What is claimed is:

1. A method of preparing a polynucleotide, the method comprising:

a) contacting a first polynucleotide composition ~~comprising:~~ with a multivalent cation salt to precipitate a first polynucleotide salt;

~~a polynucleotide having a sequence of 7 or more nucleoside subunits and at least two of the nucleoside subunits are joined by a N3′→P5′ thiophosphoramidate inter-subunit linkage; and~~

~~non-target synthetic products and reagents;~~

~~with a multivalent cation salt to precipitate a first polynucleotide salt comprising at least one multivalent cation counterion; and~~

b) separating the first polynucleotide salt from the contacted first polynucleotide composition to produce a second polynucleotide composition comprising the first polynucleotide salt~~.~~;

wherein the first polynucleotide composition comprises:

(i) a polynucleotide having a sequence of 7 or more nucleoside subunits and at least two of the nucleoside subunits are joined by a N3′→P5′ thiophosphoramidate inter-subunit linkage; and

(ii) soluble non-target synthetic products and reagents

c) contacting the second polynucleotide composition from step (b) with a reverse phase chromatography support; and

d) eluting from the reverse phase chromatography support a third polynucleotide composition comprising a second soluble polynucleotide salt.

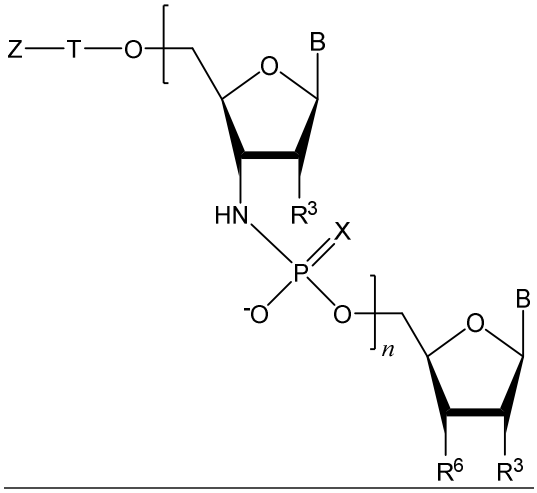
~~2. The method of claim 1, further comprising:~~

~~contacting the first polynucleotide salt with a reverse phase chromatography support; and~~

~~eluting from the chromatography support a third polynucleotide composition comprising a second polynucleotide salt.~~

2. The method of claim 1, wherein the nucleoside subunits are all joined by inter-subunit linkages each independently selected from N3′→P5′ thiophosphoramidate inter-subunit linkage and N3′→P5′ phosphoramidate inter-subunit linkage.

3. The method of claim 1 or 2, wherein the polynucleotide is described by Formula (I):



(I)

wherein:

each B is independently a purine, a protected purine, a pyrimidine or a protected pyrimidine, or an analog thereof;

each X is independently oxygen or sulfur;

each R^3 is independently hydrogen, fluoro, hydroxyl, an alkoxy, a substituted alkoxy or a protected hydroxyl;

R^6 is amino, hydroxyl, a protected amino, a protected hydroxy, -O-T-Z or –NH-T-Z;

each T is independently an optional linker;

each Z is independently H, a lipid, a carrier, an oligonucleotide, a polymer, a polypeptide, a detectable label, or a tag; and

n is an integer of 7 to 100.

~~3~~4. The method of any one of claims 1-~~2~~3, wherein:

the polynucleotide comprises a sequence comprising 13 or more nucleoside subunits complementary to the RNA component of human telomerase, or

the polynucleotide comprises between 10 and 50 contiguous nucleoside subunits complementary to the RNA component of human telomerase.

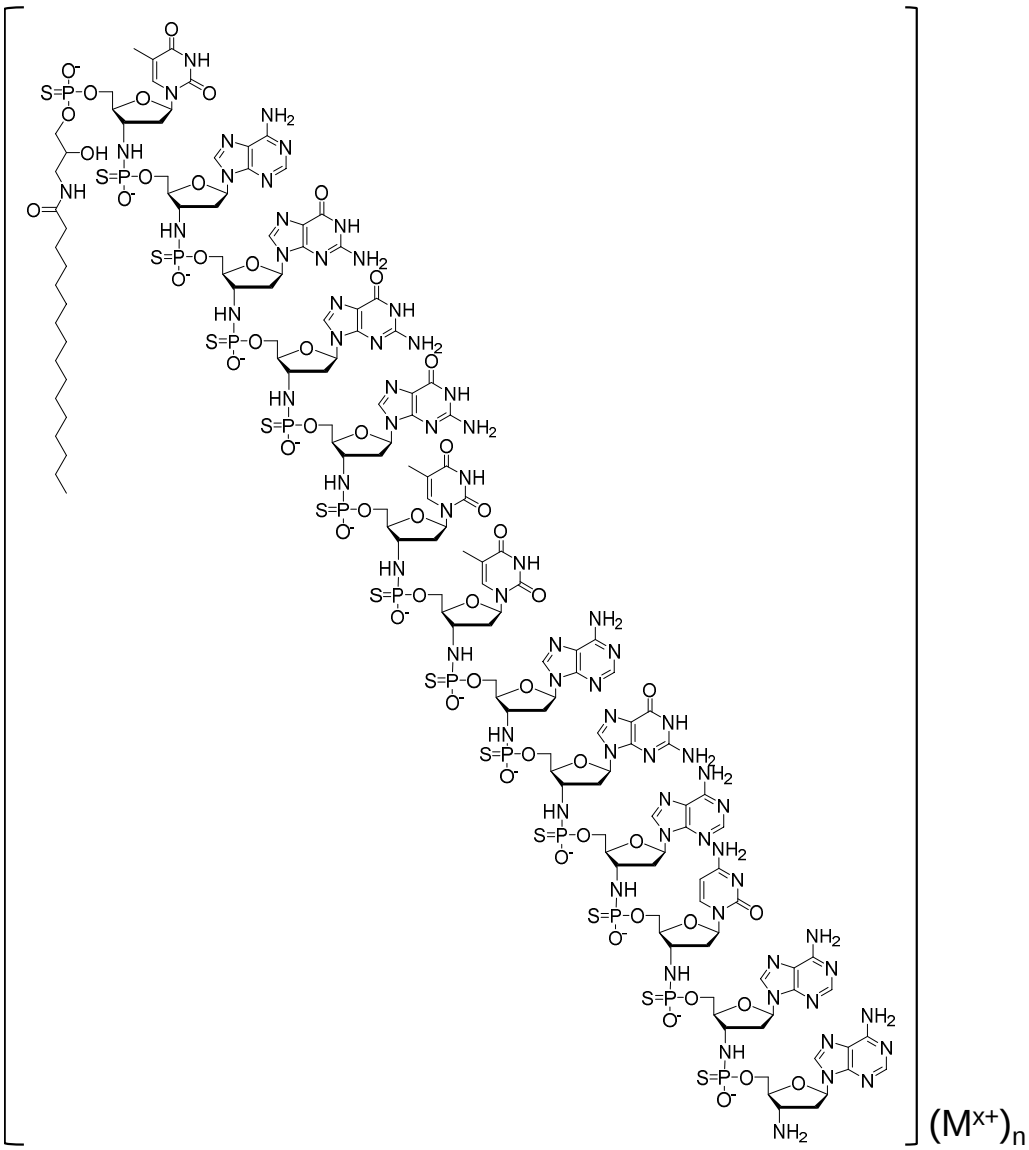
~~4. The method of any one of claims 1-3, wherein the polynucleotide comprises between 10 and 50 contiguous nucleoside subunits complementary to the RNA component of human telomerase.~~

5. The method of any one of claims ~~3~~1-4, wherein the nucleoside subunits ~~complementary to the RNA component of human telomerase~~ are all joined by N3′→P5′ thiophosphoramidate inter-subunit linkages.

6. The method of any one of claims 1-5 wherein the polynucleotide comprises a sequence selected from the group consisting of: GTTAGGGTTAG (SEQ ID NO:4), TAGGGTTAGACAA (SEQ ID NO:3) and CAGTTAGGGTTAG (SEQ ID NO:5).

7. The method of any one of claims 1-6, wherein the polynucleotide is conjugated to a lipid moiety via an optional linker.

8. The method of any one of claims ~~2~~1-7, wherein the second polynucleotide salt has the structure:



wherein each M^{x+} is independently hydrogen or a cationic counterion, each x is independently 1, 2 or 3 and n is an integer from 5 to 13.

9. The method of any one of claims ~~2~~1-8, wherein after the eluting step d) the second polynucleotide salt is a pharmaceutically acceptable salt of the polynucleotide.

10. The method of any one of claims ~~2~~1-9, wherein after the eluting step d) the second polynucleotide salt is a monovalent cation salt of the polynucleotide, preferably a sodium salt of the polynucleotide.

~~11. The method of any one of claims 2-10, wherein the second polynucleotide salt is a sodium salt of the polynucleotide.~~

~~12~~11. The method of any one of claims 1-~~5~~10, further comprising, prior to the contacting step a), cleaving the polynucleotide from a solid phase synthesis support to produce the first polynucleotide composition as a crude synthetic preparation of the polynucleotide.

~~13~~12. The method of any one of claims 1-~~12~~11, wherein prior to the contacting step a) the first polynucleotide composition comprises a monovalent cation salt of the polynucleotide.

~~14~~13. The method of any one of claims 1-~~13~~12, wherein the contacting step a) comprises loading and eluting the first polynucleotide composition from a cation exchange support.

~~15~~14. The method of any one of claims 1-~~14~~13, wherein the separating step b) comprises centrifuging the contacted first polynucleotide composition to spin down the first polynucleotide salt precipitate, or filtering the first polynucleotide salt from the contacted first polynucleotide composition.

~~16. The method of any one of claims 1-15, wherein the separating step comprises filtering the polynucleotide salt from the contacted first polynucleotide.~~

~~17~~15. The method of any one of claims 1-13 ~~claim 2~~, wherein the second polynucleotide composition of step b) is loaded directly onto the reverse phase chromatography support.

~~18~~16. The method of any one of claims 1-~~17~~15, further comprising, prior to the contacting step c), dissolving the second polynucleotide composition in a solvent.

~~19~~17. The method of any one of claims 1-~~18~~16, wherein:

the at least one multivalent cation counterion is divalent, preferably selected from the group consisting of magnesium, zinc and calcium; or

the at least one multivalent cation counterion is trivalent, preferably aluminium.

~~20. The method of claim 19, wherein the at least one multivalent cation counterion is selected from the group consisting of magnesium, zinc and calcium.~~

~~21. The method of any one of claims 1-18, wherein the at least one multivalent cation counterion is trivalent.~~

~~22. The method of claim 21, wherein the at least one multivalent cation counterion is aluminium.~~

~~23~~18. The method of any one of claims 1-~~22~~17, wherein the first polynucleotide salt further comprises a monovalent cation counterion.

~~24~~19. A composition comprising:

a salt precipitate of a polynucleotide comprising at least one multivalent cation counterion;

wherein the polynucleotide has a sequence of 7 or more nucleoside subunits complementary to the RNA component of human telomerase and at least two of the nucleoside subunits are joined by a N3′→P5′ thiophosphoramidate inter-subunit linkage.

~~25~~20. The composition of claim ~~24~~19, wherein:

the at least one multivalent cation counterion is divalent, preferably selected from the group consisting of magnesium, zinc and calcium, more preferably magnesium; or

the at least one multivalent cation counterion is trivalent, preferably aluminium.

~~26. The composition of claim 25, wherein the at least one multivalent cation counterion is selected from the group consisting of magnesium, zinc and calcium.~~

~~27. The composition of any one of claims 24-26, wherein the at least one multivalent cation counterion is magnesium.~~

~~28. The composition of claim 24, wherein the at least one multivalent cation counterion is trivalent.~~

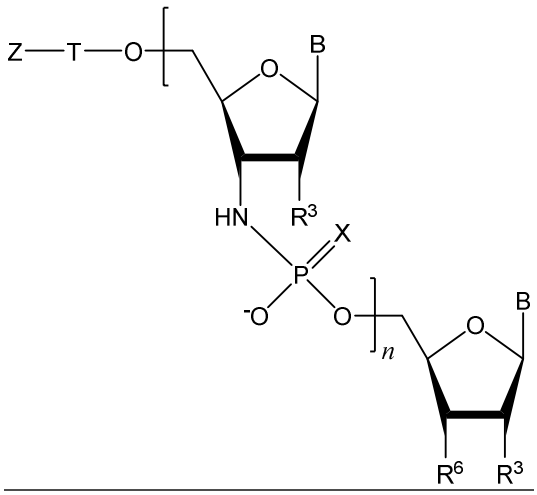
~~29. The composition of claim 28, wherein the at least one multivalent cation counterion is aluminium.~~

~~30~~21. The composition of any one of claims ~~24-29~~19-20, wherein the polynucleotide salt comprises 3 mol % or more of the multivalent cation counterion or comprises 1.0 % by weight of the multivalent cation counterion ~~relative to a polyanionic backbone of the polynucleotide~~.

~~31. The composition of any one of claims 24-29, wherein the polynucleotide comprises 1.0 % by weight or more of the multivalent cation counterion relative to the polynucleotide.~~

~~32~~22. The composition of any one of claims ~~24-31~~19-21, wherein the composition is a precipitate.

23. The composition of any one of claims 19-22, wherein the polynucleotide is described by Formula (I):



(I)

wherein:

each B is independently a purine, a protected purine, a pyrimidine or a protected pyrimidine, or an analog thereof;

each X is independently oxygen or sulfur;

each R^3 is independently hydrogen, fluoro, hydroxyl, an alkoxy, a substituted alkoxy or a protected hydroxyl;

R^6 is amino, hydroxyl, a protected amino, a protected hydroxy, -O-T-Z or –NH-T-Z;

each T is independently an optional linker;

each Z is independently H, a lipid, a carrier, an oligonucleotide, a polymer, a polypeptide, a detectable label, or a tag; and

n is an integer of 7 to 100.

~~33~~24. The composition of any one of claims ~~24-32~~19-23, wherein:

the polynucleotide comprises a sequence comprising 13 or more nucleoside subunits complementary to the RNA component of human telomerase; or

the polynucleotide comprises between 10 and 50 contiguous nucleoside subunits complementary to the RNA component of human telomerase.

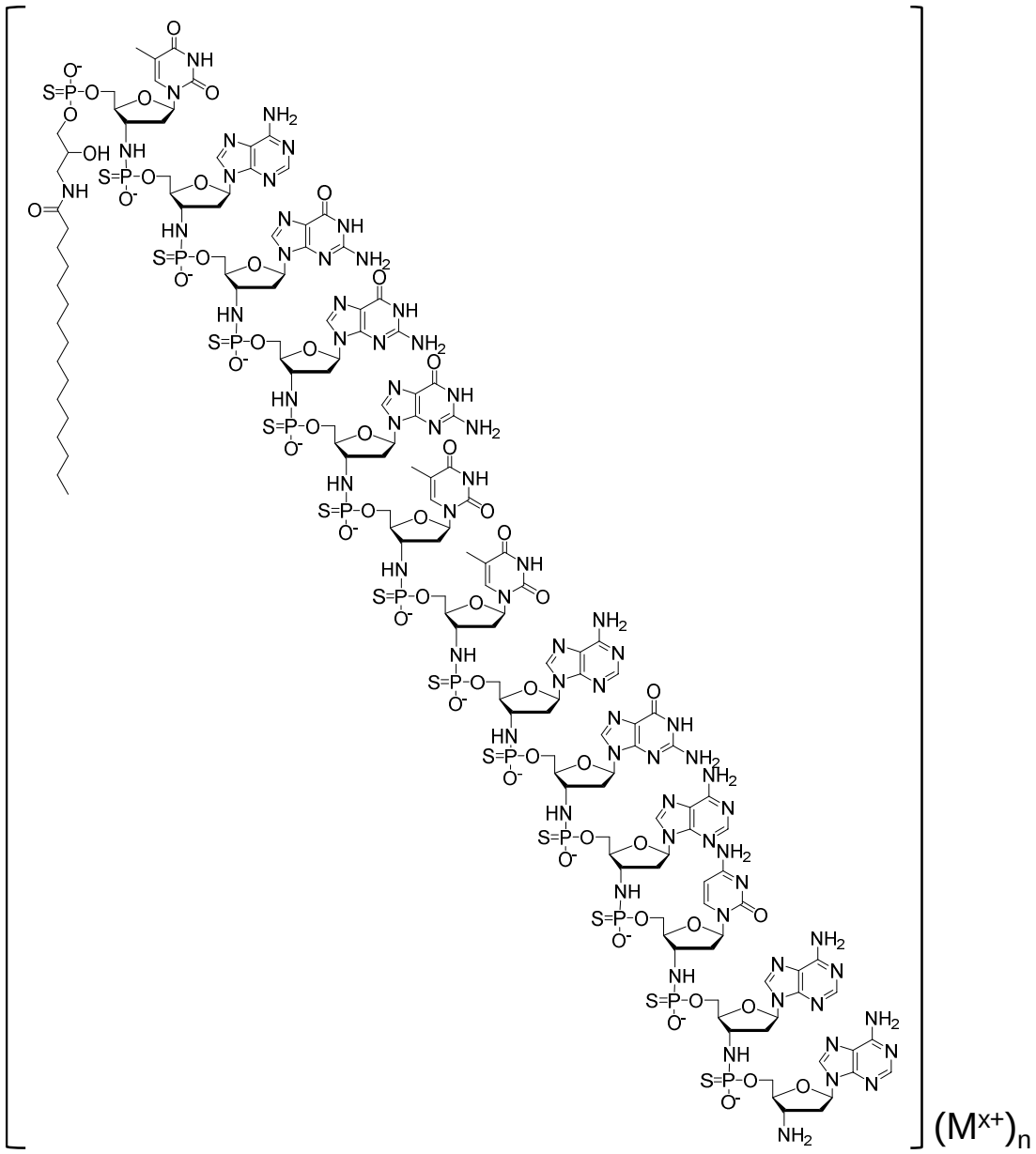
~~34. The composition of any one of claims 24-33, wherein the polynucleotide comprises between 10 and 50 contiguous nucleoside subunits complementary to the RNA component of human telomerase.~~

~~35~~25. The composition of any one of claims ~~24-34~~19-24, wherein the nucleoside subunits ~~complementary to the RNA component of human telomerase~~ are all joined by N3′→P5′ thiophosphoramidate inter-subunit linkages.

~~36~~26. The composition of any one of claims ~~24-35~~19-25, wherein the polynucleotide comprises a sequence selected from the group consisting of: GTTAGGGTTAG (SEQ ID NO:4), TAGGGTTAGACAA (SEQ ID NO:3) and CAGTTAGGGTTAG (SEQ ID NO:5).

~~37~~27. The composition of any one of claims ~~24-36~~19-26, wherein a 5’ or 3’ terminus of the polynucleotide is conjugated to a lipid moiety via an optional linker.

~~38~~28. The composition of any one of claims ~~24-37~~19-27, wherein the polynucleotide has the structure:



wherein each M^{x+} is independently a cationic counterion, each x is 1, 2 or 3 and n is 5 to 12.