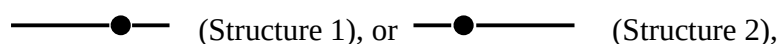


WHAT IS CLAIMED IS:

1. A multimeric oligonucleotide comprising subunits, wherein: each of the subunits independently comprises a single-stranded or double-stranded oligonucleotide; each of the subunits is joined to another subunit by a covalent linker; at least one subunit comprises at least one partial single-stranded oligonucleotide; wherein the multimeric oligonucleotide comprises:



wherein:

each — is a single-stranded oligonucleotide;

each — is a partial single-stranded oligonucleotide; and

each ● is a covalent linker.

~~2. The multimeric oligonucleotide of claim 1, wherein at least one subunit comprises two partial single-stranded oligonucleotides annealed to a complementary strand to form a double-stranded subunit.~~

~~3. The multimeric oligonucleotide of claim 1, wherein the covalent linker comprises an acid cleavable bond, a bio-cleavable bond, or an enzyme cleavable bond.~~

~~4. (Cancelled)~~

~~4.2. The~~A multimeric oligonucleotide of claim 1, further comprising Structure 3:

—●— (Structure 3), wherein:

each — is independently a partial single-stranded oligonucleotide; and

● is a covalent linker.

~~5. The multimeric oligonucleotide of claim 4, wherein Structure 3 is a homodimer.~~

~~6. The multimeric oligonucleotide of claim 4, wherein Structure 3 is a heterodimer.~~

~~7.3.~~ The multimeric oligonucleotide of claim 1, wherein at least one subunit comprises

Structure 4:

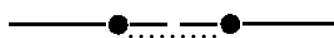
 (Structure 4), wherein:

each  is a partial single-stranded oligonucleotide;

 is a covalent linker joining the partial single-stranded oligonucleotide and an adjoining oligonucleotide subunit; and

 is a complementary strand.

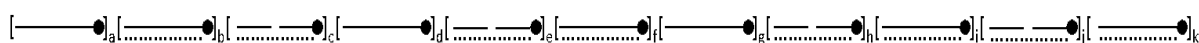
8.4. The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises Structure 5:

 (Structure 5), wherein:

each  is a covalent linker joining the single-stranded oligonucleotide to the partial single-stranded oligonucleotide; and

 is a complementary strand.

9.5. The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises Structure 6:



(Structure 6)

wherein:

each  is a covalent linker;

each  is a complementary strand; and

each of a, b, c, d, e, f, g, h, i, j and k is independently an integer greater than or equal to zero, with the proviso that at least one of c, e, h, and j is greater than or equal to 1.

~~10. The multimeric oligonucleotide of claim 9, wherein each of a, b, c, d, e, f, g, h, i, j and k is independently an integer in the range of 0 to 10, with the proviso that at least one of c, e, h and j is greater than or equal to 1.~~

11.6. The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises Structure 7:

$[\text{-----} \bullet]_m [\text{-----} \bullet]_n [\text{-----} \bullet]_o [\text{-----}]$ (Structure 7), wherein:

..... are each a complementary strand;

m and n are each independently an integer greater than or equal to 1; and

o is an integer greater than or equal to 0.

~~12. The multimeric oligonucleotide of claim 11, wherein m and n are each independently an integer in the range of 1 to 10; and o is an integer in the range of 0 to 10.~~

~~13.7.~~ The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises Structure 8

$[\text{-----} \bullet]_p [\text{-----} \bullet \text{-----}] [\bullet \text{-----}]_q$ (Structure 8),

wherein:

..... are each a complementary strand; and

p and q are each independently an integer greater than or equal to zero.

~~14. The multimeric oligonucleotide of claim 13, wherein p and q are each independently an integer in the range of 0 to 10; or wherein p and q are each independently an integer in the range of 0 to 3.~~

~~15.8.~~ The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises Structure 9:

$[\text{-----}] [\bullet \text{-----} \bullet \text{-----}]_r [\bullet \text{-----}]_s$ (Structure 9)

wherein:

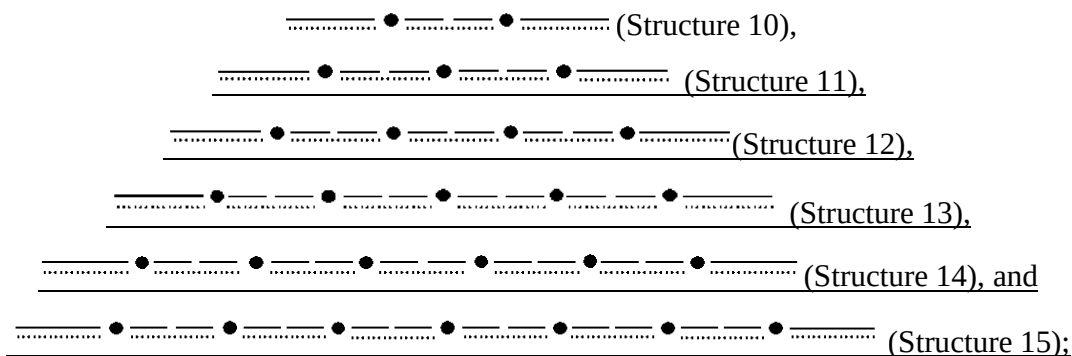
..... are each a complementary strand;

r is an integer greater than or equal to 1; and

s is an integer greater than or equal to 0.

16. ~~_____ The multimeric oligonucleotide of claim 15, wherein r is an integer in the range of 1 to 10 and s is an integer in the range of 0 to 10; or wherein r is an integer in the range of 1 to 3 and s is 0 or 1.~~

17.9 The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises one of the following structures~~Structure 10:~~



wherein each is a complementary strand.

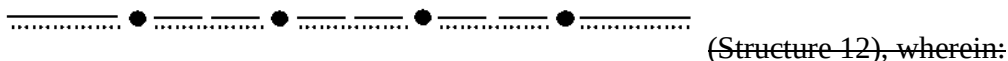
18. ~~_____ The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide~~

comprises Structure 11:  (Structure 11),

wherein:

each is a complementary strand.

19. ~~_____ The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises Structure 12:~~



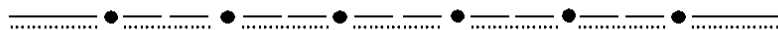
each is a complementary strand.

20. ~~_____ The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises Structure 13:~~



each is a complementary strand.

21. ~~The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises Structure 14:~~



(Structure 14),

wherein:

each is a complementary strand.

22. ~~The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises Structure 15:~~

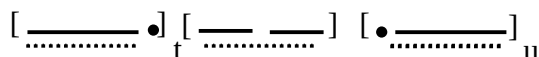


(Structure 15),

wherein:

each is a complementary strand.

23.10. The multimeric oligonucleotide of claim 1, wherein the multimeric oligonucleotide comprises Structure 16:



(Structure 16),

wherein each

each is a complementary strand; and

t and u are each independently an integer greater than or equal to 0 with the proviso that at least one of t and u are an integer greater than or equal to 1.

24. ~~The multimeric oligonucleotide of claim 23, wherein t and u are each independently an integer in the range of 0 to 10 with the proviso that at least one of t and u are an integer greater than or equal to 1; or wherein t and u are each independently an integer in the range of 0 to 3 with the proviso that at least one of t and u are an integer greater than or equal to 1.~~

25. The multimeric oligonucleotide of any of claims 1-24, wherein each partial single-

stranded oligonucleotide is 5-14 nucleotides in length.

26. ~~_____ The multimeric oligonucleotide of any of claims 1-25, wherein at least two subunits are active against different cellular targets.~~

27. ~~_____ The multimeric oligonucleotide of claim 26, wherein all of the subunits are active against different cellular targets.~~

28. ~~_____ The multimeric oligonucleotide of any of claims 1-25, wherein at least two subunits are active against the same cellular target.~~

29. ~~_____ The multimeric oligonucleotide of claim 28, wherein all of the subunits are active against different cellular targets.~~

30. ~~_____ The multimeric oligonucleotide of any of claims 1-29, wherein the multimeric oligonucleotide comprises four or more subunits.~~

31. ~~_____ The multimeric oligonucleotide of claim 30, wherein the multimeric oligonucleotide comprises four, five, six, seven, eight, nine, or ten subunits.~~

~~32-11.~~ The multimeric oligonucleotide of any of claims 1-~~34~~10, wherein each nucleic acid in the multimeric oligonucleotide is RNA, DNA, or an artificial or non-natural nucleic acid analog.

33. ~~_____ The multimeric oligonucleotide of any of claims 1-32, wherein at least one subunit is siRNA, saRNA, or miRNA.~~

34. ~~_____ The multimeric oligonucleotide of claim 33, wherein all of the subunits are siRNA.~~

35. ~~_____ The multimeric oligonucleotide of claim 33, wherein all of the subunits are saRNA.~~

36. ~~_____ The multimeric oligonucleotide of claim 33, wherein all of the subunits are miRNA.~~

~~37.12.~~ The multimeric oligonucleotide of any of claims 1-~~11~~~~32~~, wherein at least one subunit is a single-stranded subunit.

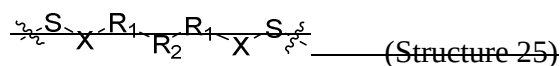
~~38.13.~~ The multimeric oligonucleotide of claim ~~37~~~~12~~, wherein the at least one single-stranded subunit is an antisense oligonucleotide.

~~39.14.~~ The multimeric oligonucleotide of any one of claims 1-~~38~~~~13~~, wherein at least one covalent linker • is a cleavable covalent linker.

~~40.15~~ The multimeric oligonucleotide of claim ~~39~~~~14~~, wherein the cleavable covalent linker comprises an acid cleavable bond, a reductant cleavable bond, a bio-cleavable bond, or an enzyme cleavable bond.

~~41.~~ ——— The multimeric oligonucleotide of claim 39 or 40, wherein the cleavable covalent linker is cleavable under intracellular conditions.

~~42.~~ ——— The multimeric oligonucleotide of any of claims 1-41, wherein each covalent linker is, independently, a disulfide bond or a compound of Structure 25:



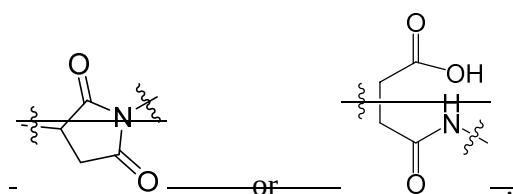
wherein:

S is attached by a covalent bond or by a linker to an oligonucleotide subunit;

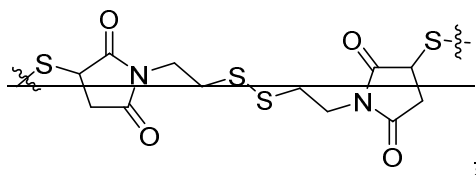
each R₁ is independently a C₂-C₁₀-alkyl, C₂-C₁₀-alkoxy, or C₁-C₁₀-aryl group;

R₂ is a thiopropionate or disulfide group; and

each X is independently selected from:

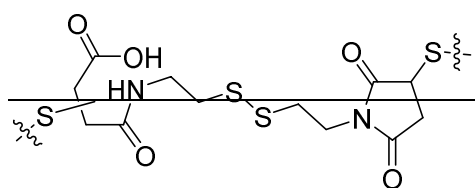


43. ~~The multimeric oligonucleotide of claim 42, wherein the compound of Structure 25 is~~



~~wherein each terminal S is attached by a covalent bond or by a linker to an oligonucleotide subunit.~~

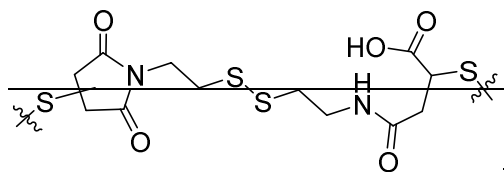
44. ~~The multimeric oligonucleotide of claim 42, wherein the compound of Structure 25 is a compound according to Structure 26:~~



(Structure 26);

~~wherein each terminal S is attached by a covalent bond or by a linker to an oligonucleotide subunit.~~

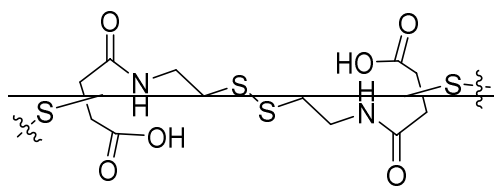
45. ~~The multimeric oligonucleotide of claim 42, wherein the compound of Structure 25 is a compound according to Structure 27:~~



(Structure 27);

~~wherein each terminal S is attached by a covalent bond or by a linker to an oligonucleotide subunit.~~

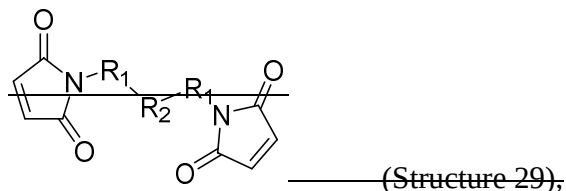
46. ~~The multimeric oligonucleotide of claim 42, wherein the compound of Structure 25 is a compound according to Structure 28:~~



(Structure 28);

wherein each terminal S is attached by a covalent bond or by a linker to an oligonucleotide subunit.

~~47. The multimeric oligonucleotide any of claims 42-46, wherein the covalent linker of Structure 25 is formed from a covalent linker precursor according to Structure 29:~~



~~wherein each R₁ is independently a C₂-C₁₀-alkyl, C₂-C₁₀-alkoxy, or C₁-C₁₀-aryl group; and R₂ is a thiopropionate or disulfide group.~~

~~48. The multimeric oligonucleotide of any of claims 1-47, wherein at least one covalent linker is attached to the 3' or 5' terminus of an oligonucleotide subunit.~~

~~49. The multimeric oligonucleotide of claim 48, wherein all covalent linkers are attached to the 3' or 5' terminus of an oligonucleotide subunit.~~

~~50. The multimeric oligonucleotide of any of claims 1-48, wherein at least one covalent linker is attached to an internal nucleotide of an oligonucleotide subunit.~~

~~51. The multimeric oligonucleotide of any of claims 1-50, wherein at least one covalent linker • comprises a nucleotide linker.~~

~~52. The multimeric oligonucleotide of claim 51, wherein the nucleotide linker is between 2-6 nucleotides in length.~~

~~53. The multimeric oligonucleotide of any of claims 1-52, wherein each covalent linker • is the same.~~

~~54. The multimeric oligonucleotide of any of claims 1-52, wherein at least one covalent linker • is different from the other covalent linkers.~~

55.16. The multimeric oligonucleotide of any of claims 1-1554, at least two subunits are joined by a covalent linker • between the 3' end of a first subunit and the 3' of a second subunit.

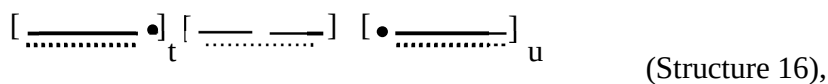
~~56. The multimeric oligonucleotide of any of claims 1-55, wherein at least two subunits are joined by a covalent linker • between the 5' end of a first subunit and the 3' of a second subunit.~~

57.17. The multimeric oligonucleotide as in any of any one of claims 1-5616, wherein at least two subunits are joined by a covalent linker • between the 5' end of a first subunit and the 5' of a second subunit.

~~58. The multimeric oligonucleotide of any of claims 1-57, further comprising a chemical or biological moiety that is not an oligonucleotide.~~

~~59. The multimeric oligonucleotide as in any of claims 1-58, wherein the multimeric oligonucleotide is at least 75, 80, 85, 90, 95, 96, 97, 98, 99, or 100% pure.~~

60.18. A method of synthesizing a multimeric oligonucleotide comprising Structure 16:



wherein each is an single-stranded oligonucleotide, each --- is a partial single-stranded oligonucleotide, each is a complementary strand; each • is a covalent linker joining adjacent oligonucleotides, and t and u are each independently an integer greater than or equal to 1; the method comprising annealing Structure 17

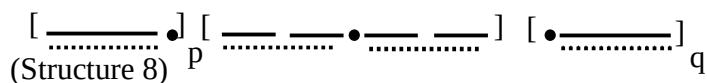


and Structure 18



with complementary strands, thereby forming Structure 16.

61.19. A method of synthesizing a multimeric oligonucleotide comprising Structure 8:



wherein each ———— is a single-stranded oligonucleotide, each — is a partial single-stranded oligonucleotide, each is a complementary strand; each $\bullet$ is a covalent linker joining adjacent oligonucleotides, and p and q are each independently an integer greater than or equal to 1;

the method comprising annealing Structure 19,



Structure 20,

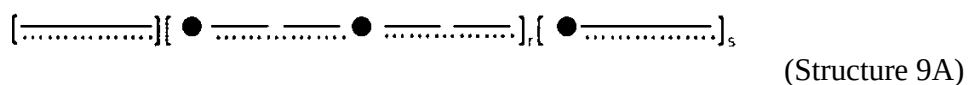


and one or more of Structure 21,



with complementary strands , thereby forming Structure 8.

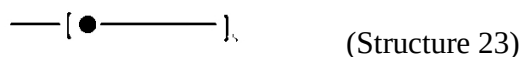
62:20. A method of synthesizing a multimeric oligonucleotide comprising Structure 9A:



wherein each ———— is a single-stranded oligonucleotide, each — is a partial single-stranded oligonucleotide, each is a complementary strand; each $\bullet$ is a covalent linker joining adjacent oligonucleotides; and r and s are each independently an integer greater than or equal to 1; the method comprising annealing Structure 22



and Structure 23

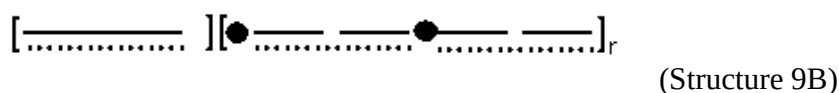


and one or more of Structure 24



with complementary strands , thereby forming Structure 9A.

63:21. A method of synthesizing a multimeric oligonucleotide comprising Structure 9B:



wherein each — is a single-stranded oligonucleotide; each — is a partial single-stranded oligonucleotide; each is a complementary strand; each • is a covalent linker joining adjacent oligonucleotides; and r is an integer greater than or equal to 1;
the method comprising annealing Structure 22,



and one or more of Structure 24



and a partial single-stranded oligonucleotide — with complementary strands ,
thereby forming Structure 9B.

~~64.22.~~ A composition comprising the multimeric oligonucleotide of any of claims 1-59~~17~~ and a pharmaceutically acceptable excipient.

~~65.23.~~ A Use of a composition comprising the multimeric oligonucleotide of any of claims 1-59~~22~~
for use in the manufacture of a medicament.

~~60.~~ A method for treating a subject comprising administering to the subject an effective amount of the multimeric oligonucleotide of any of claims 1-59.