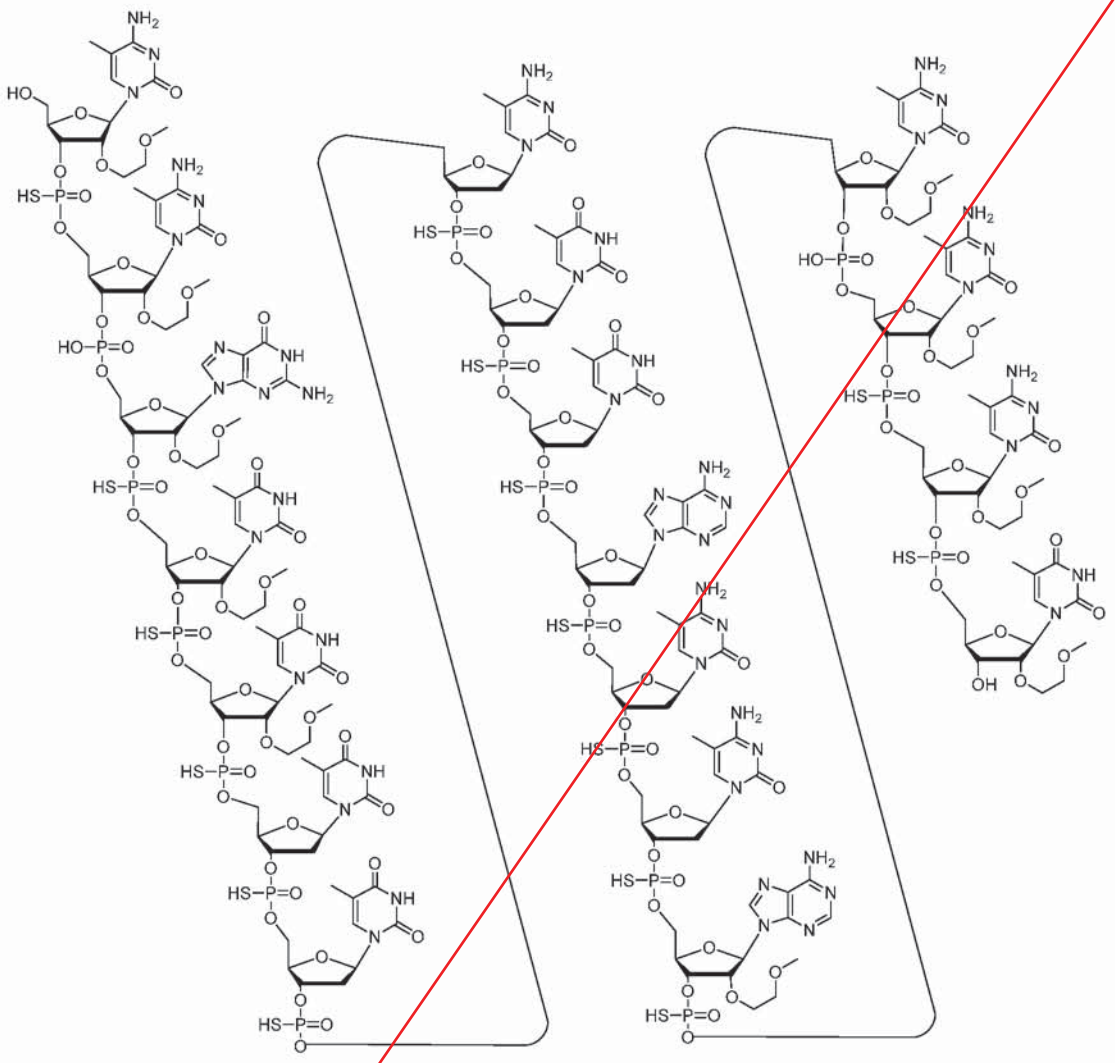
CLAIMS:

1. A modified oligonucleotide according to the following formula:



(SEQ ID NO: 8).

2. An oligomeric compound comprising a modified oligonucleotide according to the following formula:

mCes mCeo Ges Tes Tes Tds Tds mCds Tds Tds Ads mCds mCds Aes mCeo mCes mCes Te;

wherein,

A = an adenine,

mC = a 5-methylcytosine,

G = a guanine,

T = a thymine,

e = a 2'-MOE nucleoside,

d = a 2'-deoxynucleoside,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

3. The oligomeric compound of claim 2 comprising a conjugate group.

4. An oligomeric duplex comprising an oligomeric compound of claim 2 or claim 3.

5. An antisense compound comprising or consisting of a modified oligonucleotide according to claim 1, an oligomeric compound according to claim 2 or claim 3, or an oligomeric duplex according to claim 4.

6. A pharmaceutical composition comprising a modified oligonucleotide according to claim 1, an oligomeric compound according to claim 2 or claim 3, or an oligomeric duplex according to claim 4 or a salt thereof and a pharmaceutically acceptable carrier or diluent.

7. The composition of claim 6, wherein the salt is sodium.

8. A method comprising administering to an animal a pharmaceutical composition according to claim 6 or claim 7.

9. A method of treating a disease associated with Tau comprising administering to an individual having or at risk for developing a disease associated with Tau a therapeutically effective amount of a pharmaceutical composition according to claim 6 or claim 7; and thereby treating the disease associated with Tau.

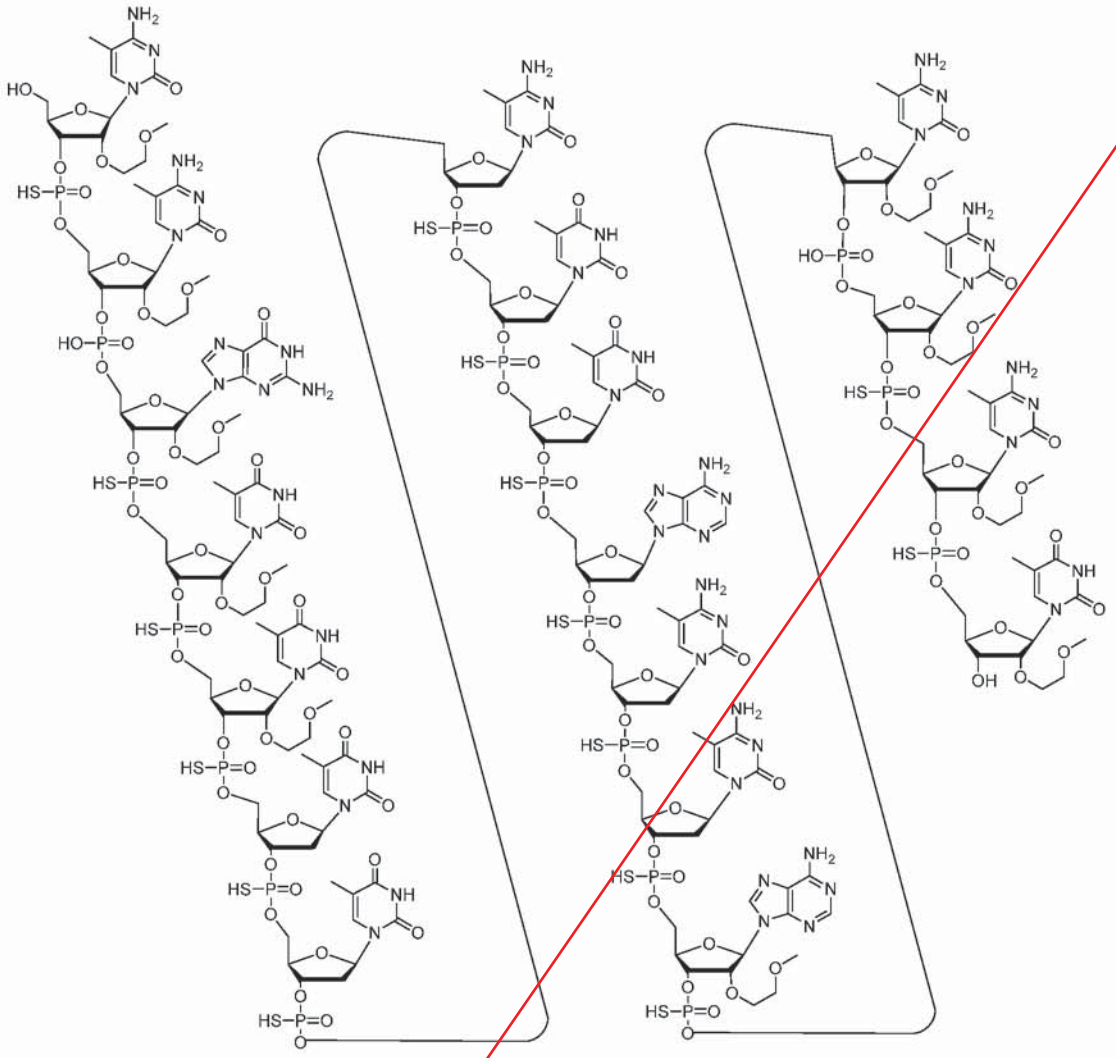
10. The method of claim 9, wherein the disease associated with Tau is a neurodegenerative disease.

11. The method of claim 10, wherein the neurodegenerative disease is any of a tauopathy, Alzheimer's Disease, Fronto-temporal Dementia (FTD), FTDP-17, Progressive Supranuclear Palsy (PSP), Chronic Traumatic Encephalopathy (CTE), Corticobasal Ganglionic Degeneration (CBD), Epilepsy, or Dravet's Syndrome.

12. The method of claim 10 or claim 11, wherein at least one symptom of the neurodegenerative disease is ameliorated.

13. The method of claim 12, wherein the symptom is any of loss of memory, loss of motor function, and increase in the number and/or volume of neurofibrillary inclusions.

14. A modified oligonucleotide according to the following formula:



(SEQ ID NO: 8)

or a salt thereof.

15. The modified oligonucleotide of claim 14, which is a sodium salt of the formula.

16. A compound comprising a modified oligonucleotide, wherein the modified oligonucleotide is a gapmer consisting of a 5' wing segment, a central gap segment, and a 3' wing segment, wherein:

the 5' wing segment consists of five 2'-MOE nucleosides,

the central gap segment consists of eight 2'-deoxynucleosides, and

the 3' wing segment consists of five 2'-MOE nucleosides;

wherein the modified oligonucleotide has the nucleobase sequence 5'-CCGTTTTCTTACCACCCT-3' (SEQ ID NO: 8), wherein each cytosine is a 5-methylcytosine; and wherein the internucleoside linkages of the modified oligonucleotide are, from 5' to 3', sosssssssssssoss, wherein each s is a phosphorothioate linkage and each o is a phosphodiester linkage.

17. A modified oligonucleotide, wherein the modified oligonucleotide is a gapmer consisting of a 5' wing segment, a central gap segment, and a 3' wing segment, wherein:

the 5' wing segment consists of five 2'-MOE nucleosides,

the central gap segment consists of eight 2'-deoxynucleosides, and

the 3' wing segment consists of five 2'-MOE nucleosides;

wherein the modified oligonucleotide has the nucleobase sequence 5'-CCGTTTTCTTACCACCCT-3' (SEQ ID NO: 8), wherein each cytosine is a 5-methylcytosine; and wherein the internucleoside linkages of the modified oligonucleotide are, from 5' to 3', sosssssssssssoss, wherein each s is a phosphorothioate linkage and each o is a phosphodiester linkage.

18. A chirally enriched population of modified oligonucleotides of any of claims 14, 15 or 17 wherein the population is enriched for modified oligonucleotides comprising at least one particular phorphorothioate internucleoside linkage having a particular stereochemical configuration.

19. The chirally enriched population of claim 18, wherein the population is enriched for modified oligonucleotides comprising at least one particular phorphorothioate internucleoside linkage having the (*S*p) configuration.

20. The chirally enriched population of claim 18, wherein the population is enriched for modified oligonucleotides comprising at least one particular phorphorothioate internucleoside linkage having the (*R*p) configuration.

21. The chirally enriched population of claim 18, wherein the population is enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage

22. The chirally enriched population of claim 21, wherein the population is enriched for modified oligonucleotides having the (*S*p) configuration at each phosphorothioate internucleoside linkage.

23. The chirally enriched population of claim 21, wherein the population is enriched for modified oligonucleotides having the (*R*p) configuration at each phosphorothioate internucleoside linkage.

24. The chirally enriched population of claim 21, wherein the population is enriched for modified oligonucleotides having the (*R*p) configuration at one particular phosphorothioate internucleoside linkage and the (*S*p) configuration at each of the remaining phosphorothioate internucleoside linkages.

25. The chirally enriched population of claim 18 or claim 21 wherein the population is enriched for modified oligonucleotides having at least 3 contiguous phosphorothioate internucleoside linkages in the *S*p, *S*p, and *R*p configurations, in the 5' to 3' direction.

26. A chirally enriched population of modified oligonucleotides of any of claims 1-17, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

27. A pharmaceutical composition comprising the modified oligonucleotide of any of claims 14, 15, or 17 and a pharmaceutically acceptable diluent or carrier.

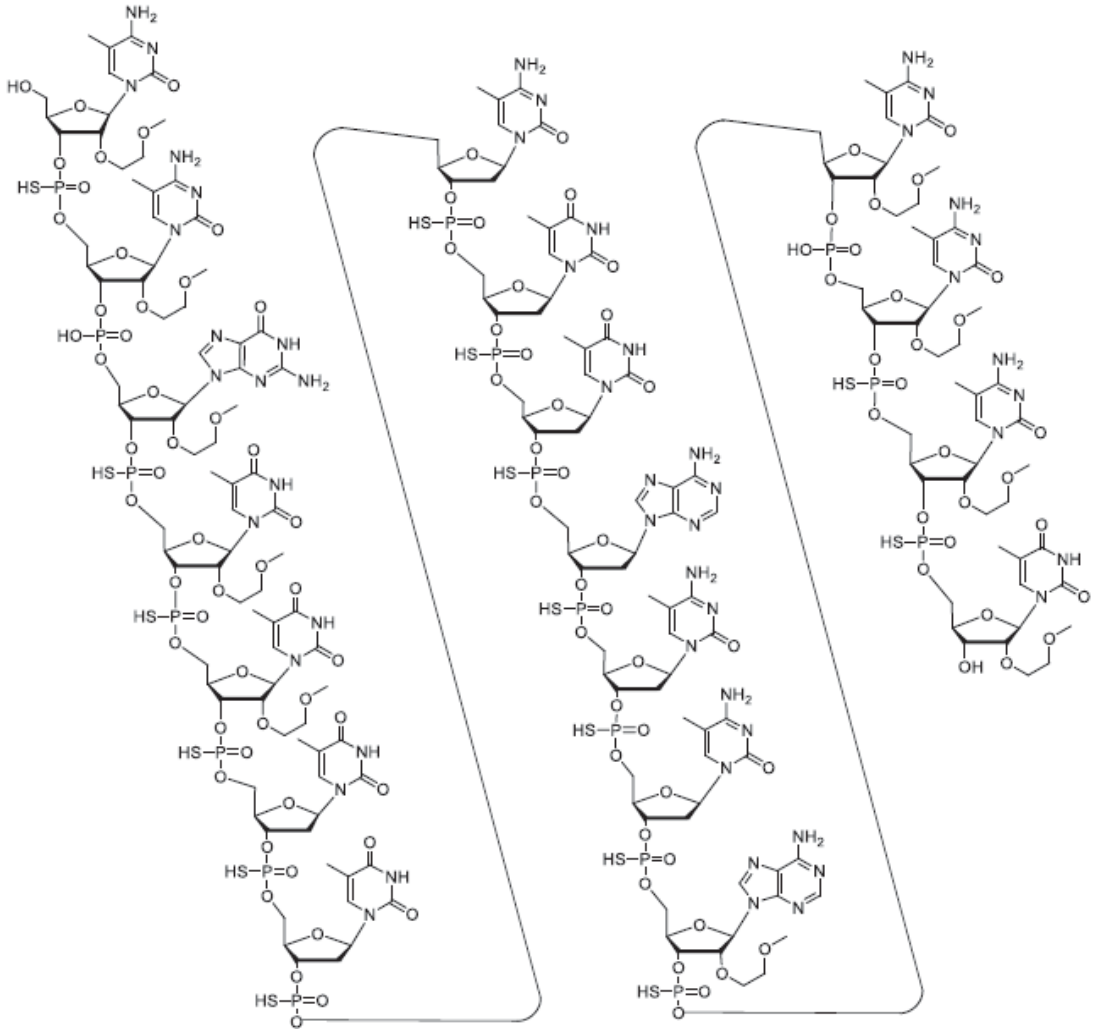
28. A pharmaceutical composition comprising the population of modified oligonucleotides of any of claims 18-26 and a pharmaceutically acceptable diluent or carrier.

29. The pharmaceutical composition of claim 27 or claim 28, wherein the pharmaceutically acceptable diluent is phosphate-buffered saline (PBS) or artificial CSF (aCSF).

30. The pharmaceutical composition of claim 27 or claim 28, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and phosphate-buffered saline (PBS) or artificial CSF (aCSF).

CLAIMS

1. A modified oligonucleotide according to the following formula:



(SEQ ID NO: 8)

or a salt thereof.

2. The modified oligonucleotide, or salt thereof, of claim 1, wherein the salt is a sodium salt.

3. A compound comprising a modified oligonucleotide, wherein the modified oligonucleotide is a gapmer consisting of a 5' wing segment, a central gap segment, and a 3' wing segment, wherein:

the 5' wing segment consists of five 2'-MOE nucleosides,
the central gap segment consists of eight 2'-deoxynucleosides, and
the 3' wing segment consists of five 2'-MOE nucleosides;

wherein the modified oligonucleotide has the nucleobase sequence 5'-CCGTTTTCTTACCACCCT-3' (SEQ ID NO: 8), wherein each cytosine is a 5-methylcytosine; and wherein the internucleoside linkages of the modified oligonucleotide are, from 5' to 3', sosssssssssssoss, wherein each s is a phosphorothioate linkage and each o is a phosphodiester linkage.

4. A modified oligonucleotide, wherein the modified oligonucleotide is a gapmer consisting of a 5' wing segment, a central gap segment, and a 3' wing segment, wherein:

the 5' wing segment consists of five 2'-MOE nucleosides,

the central gap segment consists of eight 2'-deoxynucleosides, and

the 3' wing segment consists of five 2'-MOE nucleosides;

wherein the modified oligonucleotide has the nucleobase sequence 5'-CCGTTTTCTTACCACCCT-3' (SEQ ID NO: 8), wherein each cytosine is a 5-methylcytosine; and wherein the internucleoside linkages of the modified oligonucleotide are, from 5' to 3', sosssssssssssoss, wherein each s is a phosphorothioate linkage and each o is a phosphodiester linkage.

5. A chirally enriched population of the modified oligonucleotides, or salts thereof, of claim 1 or claim 2 wherein the population is enriched for modified oligonucleotides, or salts thereof, comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.

6. The chirally enriched population of claim 5, wherein the population is enriched for modified oligonucleotides, or salts thereof, comprising at least one particular phosphorothioate internucleoside linkage having the (*S*p) configuration.

7. The chirally enriched population of claim 5, wherein the population is enriched for modified oligonucleotides, or salts thereof, comprising at least one particular phosphorothioate internucleoside linkage having the (*R*p) configuration.

8. The chirally enriched population of claim 5, wherein the population is enriched for modified oligonucleotides, or salts thereof, having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage.

9. The chirally enriched population of claim 8, wherein the population is enriched for modified oligonucleotides, or salts thereof, having the (*S*p) configuration at each phosphorothioate internucleoside linkage.

10. The chirally enriched population of claim 8, wherein the population is enriched for modified oligonucleotides, or salts thereof, having the (*R*p) configuration at each phosphorothioate internucleoside linkage.

11. The chirally enriched population of claim 8, wherein the population is enriched for modified oligonucleotides, or salts thereof, having the (*R*p) configuration at one particular phosphorothioate internucleoside linkage and the (*S*p) configuration at each of the remaining phosphorothioate internucleoside linkages.

12. The chirally enriched population of claim 5, wherein the population is enriched for modified oligonucleotides, or salts thereof, having at least 3 contiguous phosphorothioate internucleoside linkages in the *S*p, *S*p, and *R*p configurations, in the 5' to 3' direction.

13. The chirally enriched population of claim 8, wherein the population is enriched for modified oligonucleotides, or salts thereof, having at least 3 contiguous phosphorothioate internucleoside linkages in the *S*p, *S*p, and *R*p configurations, in the 5' to 3' direction.

14. A population of modified oligonucleotides, or salts thereof, of claim 1 or claim 2, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

15. A pharmaceutical composition comprising the modified oligonucleotide, or salt thereof, of claim 1 or 2 and a pharmaceutically acceptable diluent or carrier.

16. A pharmaceutical composition comprising the compound of claim 3 and a pharmaceutically acceptable diluent or carrier.

17. A pharmaceutical composition comprising the modified oligonucleotide of claim 4 and a pharmaceutically acceptable diluent or carrier.

18. The pharmaceutical composition of any one of claims 15 to 17, comprising a pharmaceutically acceptable diluent and wherein the pharmaceutically acceptable diluent is phosphate-buffered saline (PBS) or artificial CSF (aCSF).

19. The compound of claim 3, wherein the modified oligonucleotide is linked to a conjugate group.

20. An oligomeric duplex comprising the modified oligonucleotide, or salt thereof, of claim 1.

21. An oligomeric duplex comprising the compound of claim 3.

22. An oligomeric duplex comprising the modified oligonucleotide of claim 4.

23. The modified oligonucleotide or salt thereof according to claim 1 or 2, the compound according to claim 3, the modified oligonucleotide according to claim 4, or the pharmaceutical composition according to any one of claims 15 to 18 for use in therapy.

24. Use of the modified oligonucleotide or salt thereof according to claim 1 or 2, the compound according to claim 3, the modified oligonucleotide according to claim 4, or the

pharmaceutical composition according to any one of claims 15 to 18 in the manufacture of a medicament for treating a disease associated with tau in a human subject having or at risk for developing a disease associated with tau.

25. The use according to claim 24, wherein the disease associated with tau is a neurodegenerative disease.

26. The use according to claim 25, wherein the neurodegenerative disease is a tauopathy.

27. The use according to claim 25, wherein the neurodegenerative disease is Alzheimer's Disease, Fronto-temporal Dementia (FTD), FTDP-17, Progressive Supranuclear Palsy (PSP), Chronic Traumatic Encephalopathy (CTE), Corticobasal Ganglionic Degeneration (CBD), Epilepsy, or Dravet's Syndrome.

28. The use according to claim 25, wherein the neurodegenerative disease is AD.

29. The use according to claim 25, wherein the neurodegenerative disease is FTD.

30. The use according to claim 25, wherein the neurodegenerative disease is FTDP-17.

31. The use according to claim 25, wherein the neurodegenerative disease is PSP.

32. Use of the modified oligonucleotide or salt thereof according to claim 1 or 2, the compound according to claim 3, the modified oligonucleotide according to claim 4, or the pharmaceutical composition according to any one of claims 15 to 18 in the manufacture of a medicament for reducing tau messenger ribonucleic acid (mRNA) expression.

33. The use according to any one of claims 24 to 32, wherein the modified oligonucleotide, salt, compound, or pharmaceutical composition is to be administered by intrathecal administration.