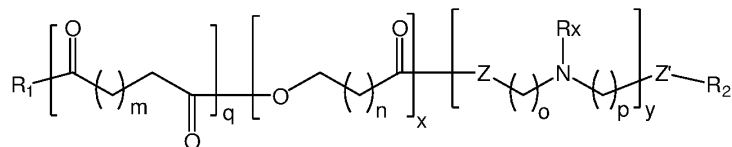


We claim:

1. A polymer of Formula I:

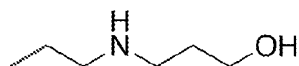


Formula I

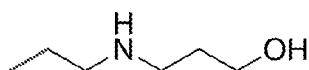
wherein n is an integer from 1-30, m, o, and p are independently integers from 1-20, x, y, and q are independently integers from 1-1000, R is hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted aryl, or substituted or unsubstituted alkoxy, Z and Z' are independently O or NR', wherein R' is hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted aryl,

wherein R₁ and R₂ are chemical entities containing a hydroxyl group, a primary amine group, a secondary amine group, a tertiary amine group, or combinations thereof.

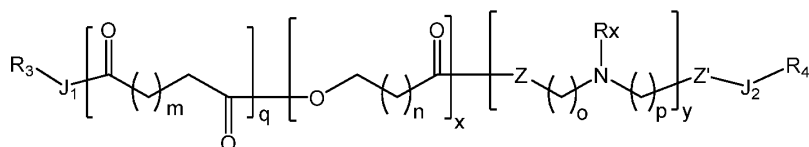
2. The polymer of claim 1, wherein R₁ and/or R₂ are not



3. The polymer of claim 1, wherein polyplexes or particles formed from the polymer show improved loading, improved cellular transfection, improved intracellular endosomal release, or a combination thereof of a mRNA, relative to corresponding polyplexes or particles wherein R₁ and/or R₂ consist of



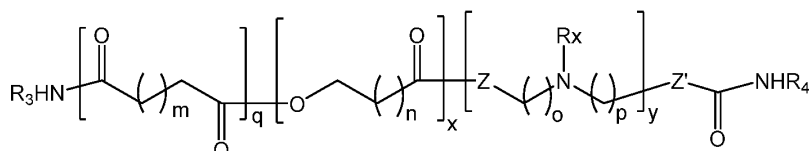
4. The polymer of claim 1, wherein the polymer has a structure of Formula II:



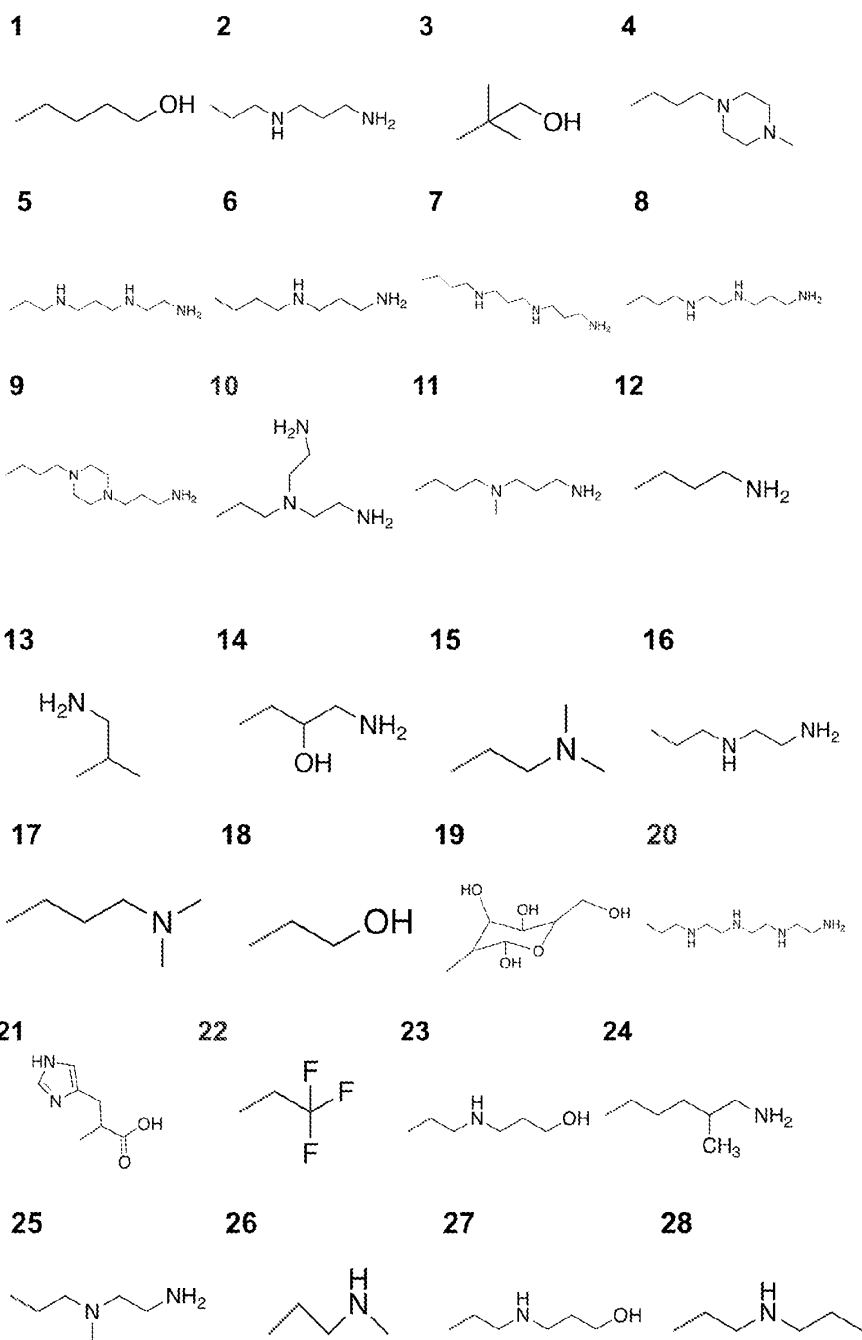
Formula II

- wherein J_1 and J_2 are independently linking moieties or absent,
 R_3 and R_4 are substituted alkyl containing a hydroxyl group, a primary amine group, a secondary amine group, a tertiary amine group, or combinations thereof.

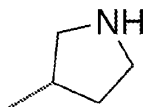
5. The polymer of claim 1, wherein the polymer has a structure of Formula III:



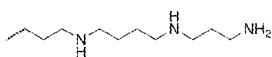
6. The polymer of claim 1, wherein Z is the same as Z' .
7. The polymer of claim 1, wherein n is 4, 10, 13, or 14.
8. The polymer of claim 1, wherein m is 5, 6, or 7.
9. The polymer of claim 1, wherein R_x is substituted or unsubstituted alkyl.
10. The polymer of claim 1, wherein the weight average molecular weight, as measured by gel permeation chromatography using narrow polydispersity polystyrene standards, is between about 2,000 Daltons and 20,000 Daltons, preferably between about 2,000 Daltons and about 10,000 Daltons, most preferably between about 2000 Daltons and about 7,000 Daltons.
11. The polymer of claim 4, wherein R_3 is the same as R_4 .
12. The polymer of claim 4, wherein R_3 and/or R_4 are independently selected from the group consisting of



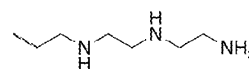
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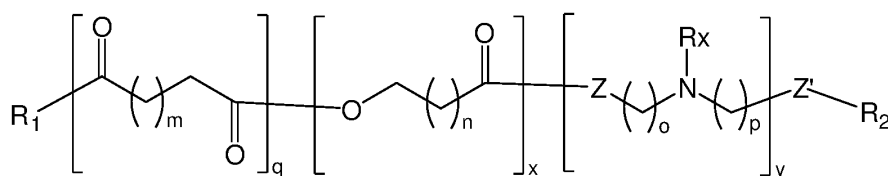
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13. The polymer of claim 4, wherein J1 is --O-- or --NH-- , J2 is --C(O)NH-- or --C(O)O-- or a combination thereof.
14. The polymer of claim 4, wherein R₃, R₄ or both contain a primary amine group, and optionally one or more secondary or tertiary amine groups.
15. The polymer of claim 4, wherein R₃, R₄ or both contain a hydroxyl group, and optionally one or more amine groups.
16. The polymer of claim 4, wherein R₃, R₄ or both contain a hydroxyl group and no amine group.
17. The polymer of claim 4, wherein at least one of R₃ and R₄ does not contain a hydroxyl group.
18. The polymer of claim 4, wherein R₃, R₄ or both are -unsubstituted C₁-C₁₀ alkylene-Aq-unsubstituted C₁-C₁₀ alkylene-Bq, -unsubstituted C₁-C₁₀ alkylene-Aq-substituted C₁-C₁₀ alkylene-Bq, -substituted C₁-C₁₀ alkylene-Aq-unsubstituted C₁-C₁₀ alkylene-Bq, or -substituted C₁-C₁₀ alkylene-Aq-substituted C₁-C₁₀ alkylene-Bq, wherein Aq is absent or $\text{--NR}_5\text{--}$, and Bq is hydroxyl, primary amine, secondary amine, or tertiary amine, wherein R₅ is hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted aryl.
19. The polymer of claim 1 wherein the poly(amine-co-ester)s or poly(amine-co-amide)s has the structure,



Formula I

wherein n is an integer from 1-30,

m, o, and p are independently integers from 1-20,

x, y, and q are independently integers from 1-1000,

R_x is hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted aryl, or substituted or unsubstituted alkoxy,

Z and Z' are independently O or NR', wherein R' is hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted aryl,

R₁ and R₂ are chemical entities containing a hydroxyl group, a primary amine group, a secondary amine group, a tertiary amine group, or combinations thereof.

20. The polymer of claim 19 wherein Z is the same as Z'.

21. The polymer of claim 20 wherein Z is O and Z' is O, Z is NR' and Z' is NR'.

22. The polymer of claim 19 wherein Z is O and Z' is NR' or Z is NR' and Z' is O.

23. The polymer of claim 19 wherein Z' is O and n is an integer from 1-24, such as 4, 10, 13, or 14, optionally wherein Z is also O.

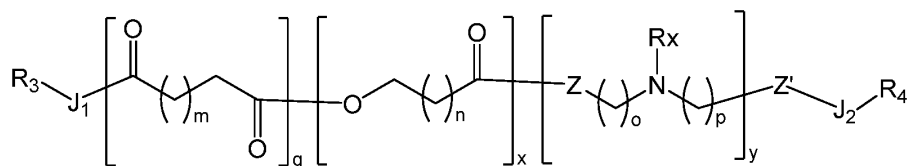
24. The polymer of claim 23 wherein m is an integer from 1-10, such as 4, 5, 6, 7, or 8, optionally wherein Z is also O.

25. The polymer of claim 19 wherein Z' is O, n is an integer from 1-24, such as 4, 10, 13, or 14, m is an integer from 1-10, such as 4, 5, 6, 7, or 8, and o and p are the same integer from 1-6, such 2, 3, or 4, optionally wherein Z is also O.

26. The polymer of claim 19 wherein Z' is O, n is an integer from 1-24, such as 4, 10, 13, or 14, m is an integer from 1-10, such as 4, 5, 6, 7, or 8, and R is alkyl, such a methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl, isobutyl, sec-butyl, cyclohexyl, (cyclohexyl)methyl, cyclopropylmethyl, or homologs and isomers of, for example, n-pentyl, n-hexyl, n-heptyl, and n-octyl, or aryl, such as phenyl, naphthalyl, anthracenyl, phenanthryl, chrysenyl, pyrenyl, tolyl, or xylyl, optionally wherein Z is also O.

27. The polymer of claim 19 wherein n is 14, optionally pentadecalactone (PDL), m is 7, optionally sebacic acid, and o and p are 2, optionally N-methyldiethanolamine (MDEA).

28. The polymer of claim 1 having a structure of Formula II:



Formula II

wherein Rx, Z, Z', m, n, o, p, q, x, and y are as described above for Formula I,

J₁ and J₂ are independently absent or linking moieties such as -C(O)-, -C(O)NH-, -C(O)O-, -O-, and -NH-,

R₃ and R₄ in Formula II are independently substituted alkyl containing a hydroxyl group, a primary amine group, a secondary amine group, a tertiary amine group, or combinations thereof.

29. The polymer of claim 28 wherein

J₁ is -O- or -NH- and

J₂ is -C(O)-, -C(O)NH-, or -C(O)O-.

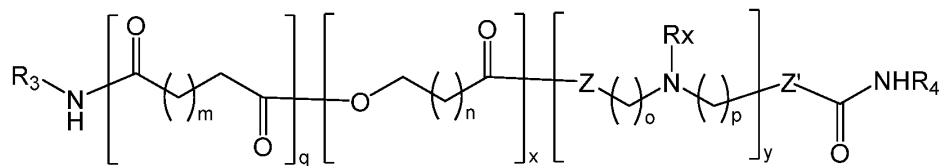
30. The polymer of claim 28 wherein R₃ is identical to R₄, optionally where R₃ and/or R₄ are linear.

31. The polymer of claim 30 wherein R₃, R₄, or both contain a hydroxyl group, and, optionally, R₃, R₄, or both contain a hydroxyl group and one or more amine groups, optionally secondary or tertiary amine groups.

32. The polymer of claim 28 wherein R₃, R₄, or both contain a hydroxyl group and no amine group.

33. The polymer of claim 28 wherein at least one of R₃ and R₄ does not contain a hydroxyl group.

34. The polymer of claim 1 having a structure of Formula III:



Formula III

wherein Rx, Z, Z', m, n, o, p, q, x, and y are as described above for Formula I,

J₁ and J₂ are independently absent or linking moieties such as -C(O)-, -C(O)NH-, -C(O)O-, -O-, and -NH-,

R₃ and R₄ in Formula II are independently substituted alkyl containing a hydroxyl group, a primary amine group, a secondary amine group, a tertiary amine group, or combinations thereof.

35. The polymer of claim 34 wherein

J₁ is -O- or -NH- and

J₂ is -C(O)-, -C(O)NH-, or -C(O)O-.

36. The polymer of claim 34 wherein R₃ is identical to R₄, optionally where R₃ and/or R₄ are linear.

37. The polymer of claim 34 wherein R₃, R₄, or both contain a hydroxyl group, and, optionally, R₃, R₄, or both contain a hydroxyl group and one or more amine groups, optionally secondary or tertiary amine groups.

38. The polymer of claim 34 wherein R₃, R₄, or both contain a hydroxyl group and no amine group.

39. The polymer of claim 34 wherein at least one of R₃ and R₄ does not contain a hydroxyl group.

40. The polymer of any of claims 19-39 wherein the weight average molecular weight of the polymer is greater than 20,000 Daltons, greater than 15,000 Daltons, greater than 10,000 Daltons, greater than 5,000 Daltons, or greater than 2,000 Daltons.

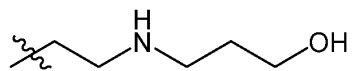
41. The polymer of claim 40 wherein the weight average molecular weight of the polymer is between about 2,000 Daltons and about 20,000 Daltons, more preferably between about 5,000 Daltons and about 10,000 Daltons.

42. The polymer of any of claims 19-41 prepared from one or more lactones, one or more amine-diols (Z and Z' = O) or triamines (Z and Z' = NR'), and one or more diacids or diesters, wherein when two or more different lactone, diacid or diester, and/or triamine or amine-diol monomers are used, the values of n, o, p, and/or m can be the same or different.

43. The polymer of any of claims 19-42 formed into polyplexes or particles thereof.

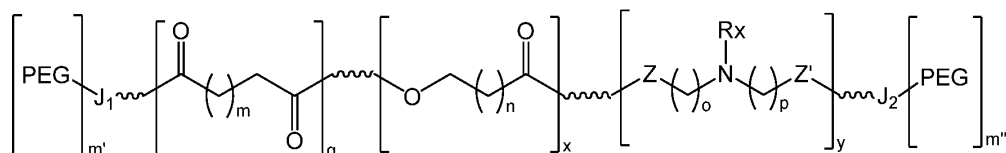
44. The polymer of claim 43 formed into polyplexes or particles thereof, having encapsulated therein one or more nucleic acids.

45. The polymer of claim 44 wherein the polyplexes or particles are formed from polymer wherein R₁ and/or R₂ do not consist of or include



46. The polymer of claim 44 formed into polyplexes or particles thereof, wherein the poly(amine-co-ester)s or poly(amine-co-amide)s are in a mixture containing the poly(amine-co-ester)s or poly(amine-co-amide)s conjugated to a polyethylene glycol (PEG), *i.e.*, PEG-conjugated poly(amine-co-ester)s or poly(amine-co-amide)s.

47. The polymer of claim 46 wherein the PEG-conjugated poly(amine-co-ester)s or poly(amine-co-amide)s contain a structure



Formula XI

wherein m' and m'' are independently 0 or 1, with the proviso that m' + m'' is 1 or 2,

J₁ and J₂ in Formulae XI are independently absent or linking moieties such as -C(O)-, -C(O)NH-, -C(O)O-, -O-, and -NH-.

In some forms of Formula XI, J₁ is -O- or -NH-. In some forms of Formula XI, J₂ is -C(O)-, -C(O)NH-, or -C(O)O-.

48. A method of administering one or more therapeutic, diagnostic, or prophylactic nucleic acid agents, or combinations thereof *in vivo*, comprising administering the polymer in the form of a polyplex or particles of any of claims 1-47 to cells or an individual in need thereof.

49. The method of claim 48 comprising transfecting cells by contacting cells with the particles or polyplex.

50. The method of claim 48 wherein the polyplex or particles are administered to the lung.