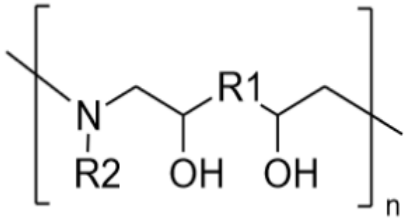
Claims

1. An ionizable polymer comprising a constitutional unit according to formula (I):



(I)

wherein

R1 represents a covalent bond or a linking moiety derived from a polyalkylene glycol; and

R2 represents a linear or branched aliphatic hydrocarbyl or a linear or branched fluorinated aliphatic hydrocarbyl group.

2. The ionizable polymer of claim 1, wherein the polyalkylene glycol is a polyethylene glycol.

3. The ionizable polymer of claim 1 or 2, wherein the polyalkylene glycol has a molecular weight of from about 200 to about 1000, optionally from about 300 to about 800, such as about 400 to about 600, e.g. about 500.

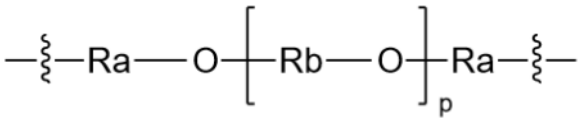
4. The ionizable polymer of any one of the preceding claims, wherein R2 is a linear or branched alkyl or fluorinated alkyl group, optionally wherein R2 has from 1 to 25 carbon atoms.

5. The ionizable polymer of any one of the preceding claims, wherein R2 is selected from the group consisting of butyl, hexyl, octyl, decyl, dodecyl, tetradecyl, hexadecyl and octadecyl.

6. The ionizable polymer of any one of claims 1 to 4, wherein R2 is selected from the group consisting of difluoroethyl, pentafluoropropyl, heptafluorobutyl, nonafluoropentyl, and pentadecafluorooctyl.

7. The ionizable polymer of any one of the preceding claims, wherein n is an integer from 1 to 10000.

8. The ionizable polymer of any one of the preceding claims, wherein R1 is according to formula (II)



(II)

wherein,

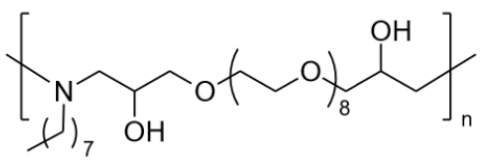
each Ra is independently a covalent bond or a linear -$C_{1\text{-}6}$alkylene-;

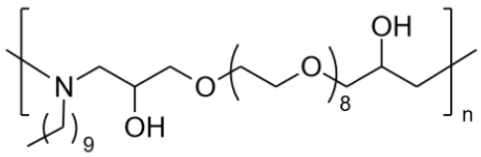
Rb is -$C_{1\text{-}6}$alkylene-, said alkylene being a linear alkylene and optionally substituted by one or more groups selected from OH, NH_2, $C_{1\text{-}4}$alkyl, and halogen;

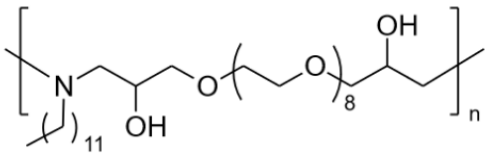
p is an integer from 1 to 10.

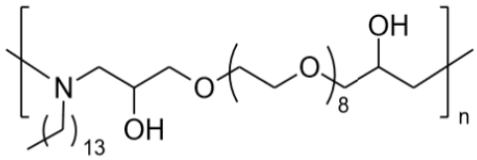
9. The ionizable polymer of any one of the preceding claims wherein each Ra is -C_1alkylene-, and Rb is a linear and unsubstituted -C_2alkylene-.

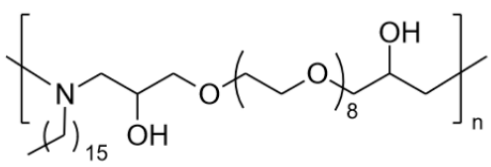
10. The ionizable polymer of claim 1, wherein the ionizable polymer comprises a constitutional unit selected from the group consisting of:

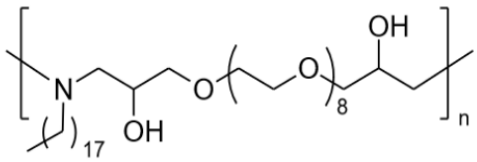
i) 

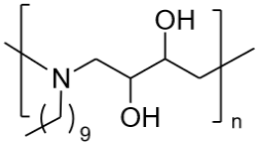
ii) 

iii) 

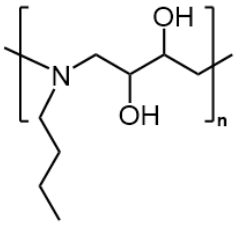
iv) 

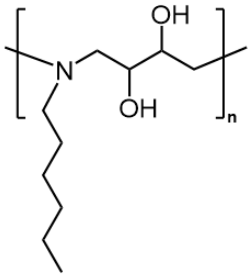
v) 

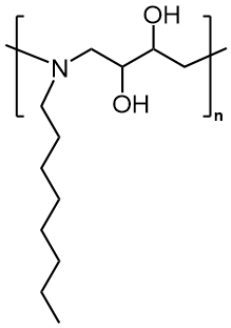
vi)  ; and

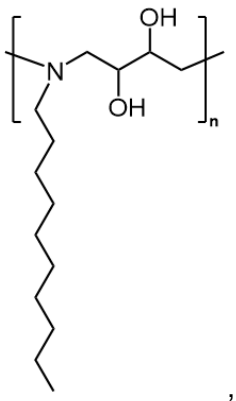
vii) .

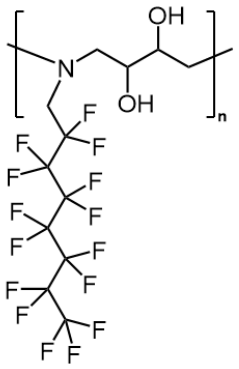
11. The ionizable polymer of claim 1, wherein the ionizable polymer comprises a constitutional unit selected from the group consisting of:

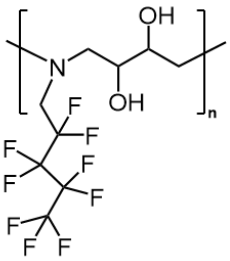
viii) ,

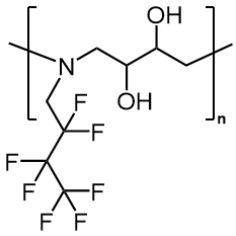
ix) ,

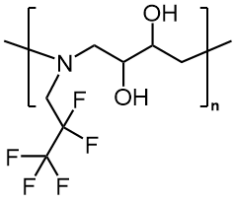
x) ,

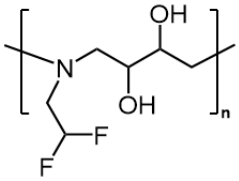
xi) ,

xii) ,

xiii) ,

xiv) ,

xv) , and

xvi) .

12. A composition comprising the ionizable polymer of any one of claims 1 to 11, and a polynucleotide, wherein the polynucleotide is complexed with polymeric nanoparticles (PNP) formed from said ionizable polymer.

13. The composition of claim 12, wherein the polynucleotide is selected from the group comprising RNA and DNA, optionally wherein the polynucleotide is mRNA or siRNA, optionally wherein:

a) R1 is derived from a polyalkylene glycol and the polynucleotide-PNP complexes are formed by mixing polynucleotide, cholesterol and ionizable polymer, optionally wherein the polyalkylene glycol is polyethylene glycol; or
b) R1 is a covalent bond and the polynucleotide-PNP complexes are formed by mixing polynucleotide and ionizable polymer.

14. The composition of any one of claims 12 or 13, wherein one or both of the following apply:

(a) the polynucleotide-PNP complex is capable of delivering said polynucleotide into a human or non-human animal cell, optionally wherein the polynucleotide is mRNA and/or wherein the human cell is a cancer cell; and

(b) wherein the polynucleotide is mRNA or DNA, and where the mRNA or DNA encodes a cancer-specific antigen, an infectious disease-specific antigen, or a therapeutic protein.

15. A pharmaceutical composition comprising the composition of any one of claims 12 to 14.

16. The pharmaceutical composition of claim 15, comprising polymeric nanoparticles (PNP) formed from a polynucleotide and an ionizable polymer, wherein:

a) R1 is a linking moiety derived from a polyethylene glycol and R2 is octadecyl, or

b) R1 is a covalent bond and R2 is decyl.

17. The pharmaceutical composition of claim 15 or 16, wherein one of the following applies:

(a) the pharmaceutical composition is for use in the treatment of a cancer, wherein the mRNA or DNA encodes a cancer-specific antigen;

(b) the pharmaceutical composition is for use in the prophylaxis or treatment of an infectious disease, wherein the mRNA or DNA encodes an infectious disease-specific antigen, optionally wherein the infectious disease is a virus-related disease, and the mRNA or DNA encodes a virus-specific antigen; or

(c) the pharmaceutical composition is for use in the treatment of a protein-deficiency disease, wherein the mRNA or DNA encodes a protein or peptide that is absent or non-functional in a subject to be treated.

18. Use of a composition of any one of claims 12-14, or a pharmaceutical composition of any one of claims 15-16 for the manufacture of a medicament for the prophylaxis or treatment of a disease selected from the group consisting of a cancer and a virus-related disease.

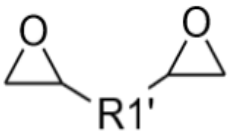
19. Use of a composition of any one of claims 12-14, or a pharmaceutical composition of any one of claims 15-16 for the manufacture of a medicament for the prophylaxis or treatment of a protein-deficiency disorder.

20. A method of producing a composition according to claim 12-14 in which the polynucleotide is mRNA or DNA, the method comprising the steps:

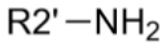
i) combining a monomer of formula (III) and a monomer of formula (IV) through amino-epoxy ring-opening polymerization to form an ionizable polymer comprising a constitutional unit according to formula (I); and

ii) mixing the ionizable polymer with an mRNA or DNA which encodes an antigenic polypeptide or a therapeutic protein,

wherein,



(III)



(IV)

wherein,

R1’ represents a covalent bond or a polyalkylene glycol moiety; and

R2’ represents a linear or branched aliphatic hydrocarbyl or a linear or branched fluorinated aliphatic hydrocarbyl group.