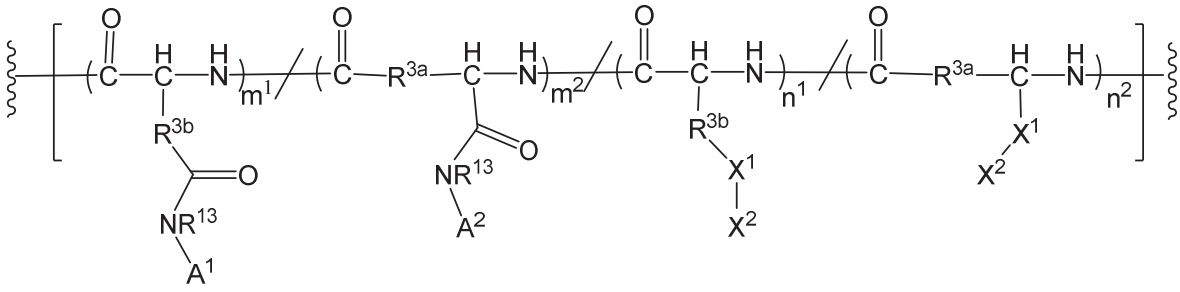
wherein p1 to p4, q1 to q6, r1 and r2, and s1 to s4 are each independently an integer of 1 to 5; each instance of R^2 is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group, or R^2 is combined with a second R^2 so as to form a heterocyclic group; each instance of R^4 is independently -C(O)O-, -C(O)NH-, -C-O-C(O)-O-C-, -O-, or -S(O)(O)-; and each instance of R^5 is independently an alkyl group, cycloalkyl group, alkenyl group, cycloalkenyl group, aryl group, heteroalkyl group, heterocyclic group, or combination thereof optionally comprising from 2 to 8 tertiary amines or a substituent comprising a tissue-specific or cell-specific targeting moiety.

[0005] The foregoing polymer of Formula 1 can further comprise an ionizable group. In some embodiments, the ionizable group is provided by R^5 of Formula 1. In other embodiments, the polymer further comprises a monomer with a side chain comprising an ionizable group.

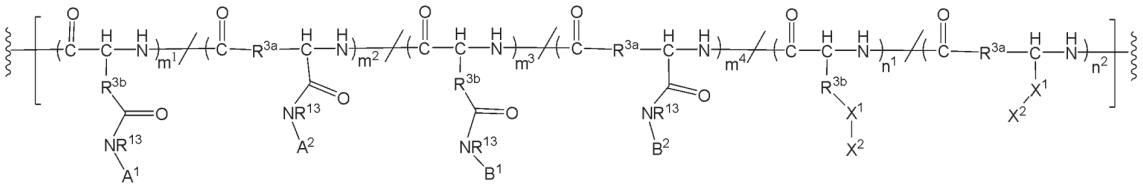
[0006] The disclosure also provides a composition comprising a polymer comprising the structure of Formula 1 and a nucleic acid and/or polypeptide. Further provided is a method of preparing a polymer comprising a structure of Formula 1, as well as methods of using the polymers and compositions comprising same, for example, to deliver a nucleic acid or protein to a cell.

[0006a] In one aspect, the present disclosure provides a method of preparing a polymer of Formula 1 as described herein, the method comprising (a) providing a polymer of Formula 4:



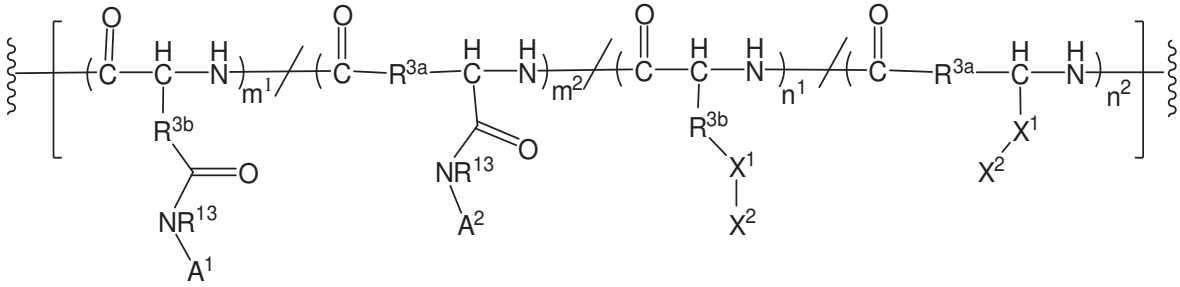
Formula 4

and (b) modifying a portion of groups A^1 and/or A^2 of the polymer of Formula 4 to provide the polymer of Formula 1



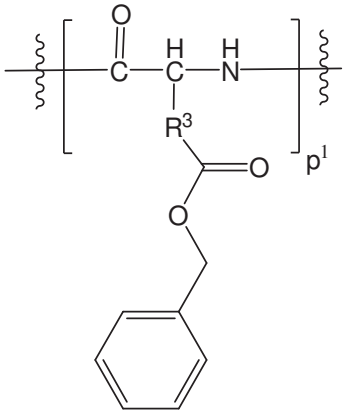
wherein m^1, m^2, m^3, m^4, n^1, n^2 R^{3a}, R^{3b}, R^{13}, X^1, X^2, A^1, A^2, B^1, and B^2 of Formulas 1 and 4 are as described herein.

[0006b] In another aspect, there is provided a method of preparing a polymer of Formula 4 as described herein:



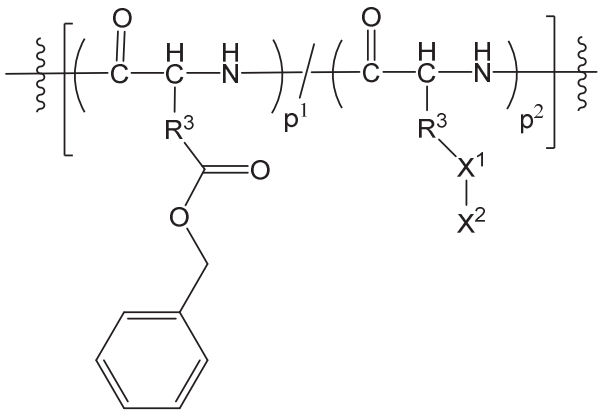
Formula 4

the method comprising (I) reacting a polymer of Formula 2:



Formula 2

with (a) a compound of the formula $HNR^{13}A^1$ and/or $HNR^{13}A^2$; and (b) a compound of formula H_2NX^2 or HOX^2, simultaneously or in any sequential order; or (II) reacting a polymer of Formula 3



Formula 3

with a compound of the formula $HNR^{13}A^1$ and/or $HNR^{13}A^2$; wherein, p^1 is an integer from 1 to 2000; p^2 is an integer from 1 to 2000; each R^3 is independently a methylene or ethylene group; and m^1, m^2, n^1, n^2, R^{3a} , R^{3b} , R^{13}, X^1 , X^2, A^1, and A^2 are as described herein.

[0006c] In yet another aspect, there is provided a method of delivering a nucleic acid and/or polypeptide to a cell, the method comprising administering the composition as described herein to the cell.

BRIEF DESCRIPTION OF THE DRAWINGS

[0007] FIG. 1 provides the amino acid sequence of Cas9 from *Streptococcus pyogene* (SEQ ID NO:1).

[0008] FIG. 2 provides the amino acid sequence of Cpf1 from *Francisella tularensis* subsp. Novicida U112 (SEQ ID NO:2).

[0009] FIG. 3 is a graph of the degree of substitution of the hydrophobic moiety of Polymer A as a result of the number of equivalents of hydrophobic moiety added in the reaction mixture.

[0010] FIG. 4 is a graph of the degree of substitution of the hydrophobic moiety of Polymer B as a result of the number of equivalents of hydrophobic moiety added in the reaction mixture.

[0011] FIG. 5 is a graph illustrating transfection efficiency of Polymer A nanoparticles in HEK293T cells as a function of RFP fluorescence, as described in Example 3.

[0012] FIG. 6 is a graph illustrating transfection efficiency of Polymer A nanoparticles in HEK293T cells as a function of RFP fluorescence, as described in Example 4.