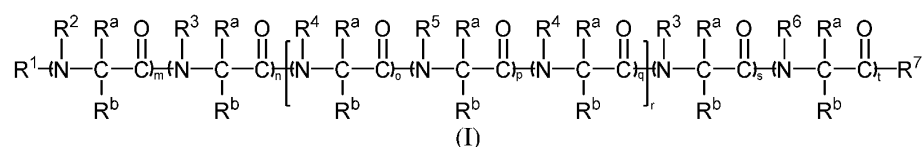


CLAIMS

What is claimed is:

1. A composition, comprising complexes of:
 - (i) one or more polyanionic compounds;
 - (ii) one or more PEG compounds; and
 - (iii) one or more cationic compounds, wherein the one or more cationic 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:



wherein:

m is 0;

n is an integer from 0 to 5;

s is an integer from 0 to 5;

t is 0;

wherein at least one of n and s is nonzero;

r is an integer from 1 to 20;

each o is independently an integer 0, 1, 2, 3 or 4;

each q is independently an integer 0, 1, 2, 3 or 4;

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

-CH₂CH₂O(CH₂CH₂O)_uCH₃, and wherein each u is independently an integer from 1 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;

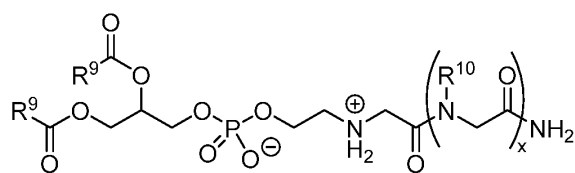
each R^6 is independently an ethylene glycol moiety of the formula

$-\text{CH}_2\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_v\text{CH}_3$, and wherein each v is independently an integer from 1 to 200;

R^7 is $-\text{H}$, alkyl, acyl, $-\text{OH}$, $-\text{OR}^{7a}$, $-\text{NH}_2$, $-\text{NHR}^{7a}$, or a lipid moiety, wherein R^{7a} is alkyl, acyl, or a lipid moiety; and

each R^a and R^b are independently $-\text{H}$, 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)

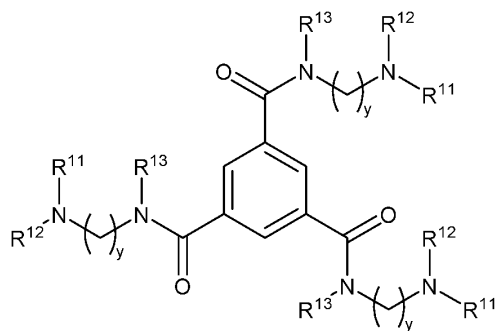
wherein:

x is a 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;

(c) one or more lipid-like compounds of formula (III):



(III)

wherein:

each R^{11} is independently substituted or unsubstituted alkyl;

each R¹² is independently substituted or unsubstituted alkyl;
each R¹³ is independently hydrogen or substituted or unsubstituted alkyl; and
each y is independently an integer from 1 to 8;
and

(d) any combination thereof;

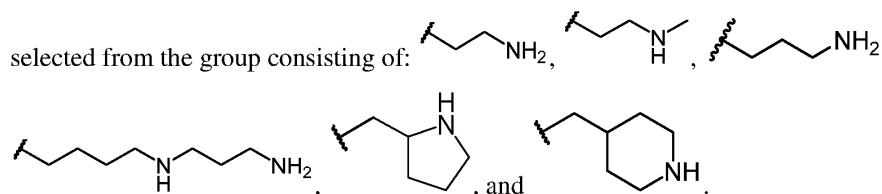
and wherein the one or more cationic compounds, the one or more PEG compounds and the one or more polyanionic compounds have a combined mass percentage of at least 90% w/w of the complexes.

2. The composition of claim 1, wherein the one or more cationic compounds are one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I).
3. The composition of claim 1 or claim 2, wherein the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds comprises a block of N-lipidated amino acid residues, wherein either *n* or *s* is at least 2.
4. The composition of any one of claims 1 to 3, wherein the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds comprises a block of N-lipidated amino acid residues, wherein either *n* or *s* is 4.
5. The composition of any one of claims 1 to 4, wherein each R³ is independently C₄-C₂₂-alkyl or C₄-C₂₂-alkenyl, and wherein the C₄-C₂₂-alkenyl is optionally mono- or poly-unsaturated.
6. The composition of any one of claims 1 to 5, wherein each R³ is independently C₈-C₁₂ alkyl.
7. The composition of any one of claims 1 to 5, wherein each R³ is independently selected from the group consisting of 2-ethylhex-1-yl, caproyl, oleyl, stearyl, linoleyl, myristyl, and lauryl.
8. The composition of any one of claims 1 to 7, wherein the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds comprises a block of N-

lipidated amino acid residues, comprising a set of mixed N-lipidated amino acid residues having one of two different lipid moieties R^{3a} and R^{3b} .

9. The composition of any one of claims 1 to 8, wherein at least one lipid moiety R^3 (or R^{3a} or R^{3b}) is a branched aliphatic moiety.
10. The composition of any one of claims 1 to 9, wherein at least one lipid moiety R^3 (or R^{3a} or R^{3b}) is 2-ethylhex-1-yl.
11. The composition of any one of claims 1 to 10, wherein at least one of the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds comprises a cationic domain comprising at least two cationic amino acid residues having cationic moieties R^5 .
12. The composition of any one of claims 1 to 11, wherein each R^5 is independently aminoalkyl, alkylaminoalkyl, aminoalkylaminoalkyl, guanidinoalkyl, N-heterocyclylalkyl or N-heteroaryl.

13. The composition of any one of claims 1 to 12, wherein each R^5 is independently selected from the group consisting of:

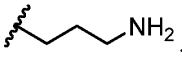
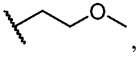
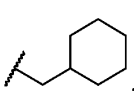
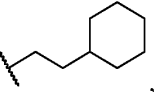
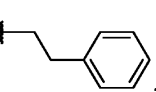
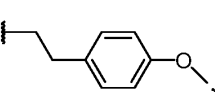
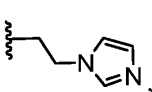
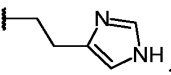
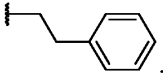


14. The composition of any one of claims 1 to 12, wherein each R^5 is a $-(C_1-C_4\text{alkylene})-NR^{5a}R^{5b}$, wherein R^{5a} and R^{5b} are independently H, C_1-C_3 alkyl, or C_6-C_{10} aryl, or R^{5a} and R^{5b} are taken together with the nitrogen atom to which they are attached to form a 4-7 membered N-heterocycloalkyl ring, wherein the N-heterocycloalkyl ring may optionally include one additional heteroatom selected from the group consisting of N and O.

15. The composition of any one of claims 1 to 14, wherein each R^5 is

16. The composition of any one of claims 1 to 14, wherein each R^5 is independently , wherein R^{5a} and R^{5b} are independently H, C_1-C_3 alkyl, or C_6-

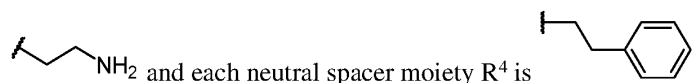
C₁₀ aryl, or R^{5a} and R^{5b} are taken together with the nitrogen atom to which they are attached to form a 4-7 membered N-heterocycloalkyl ring, wherein the N-heterocycloalkyl ring may optionally include one additional heteroatom selected from the group consisting of N and O.

17. The composition of claim 1 to 14, wherein each R⁵ is .
18. The composition of any one of claims 1 to 17, wherein each neutral spacer moiety R⁴ is independently a C₁-C₅ straight chain alkyl, a C₁-C₄-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.
19. The composition of any one of claims 1 to 18, wherein each neutral spacer moiety R⁴ is independently selected from the group consisting of: -CH₃, , , , , , , and .
20. The composition of any one of claims 1 to 19, wherein each neutral spacer moiety R⁴ is .
21. The composition of any one of claims 1 to 20, wherein at least one of the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds comprises a cationic domain comprising at least two amino acid residues having R⁵ cationic moieties and wherein each of the at least two cationic amino acid residues within the cationic domain are separated by at least one amino acid residue having a neutral spacer or lipid moiety R⁴.
22. The composition of any one of claims 1 to 21, wherein at least one of the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds comprises at

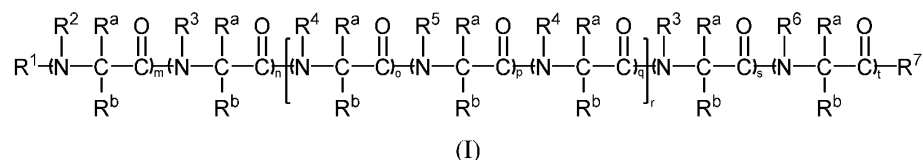
least one trimer subunit $-R^{\text{cation}}-R^{\text{neutral}}-R^{\text{neutral}}$, and wherein R^{cation} is an amino acid residue comprising a cationic moiety R^5 and each R^{neutral} is an amino acid residue comprising a neutral spacer moiety R^4 .

23. The composition of any one of claims 1 to 21, wherein at least one of the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds comprises at least one trimer subunit $-R^{\text{cation}}-R^{\text{neutral}}-R^{\text{lipid}}$, and wherein R^{cation} is an amino acid residue comprising a cationic moiety R^5 , each R^{neutral} is an amino acid residue comprising a neutral spacer moiety R^4 and each R^{lipid} is a lipid moiety R^4 .

24. The composition of any one of claims 1 to 23, wherein each cationic moiety R^5 is



25. The composition of any one of claims 1 to 24, wherein R^a and R^b are independently selected from the group consisting of $-\text{H}$ and $-\text{CH}_3$.
26. The composition of any one of claims 1 to 25, wherein R^a and R^b are $-\text{H}$.
27. The composition of any one of claims 1 to 26, wherein the one or more cationic peptide compounds and one or more PEG compounds are present at a mass ratio of peptide compound(s)-to-PEG compound(s) between 90:10 and 99:1.
28. The composition of any one of claims 1 to 27, wherein the one or more cationic peptide compounds and the one or more PEG compounds are present at a mass ratio of peptide compounds-to-PEG compound(s) between 95:5 and 98:2.
29. The composition of any one of claims 1 to 28, wherein the one or more PEG compounds comprises DMG-PEG2000.
30. The composition of any one of claims 1 to 29, wherein the one or more PEG compounds comprises one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I) or salts thereof:



wherein:

m is an integer from 0 to 15;

n is an integer from 0 to 5;

s is an integer from 0 to 5;

t is an integer from 0 to 15;

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, 2, 3 or 4;

each q is independently an integer 0, 1, 2, 3 or 4;

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

$-\text{CH}_2\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_u\text{CH}_3$, and wherein each u is independently an integer from 1 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

$-\text{CH}_2\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_v\text{CH}_3$, and wherein each v is independently an integer from 1 to 200;

R^7 is -H, alkyl, acyl, -OH, -OR^{7a}, -NH₂, -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, C₁-C₄-alkyl, or a side chain moiety found on a naturally- or non-naturally-occurring amino acid.

31. The composition of claim 30, wherein

when m is an integer from 0 to 3, each u is independently an integer from 30 to 50; and

when m is an integer from 4 to 15, each u is independently an integer from 1 to 10.

32. The composition of claim 30 or claim 31, wherein

when t is an integer from 0 to 3, each v is independently an integer from 30 to 50;

when t is an integer from 4 to 15, each v is independently an integer from 1 to 10.

33. The composition of any one of claims 30 to 32, wherein
m is 1, and u is an integer from 40 to 45; or
t is 1, and v is an integer from 40 to 45.
34. The composition of any one of claims 1 to 33, wherein the one or more polyanionic compounds comprises a nucleic acid.
35. The composition of any one of claims 1 to 34, the one or more polyanionic compounds comprises a nucleic acid and wherein the mass ratio of the one or more cationic peptide compounds to the nucleic acid is between 0.5:1 and 20:1.
36. The composition of any one of claims 1 to 35, wherein the one or more polyanionic compounds comprises a nucleic acid and wherein the nucleic acid is an mRNA encoding a polypeptide.
37. The composition of any one of claims 1 to 36, wherein the one or more polyanionic compounds comprises a nucleic acid and wherein the nucleic acid is an mRNA encoding a protein.
38. The composition of any one of claims 1 to 37, wherein the complexes further comprise one or more second agents.
39. The composition of any one of claims 1 to 38, wherein the one or more second agents are selected from the group consisting of polyethylene glycol, a targeting element, and a combination thereof.
40. The composition of any one of claims 1 to 39, wherein the complexes further comprise one or more small molecule active agents or drug substances.
41. A method of delivering a polyanionic compound to a cell comprising contacting the cell with the composition of any one of claims 1 to 40.
42. The method of claim 41, wherein the contacting is by endocytosis.
43. The method of claim 41 or claim 42, wherein the cell is contacted *in vivo* or *in vitro*.
44. The method of any one of claims 41 to 43, wherein the polyanionic compound comprises the nucleic acid which is the mRNA encoding a polypeptide and the cell expresses the polypeptide after being contacted with the composition.
45. The method of any one of claims 41 to 44, wherein the polyanionic compound comprises the nucleic acid which is the mRNA encoding a protein and the cell expresses the protein after being contacted with the composition.

46. A method of preparing a composition of any one of claims 1 to 40, comprising contacting the one or more cationic peptide compounds with the one or more PEG compounds and the one or more polyanionic compounds.
47. The method of claim 46, comprising contacting a solution comprising the one or more cationic peptide compounds and one or more PEG compounds with a solution comprising the one or more polyanionic compounds.
48. A method of delivering a polyanionic compound to lungs of a subject comprising administering to the subject the composition of claim 1, wherein the one or more cationic compounds are one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I), wherein the mass ratio of the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I) to the polyanionic compound is between 1:1 and 10:1.
49. The method of claim 48, wherein the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I) comprise compound 8, compound 24, compound 28, compound 73, compound 79, compound 93, compound 98, or compound 112, or any combinations thereof.
50. The method of claim 48 or 49, wherein the one or more cationic peptide compounds and one or more PEG compounds are present at a mass ratio of peptide compound(s)-to-PEG compound(s) between 90:10 and 99:1.
51. The method of any one of claims 48 to 50, wherein the administration is intravenous (IV) (e.g. bolus injection or intravenous infusion), subcutaneous (SC), intramuscular (IM), intrathecal, or intratumoral injection.
52. The method of any one of claims 48 to 51, wherein the polyanionic compound comprises the nucleic acid which is the mRNA encoding a polypeptide and the cell expresses the polypeptide after being contacted with the composition.
53. The method of any one of claims 48 to 52, wherein the polyanionic compound comprises the nucleic acid which is the mRNA encoding a protein and the cell expresses the protein after being contacted with the composition.

54. A method of delivering a polyanionic compound to lungs and/or spleen of a subject comprising administering to the subject the composition of claim 1, wherein the one or more cationic compounds are one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I), wherein the mass ratio of the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I) to the polyanionic compound is between 1:1 and 10:1.
55. The method of claim 54, wherein the one or more tertiary amino lipidated and/or PEGylated cationic peptide compounds of formula (I) comprise compound 8, compound 19, compound 24, compound 28, compound 73, compound 79, compound 93, compound 98, or compound 112, or any combinations thereof.
56. The method of claim 54 or 55, wherein the one or more cationic peptide compounds and one or more PEG compounds are present at a mass ratio of peptide compound(s)-to-PEG compound(s) between 90:10 and 99:1
57. The method of any one of claims 54 to 56, wherein the administration is intravenous (IV) (e.g. bolus injection or intravenous infusion), subcutaneous (SC), intramuscular (IM), intrathecal, or intratumoral injection.
58. The method of any one of claims 54 to 57, wherein the polyanionic compound comprises the nucleic acid which is the mRNA encoding a polypeptide and the cell expresses the polypeptide after being contacted with the composition.
59. The method of any one of claims 54 to 58, wherein the polyanionic compound comprises the nucleic acid which is the mRNA encoding a protein and the cell expresses the protein after being contacted with the composition.