

61

PLUS, insulin, transferrin, or an integrin-targeting peptide prior to complexing with the lipid. After 15 minutes of complexing, the DNA-lipid was added to cells. Cells were assayed for β-gal activity as described above.

LIPID	ACTIVITY (ng/βgal/cm ²)				
	DNA	DNA and PLUS*	DNA and INSU-LIN	DNA and TRANS-FERRIN	DNA and INTEGRIN-TARGETING PEPTIDE**
LipofectAMINE Compound of Formula X	10.36	28.6	ND	17.4	ND
1:1.5 DOPE 1 mg/ml	ND	37.8	ND	ND	40.9
Compound of Formula VII	29.4	637.9	195.7	21.7	587.9
1:1 DOPE 2 mg/ml					

ND = no detectable activity
 *PLUS Reagent is available from Life Technologies, Inc., Rockville, Maryland.
 **Reference: S. L. HART, et al (1998), Human Gene Therapy, 9: 575-585.

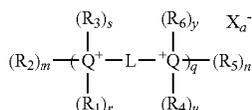
The results show that these cationic lipid formulations can deliver DNA molecules alone, but also that delivery, and ultimately gene expression, may be enhanced when the lipids are used in conjunction with peptides or proteins that bind DNA and/or act as ligands for cell surface receptors, or otherwise enhance cellular and/or nuclear uptake.

Having now fully described the present invention in some detail by way of illustration and examples for purposes of clarity of understanding, it will be obvious to one of ordinary skill in the art that the same can be performed by modifying or changing the invention within a wide and equivalent range of conditions, formulations and other parameters without affecting the scope of the invention or any specific embodiment thereof, and that such modifications or changes are intended to be encompassed within the scope of the appended claims.

All publications, patents and patent applications mentioned in this specification are indicative of the level of skill of those skilled in the art to which this invention pertains, and are herein incorporated by reference to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated by reference.

What is claimed is:

1. A method for introducing a nucleic acid into a cell, comprising the steps of contacting the nucleic acid with a polycation, thereby forming a complex; and incubating the complex with the cell, wherein the polycation has the formula:



where:

Q is N;

L is [(CH₂)_i-Y-(CH₂)_j]_k, where Y is a CH₂, an ether, an amide, a thiourea, an imine, a carbonyl, or a secondary amino group;

62

R₁, R₃, R₄, and R₆, independently of one another, are selected from H, alkyl, alkenyl, or alkynyl;

R₂ and R₅, independently of one another, are -(CH₂)_p-D-Z, wherein (CH₂)_p is optionally substituted with -OH;

D is a bond or Q;

Z is an amine, a polyamine or a diaminoalkyl optionally substituted with -OH;

X⁻ is a physiologically acceptable anion;

a is the number of positive charges divided by the valence of the anion;

m and n are 1;

r, s, u, and y are 1;

i and j are independently an integer from 0 to about 100;

k is an integer from 1 to about 100;

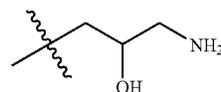
p is an integer from 1 to about 100;

q is an integer from 1 to about 100, and wherein,

i) R₁, R₃, R₄, and R₆ are optionally substituted by one or more of an alcohol, an amino alcohol, or an amine; and

ii) any two or more of R₁, R₃, R₄ and R₆ are covalently linked with each other thereby forming a cyclic moiety.

2. The method of claim 1, wherein Y is CH₂.
3. The method of claim 1, wherein D is a bond.
4. The method of claim 1, wherein p and k independently are integers from 1 to 25, and i and j independently are integers from 0 to 25.
5. The method of claim 1, wherein p and k independently are integers from 1 to 10, and i and j independently are integers from 0 to 10.
6. The method of claim 1, wherein p and k independently are integers from 1 to 4, i and j independently are integers from 0 to 4, and q is 1.
7. The method of claim 2, wherein R₂ and R₅ are (CH₂)_p-D-Z, wherein (CH₂)_p is substituted with an -OH.
8. The method of claim 7, wherein p and k independently are integers from 1 to 4, i and j independently are integers from 0 to 4, and q is 1.
9. The method of claim 7, wherein Z is a diaminoalkyl optionally substituted with -OH.
10. The method of claim 7, wherein D is a bond.
11. The method of claim 1, wherein R₁, R₃, R₄, and R₆, independent of one another, are selected from H or an alkyl group.
12. The method of claim 1, wherein R₂ and R₅ are an amino alcohol group.
13. The method of claim 1, wherein R₂ and R₅ are independently an aminoalcohol selected from aminoethanol, aminopropanol, or aminobutanol.
14. The method of claim 13, wherein the amino alcohol group has the structure



15. The method of claim 1, wherein the nucleic acid is DNA.
16. The method of claim 1, wherein the nucleic acid is RNA.
17. The method of claim 1, wherein the nucleic acid inhibits expression of nucleic acids in the cell.
18. The method of claim 1, wherein the nucleic acid catalyzes reactions.