CLAIMS

What is claimed is:

1. A composition, comprising complexes of:

one or more polyanionic compounds; and

lipid components, wherein the lipid components comprise:

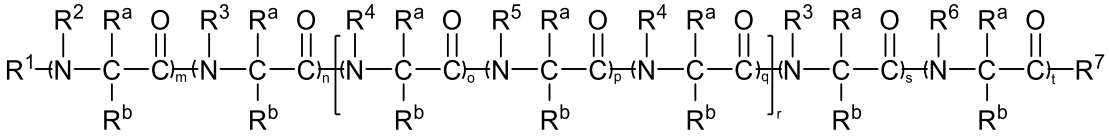
(i) optionally one or more structural lipids;

(ii) one or more phospholipids;

(iii) one or more shielding lipids; and

(iv) one or more lipidated cationic peptide compounds, wherein the one or more lipidated cationic peptide compounds are selected from the group consisting of:

(a) one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I) or salts thereof:



(I)

wherein:

m is an integer from 0 to 10;

n is an integer from 0 to 5;

s is an integer from 0 to 5;

t is an integer from 0 to 10;

wherein at least one of m, n, s, and t is nonzero;

r is an integer from 1 to 20;

each o is independently an integer 0, 1, or 2;

each q is independently an integer 0, 1, or 2;

each p is independently an integer 1 or 2;

R^1 is –H, alkyl, alkylaryl, -COR^{1a} or a lipid moiety,

wherein R^{1a} is –H, -OH, alkyl, aryl, alkylaryl, -O-alkyl, or -O-alkylaryl;

each R^2 is independently an ethylene glycol moiety of the formula $–CH_2CH_2O(CH_2CH_2O)_uCH_3$, and wherein each u is independently an integer from 2 to 200;

each R^3 is independently a lipid moiety;

each R^4 is independently a neutral spacer moiety or a lipid moiety;

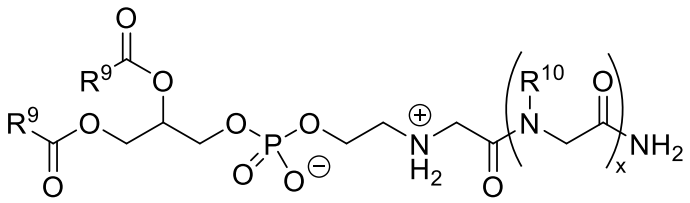
each R^5 is independently a cationic moiety;

each R^6 is independently an ethylene glycol moiety of the formula $–CH_2CH_2O(CH_2CH_2O)_vCH_3$, and wherein each v is independently an integer from 2 to 200;

R^7 is –H, alkyl, acyl, -OH, $-OR^{7a}$, $-NH_2$, $-NHR^{7a}$, or a lipid moiety, wherein R^{7a} is alkyl, acyl, or a lipid moiety; and

each R^a and R^b is independently –H, C_1-C_4-alkyl, or a side chain moiety found on a naturally- or non-naturally-occurring amino acid;

(b) one or more lipitoids of formula (II):



(II),

wherein:

x is an integer from 1 to 100;

each R^9 is independently a lipid moiety; and

each R^{10} is independently a cationic or neutral spacer moiety;

and

(c) any combination thereof.

2. The composition of claim 1, comprising 40-80% w/w one or more lipidated cationic peptide compounds of the total weight of the lipid components.

3. The composition of claim 1, wherein the one or more lipidated cationic peptide compounds are one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of the formula (I) or salts thereof.

4. The composition of claim 1, wherein at least one of n or s is nonzero.

5. The composition of claim 1, wherein each R^3 is independently C_4-C_{22}-alkyl or C_4-C_{22}-alkenyl, and wherein the C_4-C_{22}-alkenyl is optionally mono- or poly-unsaturated.

6. The composition of claim 1, wherein the one or more lipidated cationic peptide compounds are one or more lipitoids of formula (II), optionally wherein the one or more lipitoids of formula (II) are Lipitoid 1.

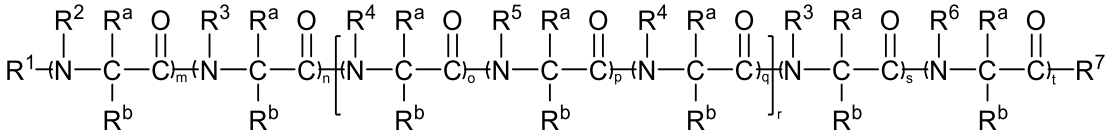
7. The composition of claim 1, comprising 0-40% w/w one or more structural lipids of the total weight of the lipid components, optionally comprising 0-25% w/w one or more structural lipids of the total weight of the lipid components, optionally wherein the one or more structural lipid are selected from the group consisting of cholesterol, fecosterol, sitosterol, ergosterol, campesterol, stigmasterol, brassicasterol, tomatidine, ursolic acid, alpha-tocopherol, and mixtures thereof.

8. The composition of claim 1, comprising 10-60% w/w one or more phospholipids of the total weight of the lipid components, optionally comprising 20-40% w/w one or more phospholipids of the total weight of the lipid components.

9. The composition of claim 1, wherein the one or more phospholipids are selected from the group consisting of 1,2-dilinoleoyl-sn-glycero-3-phosphocholine (DLPC), 1,2-dimyristoyl-sn-glycero-phosphocholine (DMPC), 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC), 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC), 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-diundecanoyl-sn-glycero-phosphocholine (DUPC), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), 1,2-di-O-octadecenyl-sn-glycero-3-phosphocholine (18:0 Diether PC), 1-oleoyl-2-cholesterylhemisuccinoyl-sn-glycero-3-phosphocholine (OChemsPC), 1-hexadecyl-sn-glycero-3-phosphocholine (C 16 Lyso PC), 1,2-dilinolenoyl-sn-glycero-3-phosphocholine, 1,2-diarachidonoyl-sn-glycero-3-phosphocholine, 1,2-didocosahexaenoyl-sn-glycero-3-phosphocholine, 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE), 1,2-diphytanoyl-sn-glycero-3-phosphoethanolamine (ME 16.0 PE), 1,2-distearoyl-sn-glycero-3-phosphoethanolamine, 1,2-dilinoleoyl-sn-glycero-3-phosphoethanolamine, 1,2-dilinolenoyl-sn-glycero-3-phosphoethanolamine, 1,2-diarachidonoyl-sn-glycero-3-phosphoethanolamine, 1,2-didocosahexaenoyl-sn-glycero-3-phosphoethanolamine, 1,2-dioleoyl-sn-glycero-3-phospho-rac-(1-glycerol) sodium salt (DOPG), sphingomyelin, and any mixtures thereof.

10. The composition of claim 1, comprising 1-5% w/w one or more shielding lipids of the total weight of the lipid components, optionally wherein the one or more shielding lipids are one or more PEG lipids selected from the group consisting of a PEG-modified phosphatidylethanolamine, a PEG-modified phosphatidic acid, a PEG-modified ceramide, a PEG-modified dialkylamine, a PEG-modified diacylglycerol, a PEG-modified dialkylglycerol, and mixtures thereof.

11. The composition of claim 1, wherein the one or more shielding lipids comprises one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I) or salts thereof:



(I)

wherein:

m is an integer from 0 to 10;

n is an integer from 0 to 5;

s is an integer from 0 to 5;

t is an integer from 0 to 10;

wherein at least one of *m* and *t* is nonzero;

r is an integer from 1 to 20;

each *o* is independently an integer 0, 1, or 2;

each *q* is independently an integer 0, 1, or 2;

each *p* is independently an integer 1 or 2;

R^1 is -H, alkyl, alkylaryl, $-COR^{1a}$ or a lipid moiety,

wherein R^{1a} is -H, -OH, alkyl, aryl, alkylaryl, -O-alkyl, or -O-alkylaryl;

each R^2 is independently an ethylene glycol moiety of the formula $-CH_2CH_2O(CH_2CH_2O)_uCH_3$, and wherein each u is independently an integer from 2 to 200;

each R^3 is independently a lipid moiety;

each R^4 is independently a neutral spacer moiety or a lipid moiety;

each R^5 is independently a cationic moiety;

each R^6 is independently an ethylene glycol moiety of the formula

$-CH_2CH_2O(CH_2CH_2O)_vCH_3$, and wherein each v is independently an integer from 2 to 200;

R^7 is-H, alkyl, acyl, -OH, $-OR^{7a}$, $-NH_2$, $-NHR^{7a}$, or a lipid moiety, wherein R^{7a} is alkyl, acyl, or a lipid moiety; and

each R^a and R^b are independently -H, C_1-C_4-alkyl, or a side chain moiety found on a naturally- or non-naturally-occurring amino acid.

12. The composition of claim 1, wherein the lipid components comprise by total weight of the lipid components:

a. 40-70% w/w one or more lipidated cationic peptide compounds;

b. 0-25% w/w cholesterol;

c. 20-40% w/w 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE); and

d. 1-5% w/w 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (DMG-PEG2000).

13. The composition of claim 1, wherein the one or more polyanionic compounds comprise a nucleic acid, optionally wherein the one or more polyanionic compounds comprise a nucleic acid and wherein the nucleic acid is an mRNA encoding a polypeptide.

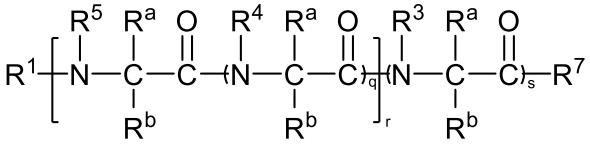
14. The composition of claim 1, wherein the mass ratio of the lipid components to the one or more polyanionic compounds is between 2:1 and 25:1.

15. A method of delivering a polyanionic compound to a cell comprising contacting the cell with the composition of claim 1, optionally wherein the polyanionic compound comprises a nucleic acid which is the mRNA encoding the polypeptide and the cell expresses the polypeptide after being contacted with the complex.

16. A method of preparing the composition according to claim 1, comprising: combining one or more lipidated cationic peptide compounds, one or more phospholipids, one or more shielding lipids, and optionally one or more structural lipids with one or more polyanionic compounds.

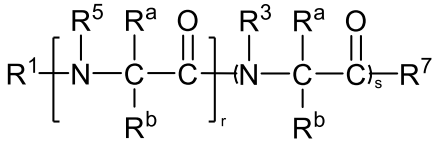
17. The composition of claim 1, wherein the one or more lipidated cationic peptide compounds are one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I) or salts thereof, wherein:

(a) m is 0; n is 0; s is an integer from 1 to 5; t is 0; r is an integer from 1 to 5; o is 0; q is 2; and p is 1, and formula (I) has a structure:



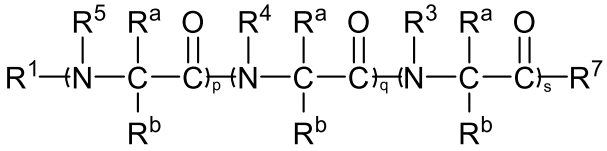
; or

(b) m is 0; n is 0; s is an integer from 1 to 5; t is 0; r is an integer from 2 to 10; o is 0; q is 0; and p is 1, and formula (I) has a structure:



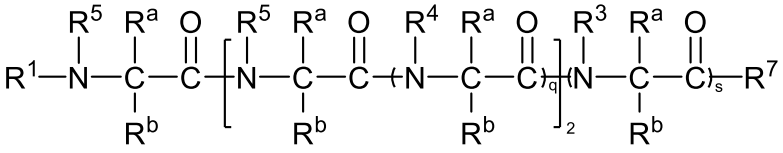
; or

(c) m is 0; n is 0; s is 3 or 4; t is 0; r is 1; o is 0; q is 2; and p is 2, and formula (I) has a structure:



; or

(d) m is 0; n is 0; s is 3 or 4; t is 0; r is 3; o is 0; q is 2; and p is 1, and formula (I) has a structure:



;

(e) or combinations thereof.

18. The composition of claim 17, wherein

R^1 is H or alkyl;

each R^3 independently is C_8-C_{24}alkyl;

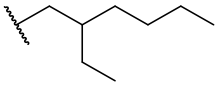
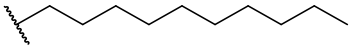
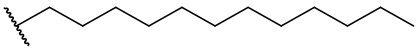
each R^4 is independently a neutral spacer moiety that is a C_1-C_4-alkyl substituted by cycloalkyl, heterocyclylalkyl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, alkoxy, alkoxyalkyl, or hydroxyalkyl, wherein each cycloalkyl, heterocyclylalkyl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, alkoxy, alkoxyalkyl, or

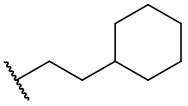
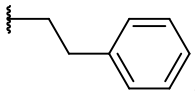
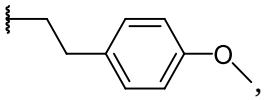
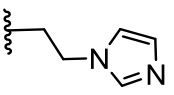
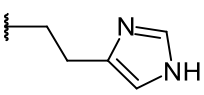
hydroxyalkyl is optionally substituted with one or more substituents –OH, halo, or alkoxy;

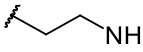
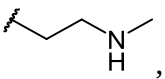
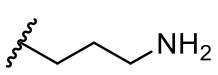
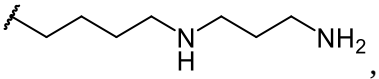
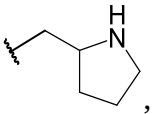
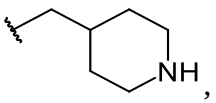
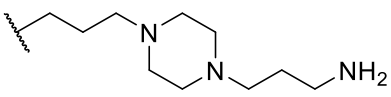
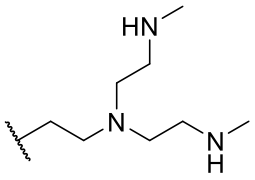
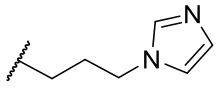
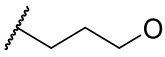
each R^5 is independently selected from the group consisting of aminoalkyl, alkylaminoalkyl, aminoalkylaminoakyl, guanidinoalkyl, N-heterocyclylalkyl, and N-heteroaryl, hydroxyalkyl, hydroxyether, alkoxyalkyl, and hydroxylheteroalkyl;

R^7 is NH_2; and

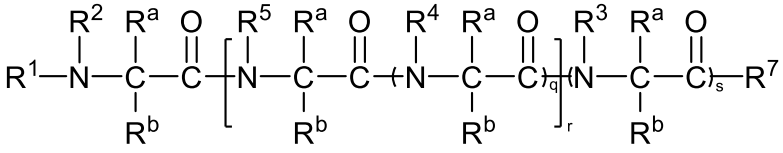
each of R^a and R^b is H, optionally wherein

each R^3 independently is ,  or ;

each R^4 independently is selected from the group consisting of , , , , and ; and

each R^5 is independently selected from the group consisting of , , , , , , , , , and .

19. The composition of claim 11 wherein m is 1; n is 0; s is 3 or 4; t is 0; r is 1 or 2; o is 0; q is 2; and p is 1, and having a structure:



, optionally wherein:

R^1 is H;

R^2 is an ethylene glycol moiety of the formula $–CH_2CH_2O(CH_2CH_2O)_uCH_3$, and wherein each u is independently an integer from 2 to 50;

each R^3 independently is C_8-C_{24}alkyl;

each R^4 is independently a neutral spacer moiety that is a C_1-C_4-alkyl substituted by cycloalkyl, heterocyclylalkyl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, alkoxy, alkoxyalkyl, or hydroxyalkyl, wherein each cycloalkyl, heterocyclylalkyl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, alkoxy, alkoxyalkyl, or hydroxyalkyl is optionally substituted with one or more substituents –OH, halo, or alkoxy;

each R^5 is independently selected from the group consisting of aminoalkyl, alkylaminoalkyl, aminoalkylaminoakyl, guanidinoalkyl, N-heterocyclylalkyl, and N-heteroaryl, hydroxyalkyl, hydroxyether, alkoxyalkyl, and hydroxylheteroalkyl;

R^7 is NH_2; and

each of R^a and R^b is H.

20. A composition, comprising complexes of:

one or more polyanionic compounds; and

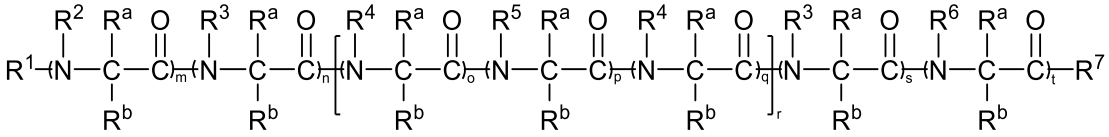
lipid components, wherein the lipid components comprise:

(i) optionally one or more structural lipids;

(ii) one or more phospholipids;

(iii) one or more shielding lipids; and

(iv) one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I) or salts thereof:



(I)

wherein:

m	is 0;
n	is 0;
s	is an integer from 1 to 5;
t	is 0;
r	is 1;
each o	is 0;
each q	0;

p is 1;

R^1 is –H;

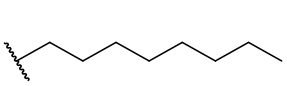
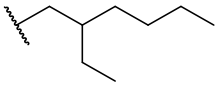
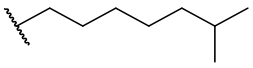
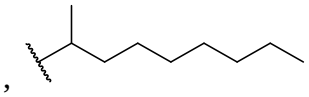
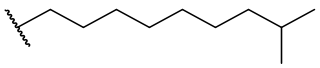
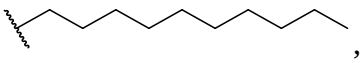
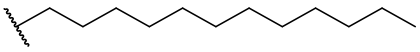
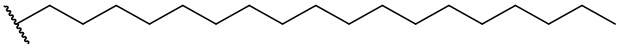
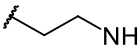
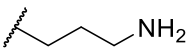
each R^3 is independently selected from C_8-C_{24}alkyl;

R^5 is selected from aminoalkyl, alkylaminoalkyl, aminoalkylaminoakyl, guanidinoalkyl, N-heterocyclylalkyl, N-heteroaryl, hydroxyalkyl, hydroxyether, alkoxyalkyl, and hydroxylheteroalkyl;

R^7 is –H, alkyl, acyl, -OH, -OR^{7a}, -NH_2, -NHR^{7a}, or a lipid moiety, wherein R^{7a} is alkyl, acyl, or a lipid moiety; and

each R^a and R^b are independently –H, C_1-C_4-alkyl, or a side chain moiety found on a naturally- or non-naturally-occurring amino acid.

21. The composition of claim 20, comprising 40-80% w/w compounds of formula (I) of the total weight of the lipid components, optionally, wherein s is 3 or 4.

22. The composition of claim 20, wherein each R^3 is independently selected from the group consisting of , , , , , , , and , optionally wherein R^5 is aminoalkyl, alkylaminoalkyl, aminoalkylaminoakyl, guanidinoalkyl, N-heterocyclylalkyl, or N-heteroaryl, optionally wherein R^5 is  or .

23. The composition of claim 20, wherein R^a and R^b are –H.

24. The composition of claim 20, comprising 0-40% w/w one or more structural lipids of the total weight of the lipid components.

25. The composition of claim 20, wherein the one or more structural lipid are selected from the group consisting of cholesterol, fecosterol, sitosterol, ergosterol, campesterol, stigmasterol, brassicasterol, tomatidine, ursolic acid, alpha-tocopherol, and mixtures thereof.

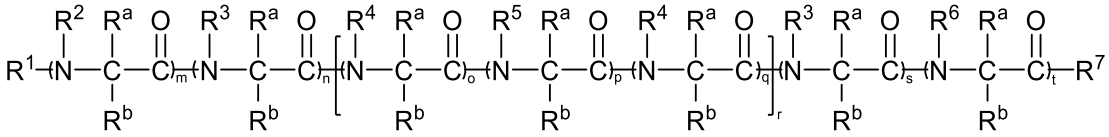
26. The composition of claim 20, comprising 10-60% w/w one or more phospholipids of the total weight of the lipid components.

27. The composition of claim 20, wherein the one or more phospholipids are selected from the group consisting of 1,2-dilinoleoyl-sn-glycero-3-phosphocholine (DLPC), 1,2-dimyristoyl-sn-glycero-phosphocholine (DMPC), 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC), 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC), 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-diundecanoyl-sn-glycero-phosphocholine (DUPC), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), 1,2-di-O-octadecenyl-sn-glycero-3-phosphocholine (18:0 Diether PC), 1-oleoyl-2-cholesterylhemisuccinoyl-sn-glycero-3-phosphocholine (OChemsPC), 1-hexadecyl-sn-glycero-3-phosphocholine (C 16 Lyso PC), 1,2-dilinolenoyl-sn-glycero-3-phosphocholine, 1,2-diarachidonoyl-sn-glycero-3-phosphocholine, 1,2-didocosahexaenoyl-sn-glycero-3-phosphocholine, 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE), 1,2-diphytanoyl-sn-glycero-3-phosphoethanolamine (ME 16.0 PE), 1,2-distearoyl-sn-glycero-3-phosphoethanolamine, 1,2-dilinoleoyl-sn-glycero-3-phosphoethanolamine, 1,2-dilinolenoyl-sn-glycero-3-phosphoethanolamine, 1,2-diarachidonoyl-sn-glycero-3-phosphoethanolamine, 1,2-didocosahexaenoyl-sn-glycero-3-phosphoethanolamine, 1,2-dioleoyl-sn-glycero-3-phospho-rac-(1-glycerol) sodium salt (DOPG), sphingomyelin, and any mixtures thereof.

28. The composition of claim 20, comprising 1-5% w/w one or more shielding lipids of the total weight of the lipid components.

29. The composition of claim 20, wherein the one or more shielding lipids are one or more PEG lipids selected from the group consisting of a PEG-modified phosphatidylethanolamine, a PEG-modified phosphatidic acid, a PEG-modified ceramide, a PEG-modified dialkylamine, a PEG-modified diacylglycerol, a PEG-modified dialkylglycerol, and mixtures thereof; or

wherein the one or more shielding lipids comprises one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I) or salts thereof:



(I)

wherein:

m is an integer from 0 to 10;

n is an integer from 0 to 5;

s is an integer from 0 to 5;

t is an integer from 0 to 10;

wherein at least one of *m* and *t* is nonzero;

r is an integer from 1 to 20;

each *o* is independently an integer 0, 1, or 2;

each *q* is independently an integer 0, 1, or 2;

each *p* is independently an integer 1 or 2;

R^1 is –H, alkyl, alkylaryl, -COR^{1a} or a lipid moiety,

wherein R^{1a} is –H, -OH, alkyl, aryl, alkylaryl, -O-alkyl, or -O-alkylaryl;

each R^2 is independently an ethylene glycol moiety of the formula $–CH_2CH_2O(CH_2CH_2O)_uCH_3$, and wherein each u is independently an integer from 2 to 200;

each R^3 is independently a lipid moiety;

each R^4 is independently a neutral spacer moiety or a lipid moiety;

each R^5 is independently a cationic moiety;

each R^6 is independently an ethylene glycol moiety of the formula $–CH_2CH_2O(CH_2CH_2O)_vCH_3$, and wherein each v is independently an integer from 2 to 200;

R^7 is–H, alkyl, acyl, -OH, -OR^{7a}, -NH_2, -NHR^{7a}, or a lipid moiety,

wherein R^{7a} is alkyl, acyl, or a lipid moiety; and

each R^a and R^b are independently –H, C_1-C_4-alkyl, or a side chain moiety found on a naturally- or non-naturally-occurring amino acid.

30. The composition of claim 20, wherein the lipid components comprise by total weight of the lipid components:

a. 40-70% w/w one or more lipidated cationic peptide compounds;
b. 0-25% w/w cholesterol;
c. 20-40% w/w 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE); and
d. 1-5% w/w 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (DMG-PEG2000).

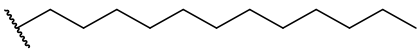
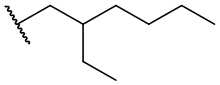
31. The composition of claim 20, wherein the one or more polyanionic compounds comprise a nucleic acid, optionally wherein the one or more polyanionic compounds comprise a nucleic acid and wherein the nucleic acid is an mRNA encoding a polypeptide, optionally wherein the mass ratio of the lipid components to the one or more polyanionic compounds is between 2:1 and 25:1.

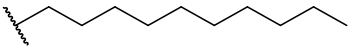
32. A method of delivering a polyanionic compound to a cell comprising contacting the cell with the composition of claim 20, optionally, wherein the polyanionic compound comprises a nucleic acid which is a mRNA encoding the polypeptide and the cell expresses the polypeptide after being contacted with the complex.

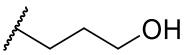
33. A method of preparing the composition according to claim 20, comprising: combining one or more lipidated cationic peptide compounds, one or more phospholipids, one or more shielding lipids, and optionally one or more structural lipids with one or more polyanionic compounds.

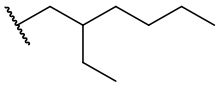
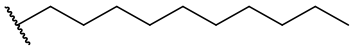
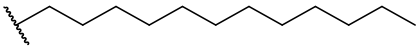
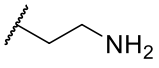
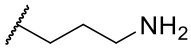
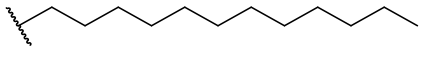
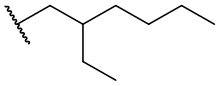
34. The composition of claim 20, wherein R^7 is NH_2.

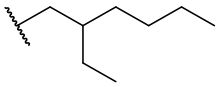
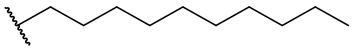
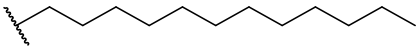
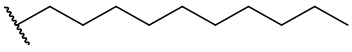
35. The composition of claim 20, wherein s is 4 and:

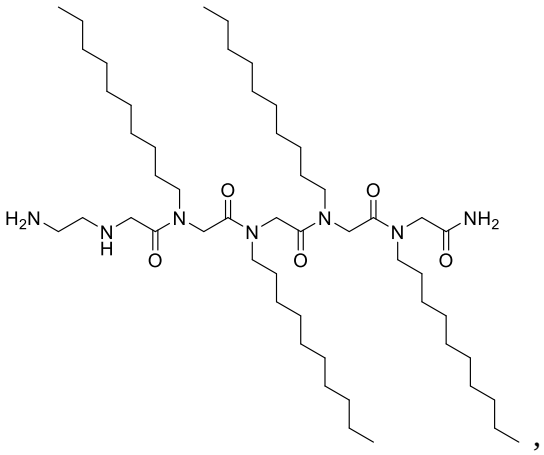
(a) two R^3 are , and two R^3 are ; or

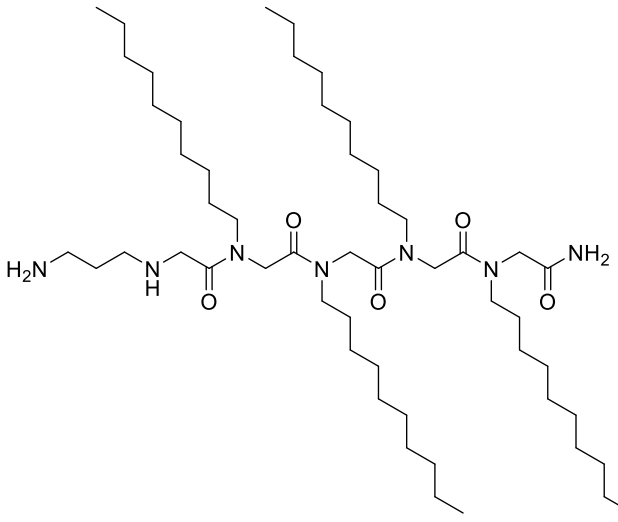
(b) each R^3 is .

36. The composition of claim 20, wherein R^5 is hydroxyalkyl, hydroxyether, alkoxyalkyl, or hydroxylheteroalkyl, optionally wherein R^5 is a hydroxyalkyl, optionally wherein R^5 is .

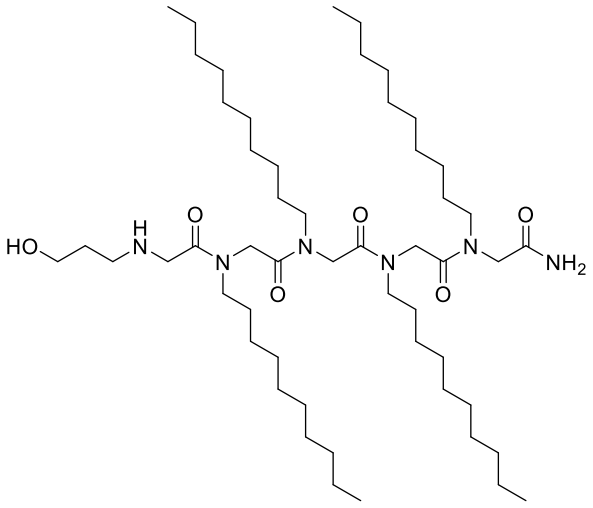
37. The composition of claim 20, wherein s is 4; each R^3 independently is , , or ; R^5 is  or ; R^7 is NH_2; and each R^a and R^b independently is H, optionally wherein two R^3 are , and two R^3 are .

38. The composition of claim 20, wherein s is 4; each R^3 independently is , , or ; R^5 is hydroxyalkyl; R^7 is NH_2; and each R^a and R^b independently is H, optionally wherein each R^3 independently is .

39. The composition of claim 20, wherein the compound of formula (I) is ,



, or



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