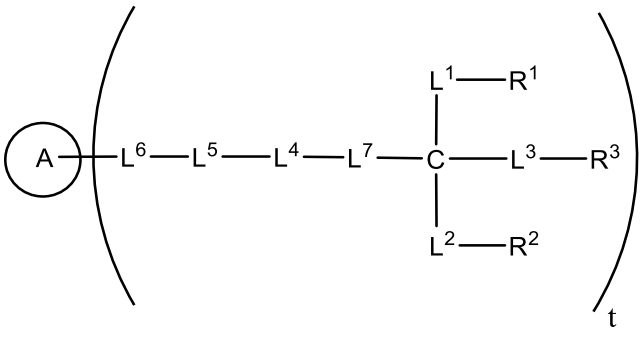
CLAIMS

1. A compound having the structure:



(I), or a pharmaceutically acceptable salt thereof,

wherein

A is nucleic acid;

L^4 and L^6 are independently a bond, -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, -OPO_2-O-, -OP(S)(O)-O-, -$OP(S)_2$-O-, -$S(O)_2$NH-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene;

L^5 is independently a bond, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene;

L^7 is independently a bond, substituted or unsubstituted alkylene or substituted or unsubstituted heteroalkylene;

L^1 is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or L^{1A}-L^{1B}-L^{1C}-L^{1D}-L^{1E};

L^2 is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or L^{2A}-L^{2B}-L^{2C}-L^{2D}-L^{2E};

L^3 is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or L^{3A}-L^{3B}-L^{3C}-L^{3D}-L^{3E};

L^{1A}, L^{1B}, L^{1C}, L^{1D}, L^{1E}, L^{2A}, L^{2B}, L^{2C}, L^{2D}, L^{2E}, L^{3A}, L^{3B}, L^{3C}, L^{3D} and L^{3E} are independently a bond, -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -$S(O)_2$C(O)-, -OPO_2-O-, -OP(S)(O)-O-, -$OP(S)_2$-O-, -S(O)NH-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_{25} alkylene, substituted or unsubstituted 2 to 25 membered heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted

heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene,

wherein L^{1A}-L^{1B}-L^{1C}-L^{1D}-L^{1E} is not a bond, substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom and at least one of L^{1A}, L^{1B}, L^{1C}, L^{1D} or L^{1E} is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene,

wherein L^{2A}-L^{2B}-L^{2C}-L^{2D}-L^{2E} is not a bond, substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom and at least one of L^{2A}, L^{2B}, L^{2C}, L^{2D} or L^{2E} is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene,

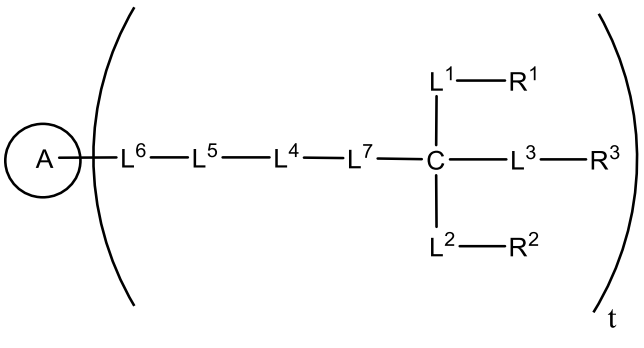
wherein L^{3A}-L^{3B}-L^{3C}-L^{3D}-L^{3E} is not a bond or substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom at least one of L^{3A}, L^{3B}, L^{3C}, L^{3D} or L^{3E} is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene;

R^1, R^2 and R^3 are independently unsubstituted C_1-C_{25} alkyl; and

t is an integer from 1 to 5.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1, R^2 and R^3 are independently unsubstituted C_7-C_{20} alkyl.

3. A compound having the structure:



(I), or a pharmaceutically acceptable salt thereof,

wherein

A is nucleic acid;

L^4 and L^6 are independently a bond, -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, -OPO_2-O-, -OP(S)(O)-O-, -$OP(S)_2$-O-, -$S(O)_2$NH-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene,

substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene;

L^5 is independently a bond, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene;

L^7 is independently a bond, substituted or unsubstituted alkylene or substituted or unsubstituted heteroalkylene;

L^1 is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or L^{1A}-L^{1B}-L^{1C}-L^{1D}-L^{1E};

L^2 is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or L^{2A}-L^{2B}-L^{2C}-L^{2D}-L^{2E};

L^3 is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or L^{3A}-L^{3B}-L^{3C}-L^{3D}-L^{3E};

L^{1A}, L^{1B}, L^{1C}, L^{1D}, L^{1E}, L^{2A}, L^{2B}, L^{2C}, L^{2D}, L^{2E}, L^{3A}, L^{3B}, L^{3C}, L^{3D} and L^{3E} are independently a bond, -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -$S(O)_2$C(O)-, -OPO_2-O-, -OP(S)(O)-O-, -$OP(S)_2$-O-, -S(O)NH-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_{25} alkylene, substituted or unsubstituted 2 to 25 membered heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene,

wherein L^{1A}-L^{1B}-L^{1C}-L^{1D}-L^{1E} is not a bond, substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom and at least one of L^{1A}, L^{1B}, L^{1C}, L^{1D} or L^{1E} is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene,

wherein L^{2A}-L^{2B}-L^{2C}-L^{2D}-L^{2E} is not a bond, substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom and at least one of L^{2A}, L^{2B}, L^{2C}, L^{2D} or L^{2E} is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene,

wherein L^{3A}-L^{3B}-L^{3C}-L^{3D}-L^{3E} is not a bond or substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom at least one of L^{3A}, L^{3B}, L^{3C}, L^{3D} or L^{3E} is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene;

R^1, R^2 and R^3 are independently unsubstituted C_8-C_{20} alkyl; and

t is an integer from 1 to 5.

4. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein L^1, L^2 and L^3 are independently subsituted or unsubstituted 2 to 50 membered heteroalkylene, optionally R^{10}-substituted or unsubstituted 2 to 50 membered heteroalkylene, wherein R^{10} is oxo, hydroxyl, or unsubstituted C_1-C_4 alkyl.

5. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein t is 1, 2, or 3.

6. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein A is a double-stranded nucleic acid, or a single-stranded nucleic acid.

7. The compound of claim 6, wherein the double-stranded nucleic acid is a small interfering RNA, a short hairpin RNA or a microRNA mimic.

8. The compound of claim 6, wherein the single-stranded nucleic acid is a single-strand small interfering RNA, an RNaseH oligonucleotide, an anti-microRNA oligonucleotide, a steric blocking oligonucleotide, exon-skipping oligonucleotide, a CRISPR guide RNA, or an aptamer.

9. The compound of claim 3, wherein the nucleic acid of A is comprises one or more modified nucleotides, optionally wherein the nucleic acid comprises one or more modified sugar moieties.

10. The compound of claim 9, wherein the nucleic acid comprises one or more modified sugar moieties, wherein the modified sugar moiety comprises a 2’ modification or an unlocked sugar modification, optionally wherein the 2’-modification is selected from 2’-fluoro modification, 2’-O-methyl modification, a 2’-O-methoxyethyl, and a bicyclic sugar modification.

11. The compound of claim 10, wherein the 2’-modification is a bicyclic sugar modification, wherein the bicyclic sugar modification is selected from a 4’-$CH(CH_3)$-O-2’

linkage, a 4'-$(CH_2)_2$-O-2' linkage, a 4'-$CH(CH_2$-OMe)-O-2' linkage, 4'-CH_2-$N(CH_3)$-O-2' linkage, and 4'-CH_2-N(H)-O-2' linkage.

5. The compound of claim 3, wherein the nucleic acid comprises one or more modified sugar moieties, wherein the modified sugar moiety is a morpholino moiety.

6. The compound of claim 3, wherein the nucleic acid comprises one or more modified internucleotide linkages, optionally wherein the modified internucleotide linkage selected from a phosphorothioate linkage and a phosphorodiamidite linkage.

14. The compound of claim 9, wherein the nucleic acid comprises a hydroxyl group, a phosphate group, or modified phosphate group, optionally wherein the modified phosphate group is a 5'-(E)-vinylphosphonate.

15. The compound of claim 3, wherein the nucleic acid is a double-stranded nucleic acid comprising an antisense strand hybridized to a sense strand, and wherein each of the antisense strand and sense strand is independently 15 to 30 nucleotides in length, optionally wherein each of the antisense strand and sense strand is independently 17 to 25 nucleotides in length, optionally wherein each of the antisense strand and sense strand is independently 19 to 23 nucleotides in length.

16. The compound of claim 3, wherein the nucleic acid is a single-stranded nucleic acid and the single-stranded nucleic acid is 8 to 30 nucleotides in length.

7. The compound of claim **Error! Reference source not found.**, wherein the single-stranded nucleic acid is 12 to 25 nucleotides in length, optionally wherein the single-stranded nucleic acid is 15 to 25 nucleotides in length, optionally wherein the single-stranded nucleic acid is 17 to 23 nucleotides in length.

18. The compound of claim 6, wherein

a) one L^6 is attached to a 3' carbon of the double-stranded nucleic acid or single-stranded nucleic acid, optionally wherein the 3' carbon is the 3' carbon of a 3' terminal nucleotide;
b) one L^6 is attached to a 5' carbon of the double-stranded nucleic acid or single-stranded nucleic acid, optionally wherein the 5' carbon is the 5' carbon of a 5' terminal nucleotide;

c) one L^6 is attached to a 2' carbon of the double-stranded nucleic acid or single-stranded nucleic acid;

d) one L^6 is attached to an oxygen of 2' hydroxy of the double-stranded nucleic acid or single-stranded nucleic acid;

e) the double-stranded nucleic acid or single-stranded nucleic acid comprises a morpholino moiety, and one L^6 is attached to a 3' nitrogen of morpholino moiety;

f) the double-stranded nucleic acid or single-stranded nucleic acid comprises a morpholino moiety, and one L^6 is attached to a 6' carbon of the morpholino moiety; or

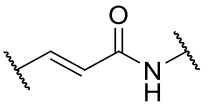
g) one L^6 is attached to a nucleobase of the double-stranded nucleic acid or single-stranded nucleic acid.

8. The compound of claim 3, wherein L^4 and L^6 are independently

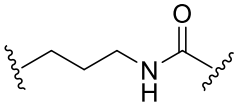
a) a bond, -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, $-OPO_2-O-$, -OP(S)(O)-O-, $-OP(S)_2-O-$, $-S(O)_2NH-$, substituted or unsubstituted alkylene or substituted or unsubstituted heteroalkylene;

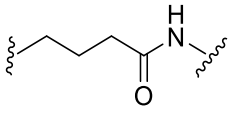
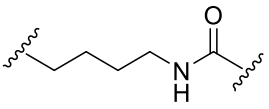
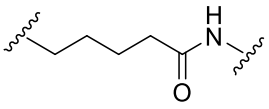
b) a bond, -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, $-OPO_2-O-$, -OP(S)(O)-O-, $-OP(S)_2-O-$, $-S(O)_2NH-$, substituted or unsubstituted C_1-C_8 alkylene or substituted or unsubstituted 2 to 8 membered heteroalkylene; or

c) -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, $-OPO_2-O-$, -OP(S)(O)-O-, $-OP(S)_2-O-$, $-S(O)_2NH-$, R^{20}-substituted or unsubstituted C_1-C_8 alkylene, or R^{20}-substituted or unsubstituted 2 to 8 membered heteroalkylene, wherein R^{20} is oxo, hydroxyl, or substituted or unsubstituted C_1-C_4 alkyl.

20. The compound of claim 3, wherein L^6 is independently  , $-OPO_2-O-$, or –O-.

21. The compound of claim 3, wherein L^4 is independently substituted or unsubstituted alkylene, substituted or unsubstituted hetoeroalkylene, $–L^{14}$-NH-C(O)- or $–L^{14}$-C(O)-NH-, wherein L^{14} is independently substituted or unsubstituted C_1-C_{20} alkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene, or wherein L^4 is independently $–L^{14}$-NH-C(O)- or $–L^{14}$-C(O)-NH-, wherein L^{14} is substituted or unsubstituted C_1-C_8 alkylene.

22. The compound of claim 3, wherein L^4 is independently  ,

 ,  , or  .

23. The compound of claim 3, wherein L^5 is

a) substituted or unsubstituted C_1-C_8 alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene;

b) substituted or unsubstituted C_3-C_6 cycloalkylene, or substituted or unsubstituted 4 to 6 membered heterocycloalkylene;

c) substituted or unsubstituted phenylene, or substituted or unsubstituted 4 to 6 heteroarylene; or

d) independently a bond.

9. The compound of claim 3, wherein L^7 is independently

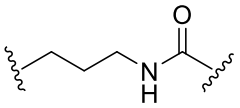
a) substituted or unsubstituted C_1-C_8 alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene

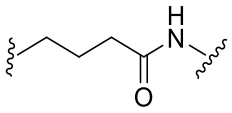
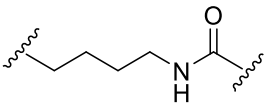
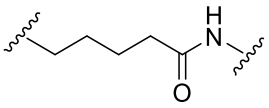
b) a bond;

c) $–L^{17}$-NH-C(O)- or $–L^{17}$-C(O)-NH-, wherein L^{17} is independently substituted or unsubstituted C_1-C_{20} alkylene, substituted or unsubstituted 2-20 membered heteroalkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene;

d) $–L^{17}$-NH-C(O)- or $–L^{17}$-C(O)-NH-, wherein L^{17} is substituted or unsubstituted C_1-C_8 alkylene; or

e) -NHC(O)-.

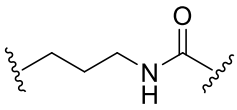
25. The compound of claim 3, wherein L^7 is independently  ,

 ,  , or  .

26. The compound of claim 3, wherein $–L^6$-L^5-L^4- is

a) independently a bond, or subsituted or unsubstituted 2 to 50 membered heteroalkylene;
b) R^{11}-substituted or unsubstituted 2 to 50 membered heteroalkylene, wherein R^{11} is oxo, hydroxyl, or unsubstituted C_1-C_4 alkyl;
c) independently $–L^{10}$-NH-C(O), or $–L^{10}$-C(O)-NH-, wherein L^{10} is independently substituted or unsubstituted C_1-C_{20} alkylene, substituted or unsubstituted heteroalkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene;
d) independently $–L^{10}$-NH-C(O)- or $–L^{10}$-C(O)-NH-, wherein L^{10} is substituted or unsubstituted C_1-C_8 alkylene;
e) independently–O-L^{10}-NH-C(O)- or –O-L^{10}-C(O)-NH-, wherein L^{10} is independently substituted or unsubstituted C_1-C_{20} alkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene;
f) independently –O-L^{10}-NH-C(O)-, or –O-L^{10}-C(O)-NH-, wherein L^{10} is substituted or unsubstituted C_1-C_8 alkylene;
g) independently -OPO_2-O-L^{10}-NH-C(O)- or -OPO_2-O-L^{10}-C(O)-NH-, wherein L^{10} is independently substituted or unsubstituted C_1-C_{20} alkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene; or
h) independently -OPO_2-O-L^{10}-NH-C(O)- or -OPO_2-O-L^{10}-C(O)-NH-, wherein L^{10} is substituted or unsubstituted C_1-C_8 alkylene.

27. The compound of claim 3, wherein – L^6-L^5-L^4- is independently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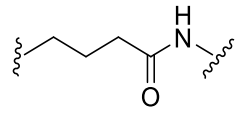
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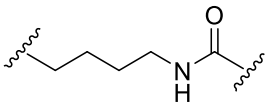
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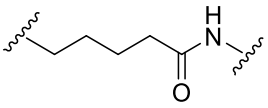
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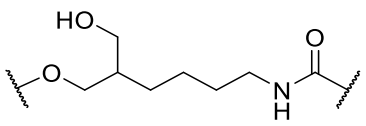
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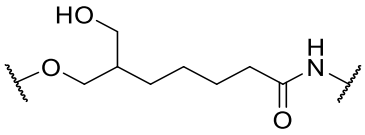
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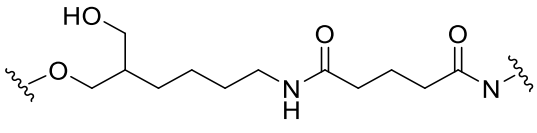
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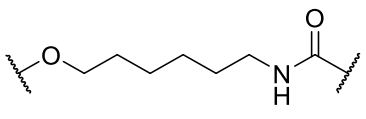
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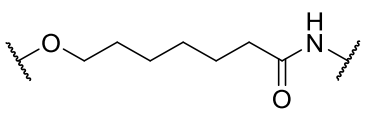
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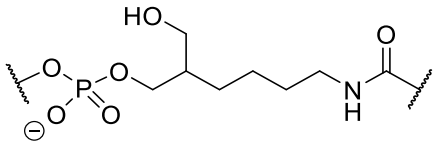
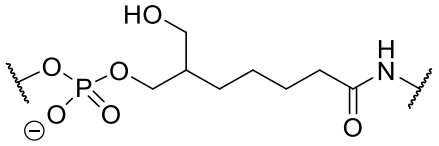
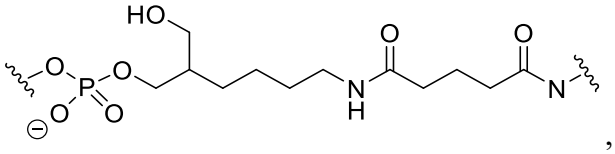
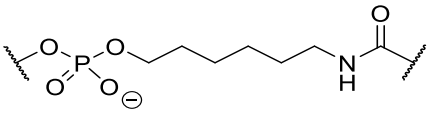
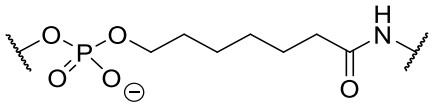
28. The compound of claim 3, wherein $–L^6-L^5-L^4-$ is independently

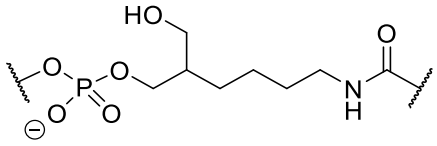
 ,  ,

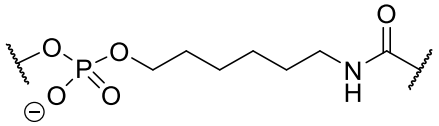
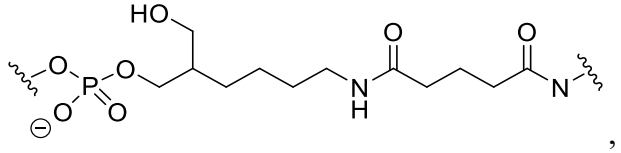
 ,  , or

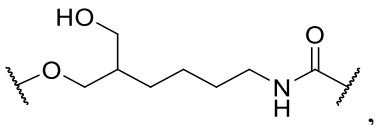
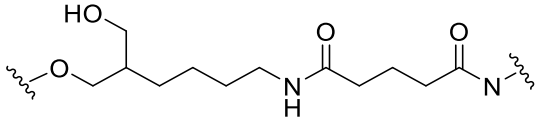
 .

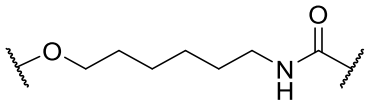
29. The compound of claim 3, wherein $–L^6-L^5-L^4-$ is selected from

Group A:

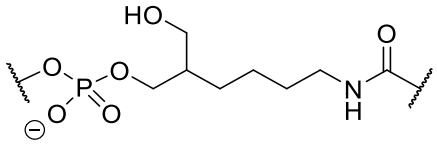
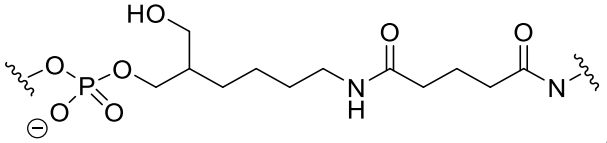
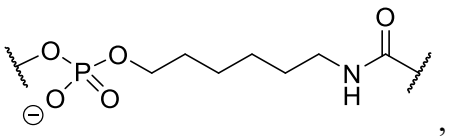
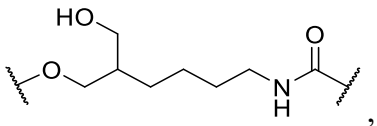
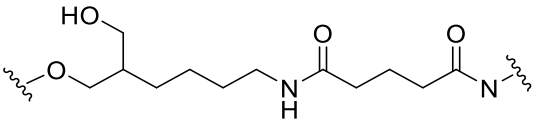
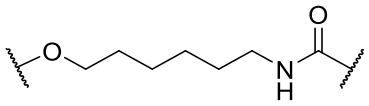
$–L^6-L^5-L^4-$ is independently  ,

 ,  ,

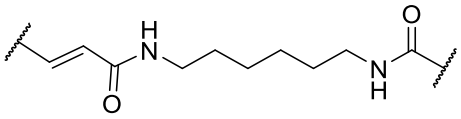
 ,  , or

 and is attached to a 3’ carbon of the double-stranded nucleic acid or single-stranded nucleic acid, optionally wherein the 3’ carbon is the 3’ carbon of a 3’ terminal nucleotide;

Group B:

–L^6-L^5-L^4- is independently  ,  ,  ,  ,  , or  and is attached to a 5’ carbon of the double-stranded nucleic acid or single-stranded nucleic acid, optionally wherein the 5’ carbon is the 5’ carbon of a 5’ terminal nucleotide; and

Group C:

wherein –L^6-L^5-L^4- is independently  and is attached to a nucleotide base of the double-stranded nucleic acid or single-stranded nucleic acid.

30. The compound of claim 3, wherein L^1 is independently -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene; or L^1 is independently –L^{11}-NH-C(O)- or –L^{11}-C(O)-NH-, wherein L^{11} is independently substituted or unsubstituted C_1-C_{20} alkylene, substituted or unsubstituted 2-20 membered heteroalkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene; or L^1 is independently –L^{11}-NH-C(O)- or –L^{11}-C(O)-NH-, wherein L^{11} is substituted or unsubstituted C_1-C_8 alkylene.

31. The compound of claim 3, wherein the compound is selected from

Group A:

L^{1A} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene;

L^{1B} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, or substituted or unsubstituted arylene;

L^{1C} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, substituted or substituted or unsubstituted heteroalkylene, or substituted or unsubstituted arylene;

L^{1D} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, or substituted or unsubstituted arylene; and

L^{1E} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene;

Group B:

L^{1A} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene;

L^{1B} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene;

L^{1C} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, substituted or unsubstituted C_2-C_8 alkynylene, substituted or substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene;

L^{1D} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene; and

L^{1E} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene; and

Group C:

L^{1A} is independently unsubstituted C_1-C_8 alkylene, or unsubstituted 2 to 8 membered heteroalkylene;

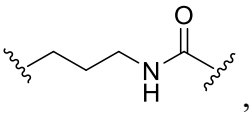
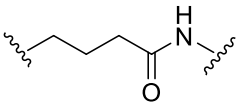
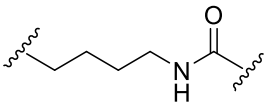
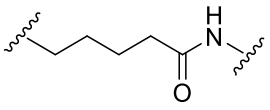
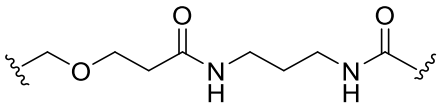
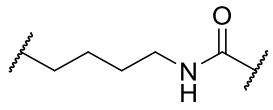
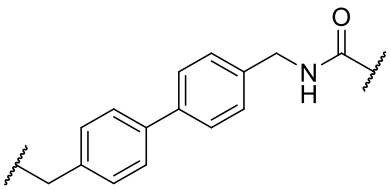
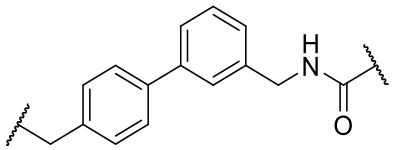
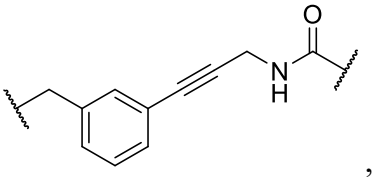
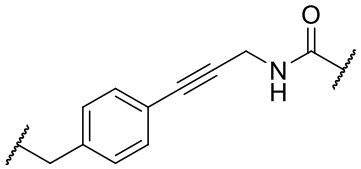
L^{1B} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, unsubstituted C_1-C_8 alkylene, unsubstituted C_2-C_8 alkynylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

L^{1C} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, unsubstituted C_1-C_8 alkylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

L^{1D} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, unsubstituted C_1-C_8 alkylene, or unsubstituted 2 to 8 membered heteroalkylene; and

L^{1E} is independently -NHC(O)-.

32. The compound of claim 3, wherein L^1 is independently -NHC(O)-,


, 
, 
, 
, a bond, 
, 
, 
, 
, 
, 
or
.

33. The compound of claim 3, wherein L^2 is independently -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene; L^2 is independently –L^{12}-NH-C(O)- or –L^{12}-C(O)-NH-, wherein L^{12} is substituted or unsubstituted C_1-C_{20} alkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene; or L^2 is independently –L^{12}-NH-C(O)- or –L^{12}-C(O)-NH-, wherein L^{12} is substituted or unsubstituted C_5-C_8 alkylene.

34. The compound of claim 3, wherein the compound is selected from Group A:

L^{2A} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene;

L^{2B} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, or substituted or unsubstituted arylene;

L^{2C} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, substituted or substituted or unsubstituted heteroalkylene, or substituted or unsubstituted arylene;

L^{2D} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, or substituted or unsubstituted arylene; and

L^{2E} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene;

Group B:

L^{2A} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene;

L^{2B} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene;

L^{2C} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, substituted or unsubstituted C_2-C_8 alkynylene, substituted or substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene;

L^{2D} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene; and

L^{2E} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene; and

Group C:

L^{2A} is independently unsubstituted C_1-C_8 alkylene, or unsubstituted 2 to 8 membered heteroalkylene;

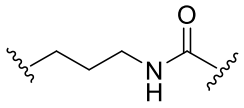
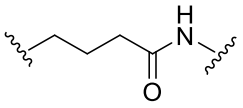
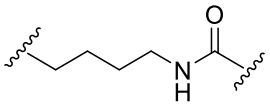
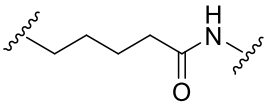
L^{2B} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, unsubstituted C_1-C_8 alkylene, unsubstituted C_2-C_8 alkynylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

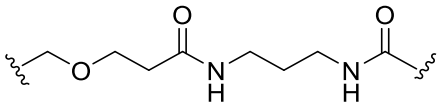
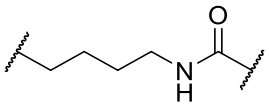
L^{2C} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, unsubstituted C_1-C_8 alkylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

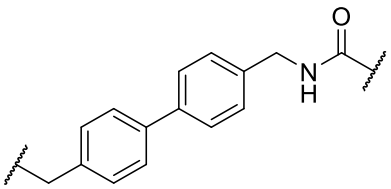
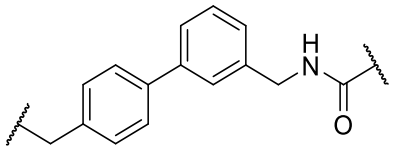
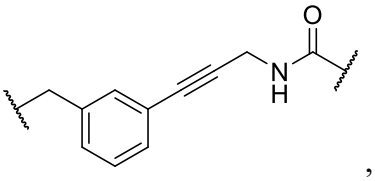
L^{2D} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, unsubstituted C_1-C_8 alkylene, or unsubstituted 2 to 8 membered heteroalkylene; and

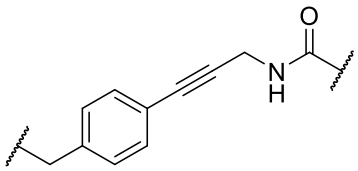
L^{2E} is independently -NHC(O)-.

35. The compound of claim 3, wherein L^2 is independently -NHC(O)-,

 ,  ,  ,  ,

a bond,  ,  ,

 ,  ,  ,

or  .

36. The compound of claim 3, wherein L^3 is independently -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene; L^3 is independently $–L^{13}$-NH-C(O)- or $–L^{13}$-C(O)-NH-, wherein L^{13} is substituted or unsubstituted C_1-C_{20} alkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene; or L^3 is independently $–L^{13}$-NH-C(O)- or $–L^{13}$-C(O)-NH-, wherein L^{13} is substituted or unsubstituted C_5-C_8 alkylene.

37. The compound of claim 3, wherein the compound is selected from Group A:

L^{3A} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene;

L^{3B} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, or substituted or unsubstituted arylene;

L^{3C} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, substituted or substituted or unsubstituted heteroalkylene, or substituted or unsubstituted arylene;

L^{3D} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, or substituted or unsubstituted arylene; and

L^{3E} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene;

Group B:

L^{3A} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene;

L^{3B} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene;

L^{3C} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, substituted or unsubstituted C_2-C_8 alkynylene, substituted or substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene;

L^{3D} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene; and

L^{3E} is independently a bond, -NHC(O)-, –C(O)NH-, substituted or unsubstituted C_1-C_8 alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene; and

Group C:

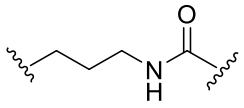
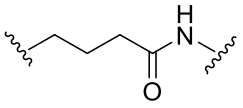
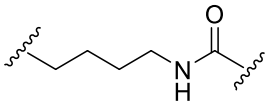
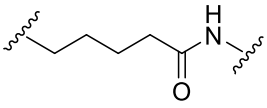
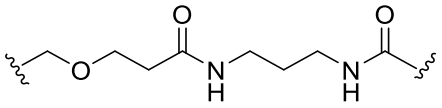
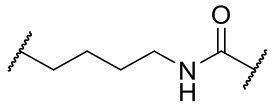
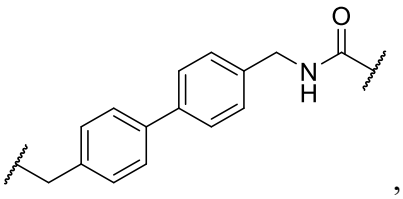
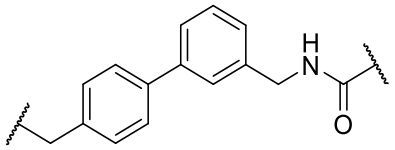
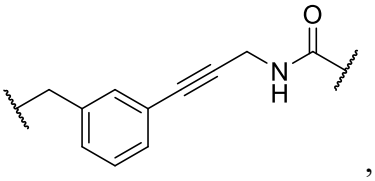
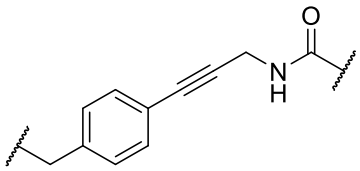
L^{3A} is independently unsubstituted C_1-C_8 alkylene, or unsubstituted 2 to 8 membered heteroalkylene;

L^{3B} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, unsubstituted C_1-C_8 alkylene, unsubstituted C_2-C_8 alkynylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

L^{3C} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, unsubstituted C_1-C_8 alkylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

L^{3D} is independently a bond, -O-, -NHC(O)-, –C(O)NH-, unsubstituted C_1-C_8 alkylene, or unsubstituted 2 to 8 membered heteroalkylene; and

L^{3E} is independently -NHC(O)-.

38. The compound of claim 3, wherein L^3 is independently -NHC(O)-,  ,  ,  ,  , a bond,  ,  ,  ,  ,  , or  .

39. The compound of claim 1, wherein R^1 is selected from

Group A:

R^1 is unsubstituted C_1-C_{25} alkyl, optionally unsubstituted unbranched C_1-C_{25} alkyl, optionally unsubstituted unbranched saturated C_1-C_{25} alkyl;

Group B:

R^1 is unsubstituted C_{11}-C_{25} alkyl, optionally unsubstituted unbranched C_{11}-C_{25} alkyl, optionally unsubstituted unbranched saturated C_{11}-C_{25} alkyl;

Group C:

R^1 is unsubstituted C_{11}-C_{17} alkyl, optionally unsubstituted unbranched C_{11}-C_{17} alkyl, optionally unsubstituted unbranched saturated C_{11}-C_{17} alkyl; and

Group D:

R^1 is unsubstituted C_{14}-C_{15} alky, optionally unsubstituted unbranched C_{14}-C_{15} alkyl, optionally unsubstituted unbranched saturated C_{14}-C_{15} alkyl.

40. The compound of claim 1, wherein R^2 is selected from

Group A:

R^2 is unsubstituted C_1-C_{25} alkyl, optionally unsubstituted unbranched C_1-C_{25} alkyl, optionally unsubstituted unbranched saturated C_1-C_{25} alkyl;

Group B:

R^2 is unsubstituted C_{11}-C_{25} alkyl, optionally unsubstituted unbranched C_{11}-C_{25} alkyl, optionally unsubstituted unbranched saturated C_{11}-C_{25} alkyl;

Group C:

R^2 is unsubstituted C_{11}-C_{17} alkyl, optionally unsubstituted unbranched C_{11}-C_{17} alkyl, optionally unsubstituted unbranched saturated C_{11}-C_{17} alkyl; and

Group D:

R^2 is unsubstituted C_{14}-C_{15} alkyl, optionally unsubstituted unbranched C_{14}-C_{15} alkyl, optionally unsubstituted unbranched saturated C_{14}-C_{15} alkyl.

41. The compound of claim 1, wherein R^3 is selected from

Group A:

R^3 is unsubstituted C_1-C_{25} alkyl, optionally unsubstituted unbranched C_1-C_{25} alkyl, optionally unsubstituted unbranched saturated C_1-C_{25} alkyl;

Group B:

R^3 is unsubstituted C_{11}-C_{25} alkyl, optionally unsubstituted unbranched C_{11}-C_{25} alkyl, optionally unsubstituted unbranched saturated C_{11}-C_{25} alkyl;

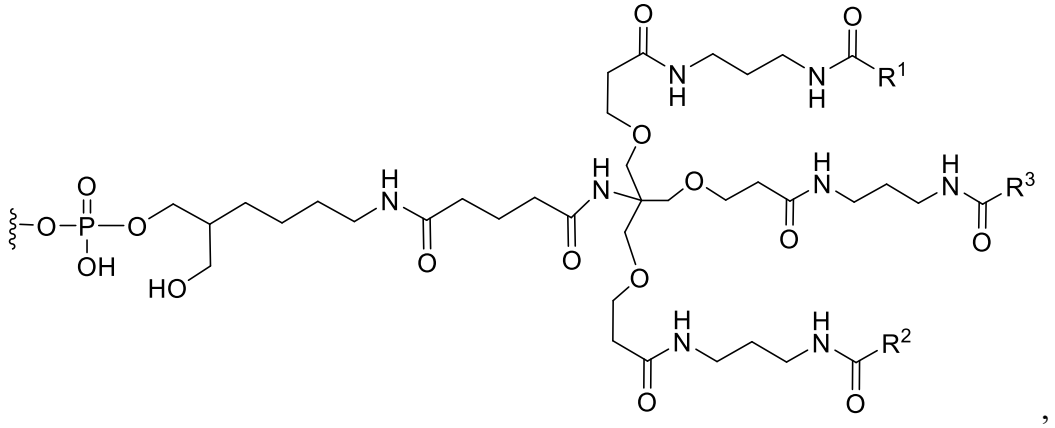
Group C:

R^3 is unsubstituted C_{11}-C_{17} alkyl, optionally unsubstituted unbranched C_{11}-C_{17} alkyl, optionally unsubstituted unbranched saturated C_{11}-C_{17} alkyl; and

Group D:

R^3 is unsubstituted C_{14}-C_{15} alkyl, optionally unsubstituted unbranched C_{14}-C_{15} alkyl, optionally unsubstituted unbranched saturated C_{14}-C_{15} alkyl.

42. The compound of claim 3, wherein the compound comprises a structure of



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wherein the wavy line represents attachment point to the nucleic acid.

43. A method comprising contacting a cell with a compound of any one of claims 1 to 42, optionally wherein contacting occurs *in vitro*, or *ex vivo*.

44. Use of the compound of any one of claims 1 to 42 in the manufacture of a medicament for the treatment of a disease or disorder of the eye, liver, kidney, heart, adipose tissue, lung, muscle or spleen in a subject, wherein the compound is to be administered to the subject.

45. A cell comprising the compound of any one of claims 1 to 42.

46. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and the compound of any one of claims 1 to 42.