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(12) **United States Patent**  
Chu et al.(10) **Patent No.:** US 7,601,872 B2  
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Carlsbad, CA (US)(\*) Notice: Subject to any disclaimer, the term of this  
patent is extended or adjusted under 35  
U.S.C. 154(b) by 0 days.This patent is subject to a terminal dis-  
claimer.(21) Appl. No.: **11/040,662**(22) Filed: **Jan. 21, 2005**(65) **Prior Publication Data**

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12, 1998.(51) **Int. Cl.****C07C 233/00** (2006.01)  
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**C12N 15/88** (2006.01)(52) **U.S. Cl.** ..... **564/295**; 564/155; 564/158;  
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424/499(58) **Field of Classification Search** ..... None  
See application file for complete search history.(56) **References Cited**

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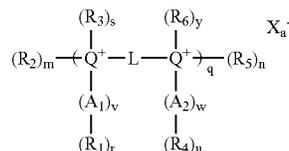
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*Primary Examiner*—Brian J Davis(57) **ABSTRACT**Disclosed are compounds capable of facilitating transport of  
biologically active agents or substances into cells having the  
general structure:

wherein

Q is selected from the group consisting of N, O and S; L is any  
bivalent organic radical capable of linking each Q, such as C,  
CH, (CH<sub>2</sub>)<sub>l</sub>, or {(CH<sub>2</sub>)<sub>i</sub>-Y-(CH<sub>2</sub>)<sub>j</sub>}<sub>k</sub>, wherein Y is selected  
from the group consisting of CH<sub>2</sub>, an ether, a polyether, an  
amide, a polyamide, an ester, a sulfide, a urea, a thiourea, a  
guanidyl, a carbamoyl, a carbonate, a phosphate, a sulfate, a  
sulfoxide, an imine, a carbonyl, and a secondary amino group  
and wherein Y is optionally substituted by -X<sub>1</sub>-L'-X<sub>2</sub>-Z or  
-Z; R<sub>1</sub>-R<sub>6</sub>, independently of one another, are selected from  
the group consisting of H, -(CH<sub>2</sub>)<sub>p</sub>-D-Z, an alkyl, an alk-  
enyl, an aryl, and an alkyl or alkyl ether optionally substituted  
by one or more of an alcohol, an aminoalcohol, an amine, an  
amide, an ether, a polyether, a polyamide, an ester, a mercap-  
tan, an alkylthio, a urea, a thiourea, a guanidyl, or a carbamoyl  
group, and wherein at least one of R<sub>1</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>6</sub> is a  
straight chain or branched, cyclic, alkyl, alkenyl, alkynyl or  
aryl group; and anyone of R<sub>1</sub>, R<sub>3</sub>, R<sub>4</sub> and/or R<sub>6</sub> may optionally  
be covalently linked with each other, with Y or with L when L  
is C or CH to form a cyclic moiety; Z is selected from the  
group consisting of amine, spermyl, carboxyspermyl,  
guanidyl, spermidinyl, putricinyl, diaminoalkyl, pyridyl, pip-  
eridinyl, pyrrolidinyl, polyamine, amino acid, peptide, and  
protein; X<sub>1</sub> and X<sub>2</sub>, independently of one another, are selected  
from the group consisting of NH, O, S, alkylene, and arylene;  
L' is selected from the group consisting of alkylene, alk-  
enylene, alkynylene, arylene, alkylene ether, and polyether; D  
is Q or a bond; A<sub>1</sub> and A<sub>2</sub>, independently of one another, are  
selected from the group consisting of CH<sub>2</sub>O, CH<sub>2</sub>S, CH<sub>2</sub>NH,  
C(O), C{NH}, C(S) and (CH<sub>2</sub>)<sub>t</sub>; X is a physiologically  
acceptable anion; m, n, r, s, u, v, w and y are 0 or 1, with the  
proviso that when both m and n are 0 at least one of r, s, u and  
y is other than 0; i, j, k, l, p and are integers from 0 to about  
100; q is an integer from 1 to about 1000; and a is the number  
of positive charge divided by the valence of the anion.

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47 Claims, 4 Drawing Sheets