(57) Abstract: Novel lipids for forming liposomes for use as nucleic acid delivery vehicles, e.g. for gene therapy, have structure with a steroid (cholesteryl) domain linked via a carbamoyl linkage to a head group which is positively charged in use (generally through protonation). The head group preferably comprises a nitrogen heterocycle, e.g. a piperazine or morpholine ring system.



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(88) Date of publication of the international search report:
16 May 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 01/02859

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07J43/00 C07J41/00 A61K31/575 A61K9/127 A61P9/00
A61P35/00

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 7 C07J A61K A61P

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, WPI Data, PAJ, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 39019 A (UNIV PITTSBURGH ;DESHMUKH HEMANT M (US); HUANG LEAF (US)) 23 October 1997 (1997-10-23) page 1, last line page 15, last paragraph -page 16, paragraph 4; examples 1-7 figures 1 and 2, compounds #2-#7; figure 3, compounds IM and PY ---	1-25
X	WO 98 45317 A (GENZYME CORP) 15 October 1998 (1998-10-15) page 2, last paragraph pages 10-11, compounds 1-7 page 14, paragraph 1 page 36, paragraph 2 page 37, line 19-21 --- -/--	1-25



Further documents are listed in the continuation of box C.



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

"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

25 September 2001

Date of mailing of the international search report

18.12.2001

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 01/02859

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 18372 A (GENZYME CORP) 20 June 1996 (1996-06-20) page 2, last paragraph page 44, paragraph 3 -page 45, paragraph 3 page 47, line 9 - line 20 figure 5, compound 97 ---	1-25
X	WO 97 04748 A (SCHREIER HANS ;CONARY JON T (US); ADVANCED THERAPIES INC (US)) 13 February 1997 (1997-02-13) page 3, line 4-13; claims 1,34 figure 12, compound 2 ---	1-25
X	WO 96 40726 A (GENTA INC) 19 December 1996 (1996-12-19) page 11, compound IX page 24, line 25 -page 25, line 21 -----	1-25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 01/02859

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.: 1-14,18-25
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:
see FURTHER INFORMATION sheet PCT/ISA/210
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 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 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.:
1-5,8,13,14,16,17 (in full) 6,7,9-12,15,18-25 (in part)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-14,18-25

Present claims 1-14 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds of formulae NCC1-NCC10 appearing in figure 2 and as claimed in claims 15-17*. The search on the subject matter of claims 18-25 (relating to compositions, uses and synthesis of these compounds) has been limited to compositions, uses and syntheses of the compounds NCC1-NCC10 mentioned above. In this regard it is further noted that claims 1,2,7 and 9-11 relate to heterocyclic derivatives of steroid compounds which do not necessarily contain Nitrogen atoms in the heterocycle, or anywhere else in the structure, (for example these claims embrace Tetrahydrofuran derivatives of steroid compounds. Such compounds are clearly unsuited to solving the stated problem of providing transfection agents, since they contain no positively charged groups which might complex with the negatively charged nucleic acids and as such embrace a large area of subject matter for which there is no support within the meaning of Article 6 PCT and Preliminary Examination Guidelines III 6.3 since the skilled person is unable to extend the described (alleged) invention over the whole claimed area. Consequently the subject matter of the search is limited also for this reason to the compounds mentioned above.

Furthermore, the initial phase of the search revealed a very large number of documents relevant to the issue of novelty of the compounds of claims 1-14. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted as indicated in the above paragraph. Furthermore, in spite of this restriction, it was found nonetheless that the compounds of claims 15-17, which were searched in full, are in any case not novel.

*The applicant's attention is also drawn to the limitation of the search by reason of a lack of unity of invention - see the finding to this effect (it is this finding of a lack of unity which precludes a full search on claim 15). It is further noted, that the same problems are considered to exist to the second invention identified in the invitation according to Article 17(3)(a) PCT and in the event of a search being conducted on this claimed invention, a further analogous limitation of the subject of the search will be necessary for the same reasons as given above (this would be a limitation to the non-cyclic amines given in figure 2 and claimed as such in claim 15).

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. Claims: 1-5,8,13,14,16,17 (in full) 6,7,9-12,15, 18-25 (in part)

Steroid-Heterocycle derivatives, liposomes and pharmaceutical compositions containing them, their complexes with nucleic acids, uses in gene therapy and process for their production.

2. Claims: 6,7,9-12,15,18-25 (in part)

Steroid-amine derivatives not containing heterocyclic groups, liposomes and pharmaceutical compositions containing them, their complexes with nucleic acids, uses in gene therapy and process for their production.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 01/02859

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9739019 A	23-10-1997	AU 715376 B AU 2457397 A CA 2251543 A EP 0904282 A	03-02-2000 07-11-1997 23-10-1997 31-03-1999
WO 9845317 A	15-10-1998	US 5912239 A AU 6874998 A	15-06-1999 30-10-1998
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