COMPOSITIONS AND METHODS FOR INHIBITING *MAPT* EXPRESSION

CROSS-REFERENCE TO RELATED APPLICATIONS

[001] The present application claims priority under 35 U.S.C. § 119(e) from U.S. Provisional Application No. 63/364,609, filed May 12, 2022, which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

[002] The disclosure relates generally to biology and medicine, and more particularly it relates to oligonucleotides and compositions including the same for inhibiting or reducing (*i.e.*, modulating) microtubule-associated protein tau (*MAPT*) gene expression, as well as their use for treating diseases and disorders associated with *MAPT* gene expression.

BACKGROUND

[003] Microtubules perform several essential roles within cells throughout the body. Within the central nervous system (CNS), microtubules provide structural support and assist in transporting substances throughout cells. Changes in microtubule mass, structure, and pattern are known factors leading to the development of many neurodegenerative diseases. Tau is an essential protein for forming microtubules, whose abnormal expression leads to neurodegenerative diseases. Tau proteins combine with tubulin to form microtubules. Alternative splicing of *MAPT* generates different Tau proteins used in microtubule assembly. Mutations (*e.g.*, insertions and mismatches) in *MAPT* that alter Tau function and expression are known causes of several diseases and disorders impacting the CNS (*e.g.*, Alzheimer's disease (AD), Parkinson's disease (PD), and tauopathies). Strategies for targeting *MAPT* gene expression to prevent such diseases and disorders are needed.

[004] The mammalian CNS is a complex system of tissues, including cells, fluids, and chemicals that interact in concert to enable a wide variety of functions, including movement, navigation, cognition, speech, vision, and emotion. Unfortunately, a variety of diseases and disorders of the CNS are known (*e.g.*, neurological disorders) and affect or disrupt some or all of these functions. Typically, treatments for diseases and disorders of the CNS have been limited to small molecule drugs, antibodies, and/or to adaptive or behavioral therapies. There exists an

ongoing need to develop treatments for diseases and disorders of the CNS associated with inappropriate *MAPT* gene expression.

BRIEF SUMMARY

[005] To address this need, the disclosure describes compositions for and methods of treating a disease, disorder, or condition associated with *MAPT* gene expression. The disclosure is based, at least in part, on discovering and developing double-stranded (ds) oligonucleotides such as RNAi oligonucleotides that effectively target and reduce *MAPT* gene expression in tissues of the CNS. Specifically, target sequences within MAPT mRNA were identified, and oligonucleotides that bind to these target sequences and inhibit MAPT mRNA expression were generated. As demonstrated herein, the oligonucleotides inhibit human and non-human primate (NHP) *MAPT* gene expression in CNS tissue. Further, MAPT mRNA expression was reduced in CNS tissue associated with AD or progressive supranuclear palsy (PSP) with both N-acetylgalactosamine (GalNAc)-conjugated and lipid-conjugated MAPT mRNA-targeting oligonucleotides. Without being bound by theory, the oligonucleotides described herein are useful for treating a disease, disorder, or condition associated with *MAPT* gene expression.

[006] Accordingly, and in some aspects, the disclosure provides a RNAi oligonucleotide for reducing *MAPT* gene expression, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein the antisense strand comprises a region of complementarity to a MAPT mRNA target sequence of any one of SEQ ID NOs: 912-1295, and wherein the region of complementarity is at least about 15 contiguous nucleotides in length.

[007] In any of the foregoing or related aspects, the sense strand is about 15 to about 50 nucleotides in length. In some aspects, the sense strand is 18 to 36 nucleotides in length. In some aspects, the antisense strand is about 15 to about 30 nucleotides in length. In some aspects, the antisense strand is 22 nucleotides in length, wherein the antisense strand and the sense strand form a duplex region of at least about 19 nucleotides in length, optionally at least 20 nucleotides in length. In some aspects, the region of complementarity is at least about 19 contiguous nucleotides

in length. In some aspects, the region of complementarity is at least about 20 contiguous nucleotides in length.

[008] In other aspects, the disclosure provides a ds RNAi oligonucleotide for reducing *MAPT* gene expression, the oligonucleotide comprising:

(i) an antisense strand of about 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is selected from SEQ ID NOs: 1296-1679, and

(ii) a sense strand of about 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[009] In some aspects, the 3' end of the sense strand comprises a stem-loop set forth as S1-L-S2, wherein S1 is complementary to S2, and wherein L forms a loop between S1 and S2 of 3-5 nucleotides in length. In some aspects, L is a triloop (triL) or a tetraloop (tetraL). In some aspects, L is a tetraL. In some aspects, the tetraL comprises the sequence 5'-GAAA-3'. In some aspects, S1 and S2 are about 1 to about 10 nucleotides in length and have the same length. In some aspects, S1 and S2 are 1 nucleotide, 2 nucleotides, 3 nucleotides, 4 nucleotides, 5 nucleotides, 6 nucleotides, 7 nucleotides, 8 nucleotides, 9 nucleotides, or 10 nucleotides in length. In some aspects, S1 and S2 are 6 nucleotides in length. In some aspects, the stem-loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 1680).

[0010] In other aspects, the oligonucleotide comprises a blunt end. In some aspects, the blunt end comprises the 3' end of the sense strand. In some aspects, the sense strand is about 20-22 nucleotides. In some aspects, the sense strand is 20 nucleotides.

[0011] In any of the foregoing or related aspects, the antisense strand comprises a 3' overhang sequence of one or more nucleotides in length. In some aspects, the overhang comprises purine nucleotides. In some aspects, the 3' overhang sequence is 2 nucleotides in length. In some aspects, the 3' overhang is selected from AA, GG, AG, and GA. In some aspects, the overhang is GG or AA. In some aspects, the overhang is GG.

[0012] In any of the foregoing or related aspects, the oligonucleotide comprises at least one modified nucleotide. In some aspects, the modified nucleotide comprises a 2'-modification. In some aspects, the 2'-modification is a modification selected from 2'-aminoethyl (EA), 2'-fluoro (2'-F), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-OME), and 2'-deoxy-2'-fluoro-β-d-arabinonucleic acid (2'-FANA). In some aspects, the modification is a 2'-modification selected from 2'-F and 2'-OMe. In some aspects, about 18% to about 23%, or 18%, 19%, 20%, 21%, 22%, or 23% of the nucleotides of the sense strand comprise a 2'-F modification. In other aspects, about 38% to about 43%, or 38%, 39%, 40%, 41%, 42%, or 43% of the nucleotides of the sense strand comprise a 2'-F modification. In some aspects, about 25% to about 35%, or 25%, 26%, 27%, 28%, 29%, 30%, 31%, 32%, 33%, 34%, or 35% of the nucleotides of the antisense strand comprise a 2'-F modification. In some aspects, about 25% to about 35%, or 25%, 26%, 27%, 28%, 29%, 30%, 31%, 32%, 33%, 34%, or 35% of the nucleotides of the oligonucleotide comprise a 2'-F modification. In some aspects, about 35-45%, 35%, 36%, 37%, 38%, 39%, 40%, 41%, 42%, 43%, 44% or 45% of the nucleotides of the oligonucleotide comprise a 2'-F modification. In some aspects, the sense strand comprises 20 nucleotides with positions 1-20 from 5' to 3', wherein each of positions 3, 5, 8, 10, 12, 13, 15, and 17 comprise a 2'-F modification. In other aspects, the sense strand comprises 36 nucleotides with positions 1-36 from 5' to 3', wherein each of positions 3, 5, 8, 10, 12, 13, 15, and 17 comprise a 2'-F modification. In some aspects, the antisense strand comprises 22 nucleotides with positions 1-22 from 5' to 3', and wherein each of positions 2, 3, 4, 5, 7, 10 14, 16, and 19 comprise a 2'-F modification. In some aspects, the remaining nucleotides comprise a 2'-OMe modification.

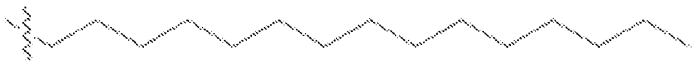
[0013] In any of the foregoing or related aspects, the oligonucleotide comprises at least one modified internucleotide linkage. In some aspects, the at least one modified internucleotide linkage is a phosphorothioate linkage. In some aspects, the antisense strand comprises a phosphorothioate linkage (i) between positions 1 and 2, and between positions 2 and 3; or (ii) between positions 1 and 2, between positions 2 and 3, and between positions 3 and 4, wherein positions are numbered 1-4 from 5' to 3'. In some aspects, the antisense strand is 22 nucleotides in length, and wherein the antisense strand comprises a phosphorothioate linkage between positions 20 and 21 and between positions 21 and 22, wherein positions are numbered 1-22 from 5' to 3'. In some aspects, the sense

strand comprises a phosphorothioate linkage between positions 1 and 2, wherein positions are numbered 1-2 from 5' to 3'. In some aspects, the sense strand is 20 nucleotides in length, and wherein the sense strand comprises a phosphorothioate linkage between positions between positions 1 and 2, between positions 18 and 19 and between positions 19 and 20, wherein positions are numbered 1-20 from 5' to 3'.

[0014] In any of the foregoing or related aspects, the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog. In some aspects, the phosphate analog is oxymethyl phosphonate, vinyl phosphonate or malonyl phosphonate, optionally wherein the phosphate analog is a 4'-phosphate analog comprising 4'-oxymethylphosphonate.

[0015] In any of the foregoing or related aspects, at least one nucleotide of the oligonucleotide is conjugated to one or more targeting ligands. In some aspects, each targeting ligand comprises a carbohydrate, amino sugar, lipid, cholesterol, or polypeptide. In some aspects, the stem-loop comprises one or more targeting ligands conjugated to one or more nucleotides of the stem-loop. In some aspects, the one or more targeting ligands is conjugated to one or more nucleotides of the loop. In some aspects, the loop comprises 4 nucleotides numbered 1-4 from 5' to 3', wherein nucleotides at positions 2, 3, and 4 each comprise one or more targeting ligands, wherein the targeting ligands are the same or different. In some aspects, each targeting ligand comprises a GalNAc moiety. In some aspects, the GalNac moiety is a monovalent GalNAc moiety, a bivalent GalNAc moiety, a trivalent GalNAc moiety, or a tetravalent GalNAc moiety. In some aspects, up to 4 nucleotides of L of the stem-loop are each conjugated to a monovalent GalNAc moiety.

[0016] In other aspects, the one or more targeting ligands is a lipid moiety. In some aspects, the lipid moiety is conjugated to the 5' terminal nucleotide of the sense strand. In some aspects, the lipid moiety is a hydrocarbon chain. In some aspects, the hydrocarbon chain is a C_8-C_{30} hydrocarbon chain. In some aspects, the hydrocarbon chain is a C_{16} hydrocarbon chain. In some aspects, the C_{16} hydrocarbon chain is represented by:



. In some aspects, the lipid moiety is conjugated to the 2' carbon of the ribose ring of the 5' terminal nucleotide.

[0017] In any of the foregoing or related aspects, the region of complementarity is fully complementary to the MAPT mRNA target sequence at nucleotide positions 2-8 of the antisense strand, wherein nucleotide positions are numbered 5' to 3'. In some aspects, the region of complementarity is fully complementary to the MAPT mRNA target sequence at nucleotide positions 2-11 of the antisense strand, wherein nucleotide positions are numbered 5' to 3'.

[0018] In any of the foregoing or related aspects, the sense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 769-803 and 1681. In some aspects, the antisense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 804-838.

[0019] In some aspects, the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 769 and 804, respectively;
b) SEQ ID NOs: 770 and 805, respectively;
c) SEQ ID NOs: 771 and 806, respectively;
d) SEQ ID NOs: 772 and 807, respectively;
e) SEQ ID NOs: 773 and 808, respectively;
f) SEQ ID NOs: 774 and 809, respectively;
g) SEQ ID NOs: 775 and 810, respectively;
h) SEQ ID NOs: 776 and 811, respectively;
i) SEQ ID NOs: 777 and 812, respectively;
j) SEQ ID NOs: 778 and 813, respectively;
k) SEQ ID NOs: 779 and 814, respectively;
l) SEQ ID NOs: 780 and 815, respectively;
m) SEQ ID NOs: 781 and 816, respectively;
n) SEQ ID NOs: 782 and 817, respectively;
o) SEQ ID NOs: 783 and 818, respectively;
p) SEQ ID NOs: 784 and 819, respectively;
q) SEQ ID NOs: 785 and 820, respectively;
r) SEQ ID NOs: 786 and 821, respectively;
s) SEQ ID NOs: 787 and 822, respectively;

t) SEQ ID NOs: 788 and 823, respectively;

u) SEQ ID NOs: 789 and 824, respectively;

v) SEQ ID NOs: 790 and 825, respectively;

w) SEQ ID NOs: 791 and 826, respectively;

x) SEQ ID NOs: 792 and 827, respectively;

y) SEQ ID NOs: 793 and 828, respectively;

z) SEQ ID NOs: 794 and 829, respectively;

aa) SEQ ID NOs: 795 and 830, respectively;

bb) SEQ ID NOs: 796 and 831, respectively;

cc) SEQ ID NOs: 797 and 832, respectively;

dd) SEQ ID NOs: 798 and 833, respectively;

ee) SEQ ID NOs: 799 and 834, respectively;

ff) SEQ ID NOs: 800 and 835, respectively;

gg) SEQ ID NOs: 801 and 836, respectively;

hh) SEQ ID NOs: 802 and 837, respectively;

ii) SEQ ID NOs: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively.

[0020] In some aspects, the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively;

j) SEQ ID NOs: 803 and 838, respectively;

k) SEQ ID NOs: 1681 and 815, respectively.

[0021] In some aspects, the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

d) SEQ ID NOs: 798 and 833, respectively;

e) SEQ ID NOs: 799 and 834, respectively;

f) SEQ ID NOs: 803 and 838, respectively; and

g) SEQ ID NOs: 1681 and 815, respectively.

[0022] In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 771, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 806. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 780, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 815. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 781, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 816. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 798, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 833. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 799, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 834. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 803, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 838. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 1681, and the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 815.

[0023] In any of the foregoing or related aspects, the antisense strand is 22 nucleotides in length. In some aspects, the antisense strand comprises a nucleotide sequence selected from SEQ ID NOs: 806, 815, 816, 833, 834, and 838. In some aspects, the sense strand is 36 nucleotides in length. In some aspects, the sense strand comprises a nucleotide sequence selected from SEQ ID NOs: 1130,

1095, 1096, 1119, 1120, and 1124. In some aspects, the sense strand comprises a nucleotide sequence selected from SEQ ID NOs: 771, 780, 781, 798, 799, and 803.

[0024] In any of the foregoing or related aspects, the sense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 839-873 and 1682. In some aspects, the antisense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 874-908.

[0025] In some aspects, the sense strand and antisense strands comprise nucleotide sequences selected from:

a) SEQ ID NOs: 839 and 874, respectively;
b) SEQ ID NOs: 840 and 875, respectively;
c) SEQ ID NOs: 841 and 876, respectively;
d) SEQ ID NOs: 842 and 877, respectively;
e) SEQ ID NOs: 843 and 878, respectively;
f) SEQ ID NOs: 844 and 879, respectively;
g) SEQ ID NOs: 845 and 880, respectively;
h) SEQ ID NOs: 846 and 881, respectively;
i) SEQ ID NOs: 847 and 882, respectively;
j) SEQ ID NOs: 848 and 883, respectively;
k) SEQ ID NOs: 849 and 884, respectively;
l) SEQ ID NOs: 850 and 885, respectively;
m) SEQ ID NOs: 851 and 886, respectively;
n) SEQ ID NOs: 852 and 887, respectively;
o) SEQ ID NOs: 853 and 888, respectively;
p) SEQ ID NOs: 854 and 889, respectively;
q) SEQ ID NOs: 855 and 890, respectively;
r) SEQ ID NOs: 856 and 891, respectively;
s) SEQ ID NOs: 857 and 892, respectively;
t) SEQ ID NOs: 858 and 893, respectively;
u) SEQ ID NOs: 859 and 894, respectively;
v) SEQ ID NOs: 860 and 895, respectively;

w) SEQ ID NOs: 861 and 896, respectively;

x) SEQ ID NOs: 862 and 897, respectively;

y) SEQ ID NOs: 863 and 898, respectively;

z) SEQ ID NOs: 864 and 899, respectively;

aa) SEQ ID NOs: 865 and 900, respectively;

bb) SEQ ID NOs: 866 and 901, respectively;

cc) SEQ ID NOs: 867 and 902, respectively;

dd) SEQ ID NOs: 868 and 903, respectively;

ee) SEQ ID NOs: 869 and 904, respectively;

ff) SEQ ID NOs: 870 and 905, respectively;

gg) SEQ ID NOs: 871 and 906, respectively;

hh) SEQ ID NOs: 872 and 907, respectively;

ii) SEQ ID NOs: 873 and 908, respectively; and

jj) SEQ ID NOs: 1682 and 885, respectively.

[0026] In other aspects, the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 860 and 895, respectively;

b) SEQ ID NOs: 865 and 900, respectively;

c) SEQ ID NOs: 868 and 903, respectively;

d) SEQ ID NOs: 869 and 904, respectively;

e) SEQ ID NOs: 873 and 908, respectively;

f) SEQ ID NOs: 841 and 876, respectively;

g) SEQ ID NOs: 846 and 881, respectively;

h) SEQ ID NOs: 850 and 885, respectively;

i) SEQ ID NOs: 851 and 886, respectively;

j) SEQ ID NOs: 852 and 887, respectively; and

k) SEQ ID NOs: 1682 and 885, respectively.

[0027] In certain aspects, the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 841 and 876, respectively;

b) SEQ ID NOs: 850 and 885, respectively;

c) SEQ ID NOs: 851 and 886, respectively;

d) SEQ ID NOs: 868 and 903, respectively;

e) SEQ ID NOs: 869 and 904, respectively;

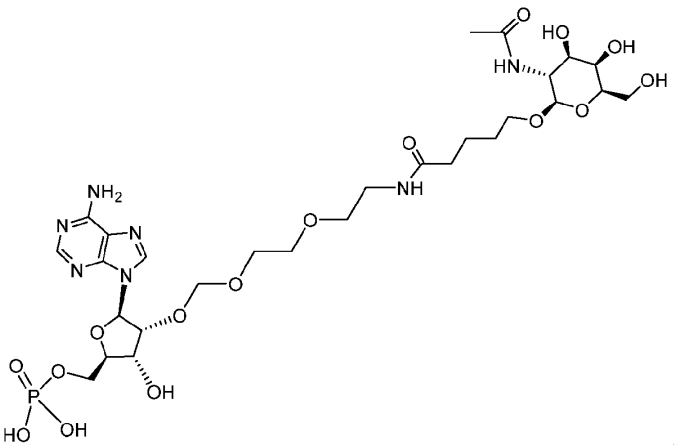
f) SEQ ID NOs: 873 and 908, respectively; and

g) SEQ ID NOs: 1682 and 885, respectively.

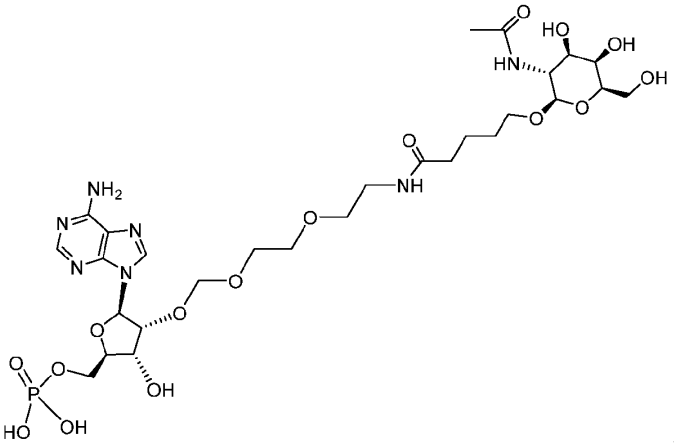
[0028] In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 841, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 876. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 850, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 885. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 851, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 886. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 868, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 903. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 869, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 904. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 873, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 908. In some aspects, the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 1682, and the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 885.

[0029] In some aspects, the sense strand comprises the sequence and all of the modifications of 5'-[mAs][mG][fA][mG][fU][mG][mU][fG][mG][fA][mA][fA][fA][mA][fA][mA][fA][mA] [mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc] [ademAGalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 841), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fCs][fU][fU][fU][mU][fU][mU][mU][fU][mU][mC][mC][fA][mC][fA][mC][mU][fC][m

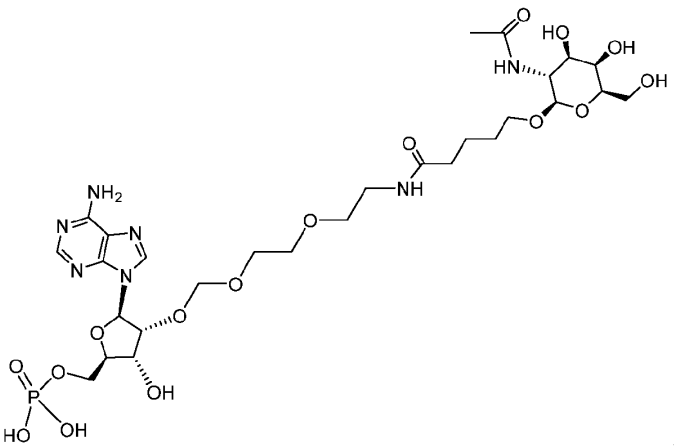
Us][mGs][mG]-3' (SEQ ID NO: 876), wherein mC, mA, mG, mU=2'-OMe ribonucleosides; fA, fC, fG, fU=2'-F ribonucleosides; s=phosphorothioate, and wherein ademA-GalNAc =



[0030] In some aspects, the sense strand comprises the sequence and all of the modifications of 5'-[mCs][mA][fG][mG][fU][mG][mG][fA][mA][fG][mU][fA][fA][mA][fA][mU][fC][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 850), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fCs][fA][fG][fA][mU][fU][mU][mU][fA][mC][mU][mU][fC][mC][fA][mC][mC][fU][mGs][mGs][mG]-3' (SEQ ID NO: 885), wherein mC, mA, mG, mU=2'-OMe ribonucleosides; fA, fC, fG, fU=2'-F ribonucleosides; s=phosphorothioate, and wherein ademA-GalNAc =

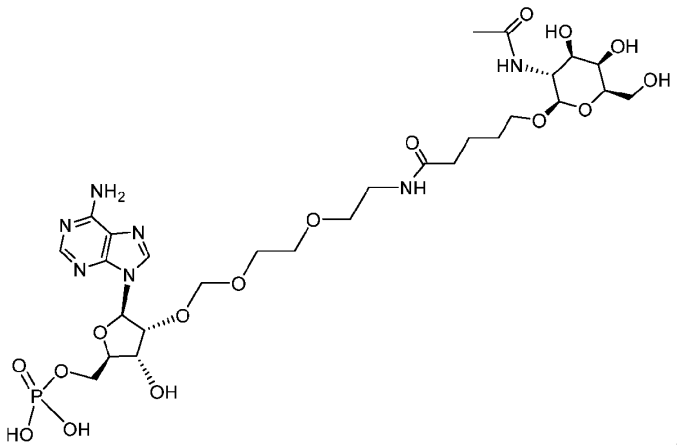


[0031] In some aspects, the sense strand comprises the sequence and all of the modifications of 5'-[mAs][mG][fG][mU][fG][mG][mA][fA][mG][fU][mA][fA][fA][mA][fU][mC][fU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 851), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fUs][fC][fA][fG][mA][fU][mU][mU][fU][mA][mC][mU][fU][mC][fC][mA][mC][fC][mUs][mGs][mG]-3' (SEQ ID NO: 886), wherein mC, mA, mG, mU=2'-OMe ribonucleosides; fA, fC, fG, fU=2'-F ribonucleosides; s=phosphorothioate, and wherein ademA-GalNAc =

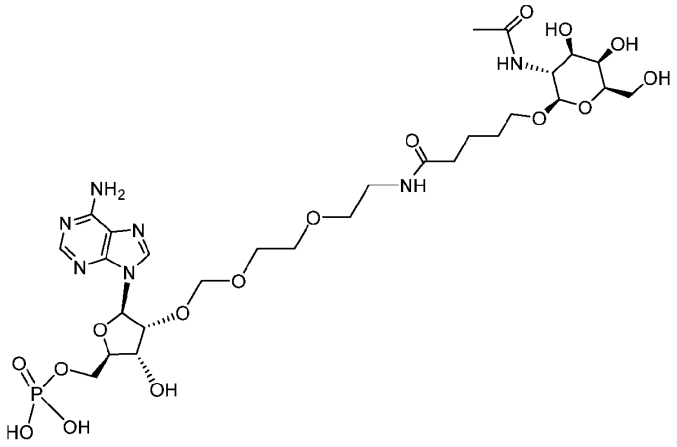


[0032] In some aspects, the sense strand comprises the sequence and all of the modifications of 5'-[mAs][mG][fG][mA][fA][mA][mU][fA][mA][fA][mA][fA][fG][mA][fU][mU][fG][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 868), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fUs][fU][fC][fA][mA][fU][mC][mU][fU][mU][mU][mU][fA][mU][fU][mU][mC][fC][mUs][mGs][mG]-3' (SEQ ID NO: 903), wherein mC, mA, mG, mU=2'-OMe ribonucleosides; fA,

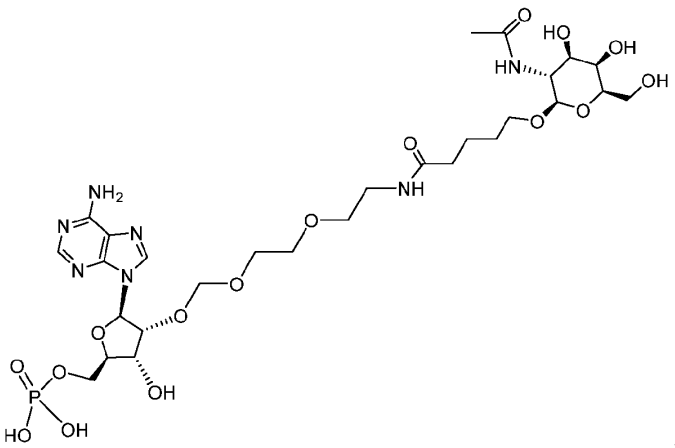
fC, fG, fU=2'-F ribonucleosides; s=phosphorothioate, and wherein ademA-GalNAc =



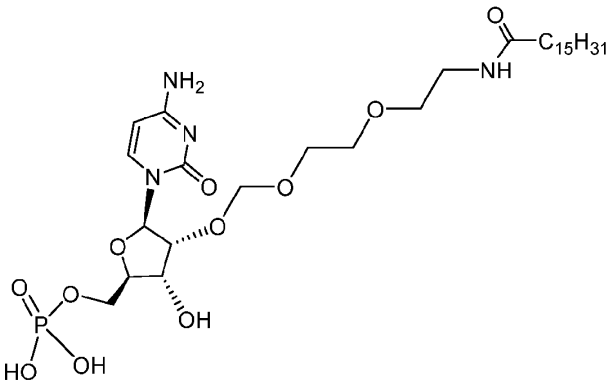
[0033] In some aspects, the sense strand comprises the sequence and all of the modifications of 5'-[mGs][mG][fA][mA][fA][mU][mA][fA][mA][fA][mA][fG][fA][mU][fU][mG][fA][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 869), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fUs][fU][fU][fC][mA][fA][mU][mC][fU][mU][mU][mU][fU][mA][fU][mU][mU][fC][mCs][mGs][mG]-3' (SEQ ID NO: 904), wherein mC, mA, mG, mU=2'-OMe ribonucleosides; fA, fC, fG, fU=2'-F ribonucleosides; s=phosphorothioate, and wherein ademA-GalNAc =



[0034] In some aspects, the sense strand comprises the sequence and all of the modifications of 5'-[mAs][mU][fA][mA][fA][mA][mA][fG][mA][fU][mU][fG][fA][mA][fA][mC][fC][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 873), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fUs][fG][fG][fG][mU][fU][mU][mC][fA][mA][mU][mC][fU][mU][fU][mU][mU][fA][mUs][mGs][mG]-3' (SEQ ID NO: 908), wherein mC, mA, mG, mU=2'-OMe ribonucleosides; fA, fC, fG, fU=2'-F ribonucleosides; s=phosphorothioate, and wherein ademA-GalNAc =



[0035] In some aspects, the sense strand comprises the sequence and all of the modifications of 5'-[ademCs-C_{16}][mA][fG][mG][fU][mG][mG][fA][mA][fG][mU][fA][fA][mA][fA][mU][fC][mUs][mGs][mA]-3' (SEQ ID NO: 1682), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fCs][fA][fG][fA][mU][fU][mU][mU][fA][mC][mU][mU][fC][mC][fA][mC][mC][fU][mGs][mGs][mG]-3' (SEQ ID NO: 885), wherein mC, mA, mG, mU=2'-OMe ribonucleosides; fA, fC, fG, fU=2'-F ribonucleosides; s=phosphorothioate, and [ademCs-C_{16}]=cytosine conjugated to C_{16} hydrocarbon chain:



[0036] In some aspects, the disclosure provides a pharmaceutical composition comprising a RNAi oligonucleotide described herein, and a pharmaceutically acceptable carrier, delivery agent or excipient.

[0037] In other aspects, the disclosure provides a method for treating a subject having a disease, disorder or condition associated with *MAPT* gene expression, the method comprising administering to the subject a therapeutically effective amount of a RNAi oligonucleotide described herein, or pharmaceutical composition thereof, thereby treating the subject.

[0038] In further aspects, the disclosure provides a method of delivering an oligonucleotide to a subject, the method comprising administering a pharmaceutical composition described herein to the subject.

[0039] In yet further aspects, the disclosure provides, a method for reducing *MAPT* gene expression in a cell, a population of cells or a subject, the method comprising the step of:

i. contacting the cell or the population of cells with a RNAi oligonucleotide or pharmaceutical composition described herein; or

ii. administering to the subject a RNAi oligonucleotide or pharmaceutical composition described herein.

[0040] In some aspects, reducing *MAPT* gene expression comprises reducing an amount or level of MAPT mRNA, an amount or level of Tau protein, or both. In some aspects, a RNAi oligonucleotide or pharmaceutical composition described herein the subject has a disease, disorder, or condition associated with *MAPT* gene expression. In some aspects, the disease, disorder, or condition associated with *MAPT* gene expression is AD, frontotemporal dementia (FTD), PSP,

PD, Tau protein-associated diseases, primary age-related tauopathy, chronic traumatic encephalopathy, corticobasal degeneration, Lytico-bodig disease, ganglioglioma, meningioangiomatosis, postencephalitic parkinsonism, or subacute sclerosing panencephalitis.

[0041] In any of the foregoing or related aspects, *MAPT* gene expression is reduced in tissue of one or more regions of the CNS, wherein the tissue is associated with AD. In some aspects, tissue associated with AD is selected from: prefrontal cortex, motor cortex, temporal cortex, parietal cortex, and hippocampus. In some aspects, *MAPT* gene expression is reduced in tissue of one or more regions of the CNS, wherein the tissue is associated with PSP. In some aspects, tissue associated with PSPy is selected from: caudate nucleus, globus pallidus, thalamus, midbrain tegmentum, substantia nigra, pons, cerebellar white matter, cerebellar dentate nucleus, medulla, cervical spinal cord, thoracic spinal cord, and lumbar spinal cord. In some aspects, *MAPT* gene expression is reduced in one or more regions of the CNS selected from: cervical spinal cord, thoracic spinal cord, lumbar spinal cord, frontal cortex, temporal cortex, cerebellum, midbrain, occipital cortex, parietal cortex, hippocampus, caudate nucleus, thalamus, brainstem, motor cortex, globus pallidus, midbrain tegmentum, substantia nigra, pons, cerebellar white matter, and cerebellar dentate nucleus.

[0042] In any of the foregoing or related aspects, the RNAi oligonucleotide, or pharmaceutical composition is administered in combination with a second composition or therapeutic agent.

[0043] In other aspects, the disclosure provides use of a RNAi oligonucleotide or pharmaceutical composition described herein in the manufacture of a medicament for the treatment of a disease, disorder, or condition associated with *MAPT* gene expression.

[0044] In further aspects, the disclosure provides a RNAi oligonucleotide or pharmaceutical composition described herein for use, or adaptable for use, in the treatment of a disease, disorder, or condition associated with *MAPT* gene expression.

[0045] In some aspects, the disclosure provides a kit comprising the a RNAi oligonucleotide described herein, an optional pharmaceutically acceptable carrier, and a package insert comprising instructions for administration to a subject having a disease, disorder, or condition associated with *MAPT* gene expression.

[0046] In any of the foregoing or related aspects, the disease, disorder, or condition associated with *MAPT* gene expression is AD, FTD, PD, PSP, Tau protein-associated diseases, primary age-related tauopathy, chronic traumatic encephalopathy, corticobasal degeneration, Lytico-bodig disease, ganglioglioma, meningioangiomatosis, postencephalitic parkinsonism, or subacute sclerosing panencephalitis.

BRIEF DESCRIPTION OF THE FIGURES

[0047] The advantages, effects, features, and objects other than those set forth above will become more readily apparent when consideration is given to the detailed description below. Such detailed description refers to the following drawings, where:

[0048] FIGs. 1A and 1B provide graphs depicting the percent (%) of human MAPT mRNA remaining in the liver of mice exogenously expressing human *MAPT* (hydrodynamic injection model) after treatment with GalNAc-conjugated MAPT oligonucleotides specific for human (Hs) *MAPT* or human and NHP (Hs-Mf; "double-common") *MAPT*. CD-1 mice were dosed subcutaneously with 3 mg/kg of the indicated GalNAc-conjugated *MAPT*-targeting oligonucleotide formulated in PBS. Four days post-dose, mice were hydrodynamically injected (HDI) with a DNA plasmid encoding human *MAPT*. The level of human MAPT mRNA was determined from livers collected 18 hours later.

[0049] FIGs. 2A and 2B provide graphs depicting the dose response of GalNAc-conjugated *MAPT*-targeting oligonucleotides selected based on inhibitory efficacy shown in FIGs. 1A-1B in addition to GalNAc-conjugated *MAPT*-targeting oliognucleotides specific for human (Hs), NHP (Mf), and murine (Mm) *MAPT*. The percent (%) of MAPT mRNA remaining in liver tissue was measured in CD-1 HDI mice as described in FIGs. 1A-1B. Following injection with 0.3 mg/kg, 1.0 mg/kg, or 3.0 mg/kg of the indicated GalNAc-conjugated *MAPT*-targeting oligonucleotide, percent (%) mRNA remaining was determined in two cohorts, FIG. 2A (Set I) and FIG. 2B (Set II). Hs = construct is human MAPT specific; Hs-Mf = construct is human and monkey MAPT specific.

[0050] FIGs. 3A-3M provide graphs depicting the percent (%) of human MAPT mRNA remaining in the CNS of NHP after treatment with GalNAc-conjugated *MAPT*-targeting

oligonucleotides. NHPs were dosed by intra cisterna magna (i.c.m) injection with 50 mg of the indicated GalNAc-conjugated *MAPT*-targeting oligonucleotide formulated in artificial cerebrospinal fluid (aCSF) on study days 0 and 7. The level of MAPT mRNA was determined relative to the percent (%) of MAPT mRNA remaining in aCSF-treated animals. CNS tissues measured included cervical spinal cord (FIG. 3A), thoracic spinal cord (FIG. 3B), lumbar spinal cord (FIG. 3C), frontal cortex (FIG. 3D), temporal cortex (FIG. 3E), cerebellum (FIG. 3F), midbrain (FIG. 3G), occipital cortex (FIG. 3H), parietal cortex (FIG. 3I), hippocampus (FIG. 3J), caudate nucleus (FIG. 3K), thalamus (FIG. 3L), and brainstem (FIG. 3M).

[0051] FIGs. 4A-4B provide schematics of a lipid-conjugated RNAi oligonucleotide (FIG. 4A) and a GalNAc-conjugated RNAi oligonucleotide (FIG. 4B).

[0052] FIGs. 5A-5B provide graphs depicting the percent (%) of NHP (Mf) MAPT mRNA remaining (FIG. 5A) and concentration of oligonucleotide (FIG. 5B) in CNS tissue associated with AD. NHPs were intrathecally administered MAPT-2357 conjugated to a C_{16} lipid or GalNAc, as shown in the modification patterns of FIGs. 4A-4B. Tissue was collected and analyzed 28 days after administration of the indicated oligonucleotide.

[0053] FIGs. 6A-6B provide graphs depicting the percent (%) of NHP (Mf) MAPT mRNA remaining (FIG. 6A) and concentration of oligonucleotide (FIG. 6B) in CNS tissue associated with PSP. NHPs were intrathecally administered MAPT-2357 conjugated to a C_{16} lipid or GalNAc, as shown in the modification patterns of FIGs. 4A-4B. Tissue was collected and analyzed 28 days after administration of the indicated oligonucleotide.

DETAILED DESCRIPTION

[0054] According to some aspects, the disclosure provides oligonucleotides such as RNAi oligonucleotides that reduce *MAPT* gene expression in the CNS. In some embodiments, the oligonucleotides provided herein are designed to treat diseases associated with *MAPT* gene expression in the CNS. In some respects, the disclosure provides methods of treating a disease associated with *MAPT* by reducing *MAPT* gene expression in cells (*e.g.*, cells of the CNS).

[0055] Oligonucleotide Inhibitors of *MAPT* Gene Expression

[0056] The disclosure provides, *inter alia,* oligonucleotides that inhibit *MAPT* gene expression (*e.g.*, RNAi oligonucleotides). In some embodiments, the oligonucleotide that inhibits *MAPT* gene expression is targeted to a MAPT mRNA.

[0057] ***MAPT Target Sequences***

[0058] In some embodiments, an oligonucleotide herein (*e.g.*, a RNAi oligonucleotide) is targeted to a target sequence comprising a MAPT mRNA. In some embodiments, the oligonucleotide is targeted to a target sequence within a MAPT mRNA sequence.

[0059] In some embodiments, the oligonucleotide corresponds to a target sequence within a MAPT mRNA sequence. In some embodiments, the oligonucleotide, or a portion, fragment, or strand thereof (*e.g.*, an antisense strand or a guide strand of a RNAi oligonucleotide) binds or anneals to a target sequence comprising MAPT mRNA, thereby inhibiting *MAPT* gene expression.

[0060] In some embodiments, the oligonucleotide is targeted to a *MAPT* target sequence for the purpose of inhibiting *MAPT* gene expression *in vivo*. In some embodiments, the amount or extent of inhibition of *MAPT* gene expression by the oligonucleotide targeted to a *MAPT* target sequence correlates with the potency of the oligonucleotide. In some embodiments, the amount or extent of *MAPT* gene expression inhibition by the oligonucleotide targeted to a *MAPT* target sequence correlates with the amount or extent of therapeutic benefit in a subject or patient having a disease, disorder, or condition associated with *MAPT* gene expression treated with the oligonucleotide.

[0061] In some embodiments, a sense strand of the oligonucleotide comprises a *MAPT* target sequence. In some embodiments, a portion or region of the sense strand of the oligonucleotide (*e.g.*, a RNAi oligonucleotide) comprises a *MAPT* target sequence. In some embodiments, the *MAPT* target sequence comprises, or consists of, a nucleotide sequence of any one of SEQ ID NOs: 912-1295. In some embodiments, the *MAPT* target sequence comprises, or consists of, a nucleotide sequence of any one of SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, 1124, and 924. In some embodiments, the *MAPT* target sequence comprises, or consists of, a nucleotide sequence of any one of SEQ ID NOs: 1061, 1108, 1119, 1120, 1124, 1130, 1065, 1095, 1096, and 1102. In some embodiments,

the *MAPT* target sequence comprises, or consists of, a nucleotide sequence of any one of SEQ ID NOs: 1130, 1095, 1096, 1119, 1120, and 1124. In some embodiments, the *MAPT* target sequence comprises the nucleotide sequence set forth in SEQ ID NO: 1130. In some embodiments, the *MAPT* target sequence comprises the nucleotide sequence set forth in SEQ ID NO: 1095. In some embodiments, the *MAPT* target sequence comprises the nucleotide sequence set forth in SEQ ID NO: 1096. In some embodiments, the *MAPT* target sequence comprises the nucleotide sequence set forth in SEQ ID NO: 1119. In some embodiments, the MAPT target sequence comprises the nucleotide sequence set forth in SEQ ID NO: 1120. In some embodiments, the *MAPT* target sequence comprises the nucleotide sequence set forth in SEQ ID NO: 1124.

[0062] ***MAPT mRNA Targeting Sequences***

[0063] In some embodiments, an oligonucleotide herein (*e.g.*, a RNAi oligonucleotide) has a region of complementarity to MAPT mRNA (*e.g.*, within a target sequence of MAPT mRNA) for purposes of targeting the mRNA in cells and inhibiting its expression. In some embodiments, the oligonucleotide comprises a MAPT mRNA target sequence (*e.g.*, an antisense strand or a guide strand of a ds oligonucleotide such as a RNAi oligonucleotide) having a region of complementarity that binds or anneals to a MAPT target sequence by complementary (Watson-Crick) base pairing. The targeting sequence or region of complementarity is generally of suitable length and base content to enable binding or annealing of the oligonucleotide (or a strand thereof) to a MAPT mRNA for purposes of inhibiting its expression. In some embodiments, the targeting sequence or region of complementarity is at least about 12, at least about 13, at least about 14, at least about 15, at least about 16, at least about 17, at least about 18, at least about 19, at least about 20, at least about 21, at least about 22, at least about 23, at least about 24, at least about 25, at least about 26, at least about 27, at least about 28, at least about 29 or at least about 30 nucleotides in length. In some embodiments, the targeting sequence or region of complementarity is at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or at least 20 nucleotides. In some embodiments, the targeting sequence or region of complementarity is about 12 to about 30 (*e.g.*, 12 to 30, 12 to 22, 15 to 25, 17 to 21, 18 to 27, 19 to 27, or 15 to 30) nucleotides in length. In some embodiments, the targeting sequence or region of complementarity is about 12, 13, 14,

15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. In some embodiments, the targeting sequence or region of complementarity is 18 nucleotides in length. In some embodiments, the targeting sequence or region of complementarity is 19 nucleotides in length. In some embodiments, the targeting sequence or region of complementarity is 20 nucleotides in length. In some embodiments, the targeting sequence or region of complementarity is 21 nucleotides in length. In some embodiments, the targeting sequence or region of complementarity is 22 nucleotides in length. In some embodiments, the targeting sequence or region of complementarity is 23 nucleotides in length. In some embodiments, the targeting sequence or region of complementarity is 24 nucleotides in length. In some embodiments, the oligonucleotide comprises a target sequence or region of complementarity complementary to a sequence of any one of SEQ ID NOs: 912-1295, and the targeting sequence or region of complementarity is 18 nucleotides in length. In some embodiments, the oligonucleotide comprises a target sequence or region of complementarity complementary to a sequence of any one of SEQ ID NOs: 912-1295, and the targeting sequence or region of complementarity is 19 nucleotides in length. In some embodiments, the oligonucleotide comprises a target sequence or region of complementarity complementary to a sequence of any one of SEQ ID NOs: 1-384, and the targeting sequence or region of complementarity is 20 nucleotides in length. In some embodiments, the oligonucleotide comprises a target sequence or region of complementarity complementary to a sequence of any one of SEQ ID NOs: 1-384, and the targeting sequence or region of complementarity is 21 nucleotides in length. In some embodiments, the oligonucleotide comprises a target sequence or region of complementarity complementary to a sequence of any one of SEQ ID NOs: 1-384, and the targeting sequence or region of complementarity is 22 nucleotides in length. In some embodiments, the oligonucleotide comprises a target sequence or region of complementarity complementary to a sequence of any one of SEQ ID NOs: 1-384, and the targeting sequence or region of complementarity is 23 nucleotides in length. In some embodiments, the oligonucleotide comprises a target sequence or region of complementarity complementary to a sequence of any one of SEQ ID NOs: 1-384, and the targeting sequence or region of complementarity is 24 nucleotides in length.

[0064] In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementarity (*e.g.*, an antisense strand or a guide strand of a ds oligonucleotide) that is fully complementary to a MAPT mRNA target sequence. In some embodiments, the targeting sequence or region of complementarity is partially complementary to a MAPT mRNA target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to a sequence of any one of SEQ ID NOs: 912-1295. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to a sequence of any one of SEQ ID NOs: 912-1295. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to a sequence of any one of SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, 1124, or 924. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to a sequence of any one of SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, 1124, or 924. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to a sequence of any one of SEQ ID NOs: 1061, 1108, 1119, 1120, 1124, 1130, 1065, 1095, 1096, or 1102. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to a sequence of any one of SEQ ID NOs: 1061, 1108, 1119, 1120, 1124, 1130, 1065, 1095, 1096, or 1102. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to a sequence of any one of SEQ ID NOs: 1130, 1095, 1096, 1119, 1120, and 1124. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to a sequence of any one of SEQ ID NOs: 1130, 1095, 1096, 1119, 1120, and 1124. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to the sequence set forth in SEQ ID NO: 1130. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully

complementary to the sequence set forth in SEQ ID NO: 1095. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to the sequence set forth in SEQ ID NO: 1096. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to the sequence set forth in SEQ ID NO: 1119. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to the sequence set forth in SEQ ID NO: 1120. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to the sequence set forth in SEQ ID NO: 1124. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to a sequence of any one of SEQ ID NOs: 1130. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to the sequence of SEQ ID NO: 1095. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to the sequence of SEQ ID NO: 1096. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to the sequence of SEQ ID NO: 1119. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to the sequence of SEQ ID NO: 1120. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to the sequence of SEQ ID NO: 1124.

[0065] In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is complementary to a contiguous sequence of nucleotides comprising a MAPT mRNA, wherein the contiguous sequence of nucleotides is about 12 to about 30 nucleotides in length (*e.g.*, 12 to 30, 12 to 28, 12 to 26, 12 to 24, 12 to 20, 12 to 18, 12 to 16, 14 to 22, 16 to 20, 18 to 20, or 18 to 19 nucleotides in length). In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is complementary to a contiguous sequence of nucleotides comprising a MAPT mRNA, wherein the contiguous sequence of nucleotides is 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides in length. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity

that is complementary to a contiguous sequence of nucleotides comprising a MAPT mRNA, wherein the contiguous sequence of nucleotides is 19 nucleotides in length. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is complementary to a contiguous sequence of nucleotides comprising a MAPT mRNA, wherein the contiguous sequence of nucleotides is 20 nucleotides in length.

[0066] In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementarity that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 912-1295, optionally where the contiguous sequence of nucleotides is 19 nucleotides in length. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementarity that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, 1124, and 924, optionally wherein the contiguous sequence of nucleotides is 19 nucleotides in length. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementarity that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1061, 1108, 1119, 1120, 1124, 1130, 1065, 1095, 1096, and 1102, optionally where the contiguous sequence of nucleotides is 19 nucleotides in length. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementarity that is complementary to a contiguous sequence of nucleotides of SEQ ID NO: 1130, 1095, 1096, 1119, 1120, and 1124, optionally where the contiguous sequence of nucleotides is 19 nucleotides in length.

[0067] In some embodiments, the targeting sequence or region of complementarity of the oligonucleotide is complementary to contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 912-1295 and spans the entire length of the antisense strand. In some embodiments, the targeting sequence or region of complementarity of the oligonucleotide is complementary to contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 912-1295 and spans a portion of the entire length of an antisense strand. In some embodiments, the oligonucleotide comprises a region of complementarity (*e.g.*, on an antisense strand of a ds oligonucleotide) that is at least partially (*e.g.*, fully) complementary to a contiguous stretch of

nucleotides spanning nucleotides 1-20 of a sequence as set forth in any one of SEQ ID NOs: 912-1295. In some embodiments, the targeting sequence or region of complementarity of the oligonucleotide is complementary to contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 1-384 and spans the entire length of an antisense strand. In some embodiments, the region of complementarity of the oligonucleotide is complementary to contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 1-384 and spans a portion of the entire length of an antisense strand. In some embodiments, the oligonucleotide comprises the region of complementarity (*e.g.*, on an antisense strand of a ds oligonucleotide) that is at least partially (*e.g.*, fully) complementary to a contiguous stretch of nucleotides spanning nucleotides 1-19 of a sequence as set forth in any one of SEQ ID NOs: 1-384.

[0068] In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having one or more base pair (bp) mismatches with the corresponding MAPT mRNA target sequence. In some embodiments, the targeting sequence or region of complementarity may have up to about 1, up to about 2, up to about 3, up to about 4, up to about 5, *etc.* mismatches with the corresponding MAPT mRNA target sequence provided that the ability of the targeting sequence or region of complementarity to bind or anneal to MAPT mRNA under appropriate hybridization conditions and/or the ability of the oligonucleotide to inhibit *MAPT* gene expression is maintained. Alternatively, in some embodiments, the targeting sequence or region of complementarity comprises no more than 1, no more than 2, no more than 3, no more than 4, or no more than 5 mismatches with the corresponding MAPT mRNA target sequence provided that the ability of the targeting sequence or region of complementarity to bind or anneal to MAPT mRNA under appropriate hybridization conditions and/or the ability of the oligonucleotide to inhibit *MAPT* gene expression is maintained. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having 1 mismatch with the corresponding target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having 2 mismatches with the corresponding target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having 3 mismatches with the corresponding target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having 4 mismatches

with the corresponding target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having 5 mismatches with the corresponding target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity more than one mismatch (*e.g.*, 2, 3, 4, 5, or more mismatches) with the corresponding target sequence, wherein at least 2 (*e.g.*, all) of the mismatches are positioned consecutively (*e.g.*, 2, 3, 4, 5, or more mismatches in a row), or wherein the mismatches are interspersed in any position throughout the targeting sequence or region of complementarity. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity more than one mismatch (*e.g.*, 2, 3, 4, 5, or more mismatches) with the corresponding target sequence, wherein at least 2 (*e.g.*, all) of the mismatches are positioned consecutively (*e.g.*, 2, 3, 4, 5, or more mismatches in a row), or wherein at least one or more non-mismatched base pair is located between the mismatches, or a combination thereof.

[0069] In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 912-1295, wherein the targeting sequence or region of complementarity may have up to about 1, up to about 2, up to about 3, up to about 4, up to about 5, *etc.* mismatches with the corresponding MAPT mRNA target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 912-1295, wherein the targeting sequence or region of complementarity may have no more than 1, no more than 2, no more than 3, no more than 4, or no more than 5 mismatches with the corresponding MAPT mRNA target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, 1124, and 924, wherein the targeting sequence or region of complementarity may have up to about 1, up to about 2, up to about 3, up to about 4, up to about 5, *etc.* mismatches with the corresponding MAPT mRNA target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is

complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, 1124, and 924, wherein the targeting sequence or region of complementarity may have no more than 1, no more than 2, no more than 3, no more than 4, or no more than 5 mismatches with the corresponding MAPT mRNA target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1061, 1108, 1119, 1120, 1124, 1130, 1065, 1095, 1096, and 1102, wherein the targeting sequence or region of complementarity may have up to about 1, up to about 2, up to about 3, up to about 4, up to about 5, *etc.* mismatches with the corresponding MAPT mRNA target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1061, 1108, 1119, 1120, 1124, 1130, 1065, 1095, 1096, and 1102, wherein the targeting sequence or region of complementarity may have no more than 1, no more than 2, no more than 3, no more than 4, or no more than 5 mismatches with the corresponding MAPT mRNA target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1130, 1095, 1096, 1119, 1120, and 1124, wherein the targeting sequence or region of complementarity may have up to about 1, up to about 2, up to about 3, up to about 4, up to about 5, *etc.* mismatches with the corresponding MAPT mRNA target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1130, 1095, 1096, 1119, 1120, and 1124, wherein the targeting sequence or region of complementarity may have no more than 1, no more than 2, no more than 3, no more than 4, or no more than 5 mismatches with the corresponding MAPT mRNA target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of SEQ ID NO: 1095, wherein the targeting sequence or region of complementarity may have up to about 1, up to about 2, up to about 3, up to about 4, up to about

5, *etc.* mismatches with the corresponding MAPT mRNA target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of SEQ ID NO: 1095, wherein the targeting sequence or region of complementarity may have no more than 1, no more than 2, no more than 3, no more than 4, or no more than 5 mismatches with the corresponding MAPT mRNA target sequence.

[0070] ***Types of Oligonucleotides***

[0071] A variety of oligonucleotide types and/or structures are useful for targeting MAPT mRNA in the methods herein including, but not limited to, RNAi oligonucleotides. Any of the oligonucleotide types described herein or elsewhere are contemplated for use as a framework to incorporate a MAPT mRNA targeting sequence herein for the purposes of inhibiting *MAPT* gene expression.

[0072] In some embodiments, the oligonucleotides herein inhibit *MAPT* gene expression by engaging with RNA interference (RNAi) pathways upstream or downstream of Dicer involvement (*e.g.*, a RNAi oligonucleotide). For example, RNAi oligonucleotides have been developed with each strand having sizes of about 19-25 nucleotides with at least one 3' overhang of about 1 to about 5 nucleotides (*see*, *e.g.*, US Patent No. 8,372,968). Longer oligonucleotides also have been developed that are processed by Dicer to generate active RNAi products (*see*, *e.g.*, US Patent No. 8,883,996). Further work produced extended ds oligonucleotides where at least one end of at least one strand is extended beyond a duplex targeting region, including structures where one of the strands includes a thermodynamically-stabilizing tetraL structure (*see*, *e.g.*, US Patent Nos. 8,513,207 and 8,927,705, as well as Intl. Patent Application Publication No. WO 2010/033225). Such structures may include single-stranded (ss) extensions (on one or both sides of the molecule) as well as ds extensions.

[0073] In some embodiments, the oligonucleotide engages with the RNAi pathway downstream of the involvement of Dicer (*e.g.*, Dicer cleavage). In some embodiments, the oligonucleotide has an overhang (*e.g.*, of 1, 2, or 3 nucleotides in length) in the 3' end of the sense strand. In some embodiments, the oligonucleotide comprises a 21-nucleotide antisense strand that is antisense to a

target mRNA (*e.g.*, MAPT mRNA) and a complementary sense strand, in which both strands anneal to form a 19-bp duplex and 2 nucleotide overhangs at either or both 3' ends. Longer oligonucleotide designs also are contemplated including oligonucleotides having an antisense strand of 23 nucleotides and a sense strand of 21 nucleotides, where there is a blunt end on the right side of the oligonucleotide (3' end of sense strand/5' end of antisense strand) and a two nucleotide 3' guide strand overhang on the left side of the oligonucleotide (5' end of the sense strand/3' end of the antisense strand). In such molecules, there is a 21 bp duplex region. *See*, *e.g.*, US Patent Nos. 9,012,138; 9,012,621; and 9,193,753.

[0074] In some embodiments, the oligonucleotide comprises sense and antisense strands that are both in the range of about 17 to about 36 (*e.g.*, 17 to 26, 20 to 25, or 21-23) nucleotides in length. In some embodiments, the oligonucleotide comprises an antisense strand of 19-30 nucleotides in length and a sense strand of 19-50 nucleotides in length, where the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand. In some embodiments, the oligonucleotide comprises sense and antisense strands that are both in the range of about 19-22 nucleotides in length. In some embodiments, the sense and antisense strands are of equal length. In some embodiments, the oligonucleotide comprises sense and antisense strands, such that there is a 3' overhang on either the sense strand or the antisense strand, or both the sense and antisense strand. In some embodiments, for oligonucleotides that have sense and antisense strands that are both in the range of about 21-23 nucleotides in length, a 3' overhang on the sense, antisense, or both is/are 1 or 2 nucleotides in length. In some embodiments, the oligonucleotide has a guide strand of 22 nucleotides and a passenger strand of 20 nucleotides, where there is a blunt end on the right side of the molecule (3' end of passenger strand/5' end of guide strand) and a 2 nucleotide 3' guide strand overhang on the left side of the molecule (5' end of the passenger strand/3' end of the guide strand). In such molecules, there is a 20 bp duplex region.

[0075] Other oligonucleotide designs for use with the compositions and methods herein include: 16-mer siRNAs (*see*, *e.g.*, NUCLEIC ACIDS IN CHEMISTRY AND BIOLOGY, Blackburn (ed.), Royal Society of Chemistry, 2006), shRNAs (*e.g.*, having 19 bp or shorter stems; *see*, *e.g.*, Moore *et al.* (2010) METHODS MOL. BIOL. 629:141-58), blunt siRNAs (*e.g.*, of 19 bps in length;

see, e.g., Kraynack & Baker (2006) *RNA* 12:163-76), asymmetrical siRNAs (aiRNA; *see, e.g.*, Sun *et al.* (2008) NAT. BIOTECHNOL. 26:1379-82), asymmetric shorter-duplex siRNA (*see, e.g.*, Chang *et al.* (2009) MOL. THER. 17:725-732), fork siRNAs (*see, e.g.*, Hohjoh (2004) FEBS LETT. 557:193-98), single-stranded siRNAs (Elsner (2012) NAT. BIOTECHNOL. 30:1063), dumbbell-shaped circular siRNAs (*see, e.g.*, Abe *et al.* (2007) J. AM. CHEM. SOC. 129:15108-09), and small internally segmented interfering RNA (siRNA; *see, e.g.*, Bramsen *et al.* (2007) NUCLEIC ACIDS RES. 35:5886-97). Further non-limiting examples of an oligonucleotide structure that may be used in some embodiments to reduce or inhibit the expression of *MAPT* are microRNA (miRNA), short hairpin RNA (shRNA), and short siRNA (*see, e.g.*, Hamilton *et al.* (2002) *EMBO J.* 21:4671-79; *see also*, US Patent Application Publication No. 2009/0099115).

[0076] Still, in some embodiments, the oligonucleotide for reducing or inhibiting *MAPT* gene expression herein is ss. Such structures may include, but are not limited to, ss RNAi molecules. Recent efforts have demonstrated the activity of ss RNAi molecules (*see, e.g.*, Matsui *et al.* (2016) *Mol. Ther.* 24:946-955). However, in some embodiments, the oligonucleotide is an antisense oligonucleotide (ASO). An ASO is a ss oligonucleotide that has a nucleobase sequence which, when written or depicted in the 5' to 3' direction, comprises the reverse complement of a targeted segment of a particular nucleic acid and is suitably modified (*e.g.*, as a gapmer) so as to induce RNaseH-mediated cleavage of its target RNA in cells or (*e.g.*, as a mixmer) so as to inhibit translation of the target mRNA in cells. ASOs for use herein may be modified in any suitable manner known in the art including, for example, as shown in US Patent No. 9,567,587 (including, *e.g.*, length, sugar moieties of the nucleobase (pyrimidine, purine), and alterations of the heterocyclic portion of the nucleobase). Further, ASOs have been used for decades to reduce expression of specific target genes (*see, e.g.*, Bennett *et al.* (2017) *Annu. Rev. Pharmacol.* 57:81-105).

[0077] In some embodiments, the ASO shares a region of complementarity with MAPT mRNA. In some embodiments, the ASO targets various areas of the human *MAPT* identified as NM_001123066.3. In some embodiments, the ASO is about 15-50 nucleotides in length. In some embodiments, the ASO is about 15-25 nucleotides in length. In some embodiments, the ASO is 22 nucleotides in length. In some embodiments, the ASO is complementary to any one of SEQ ID

NOs: 912-1295. In some embodiments, the ASO is at least 15 contiguous nucleotides in length. In some embodiments, the ASO is at least 19 contiguous nucleotides in length. In some embodiments, the ASO is at least 20 contiguous nucleotides in length. In some embodiments, the ASO differs by 1, 2, or 3 nucleotides from the target sequence.

[0078] ***Double-Stranded RNAi Oligonucleotides***

[0079] In some aspects, the disclosure provides ds RNAi oligonucleotides for targeting MAPT mRNA and inhibiting *MAPT* gene expression (*e.g.*, *via* the RNAi pathway) comprising a sense strand (also referred to herein as a passenger strand) and an antisense strand (also referred to herein as a guide strand). In some embodiments, the sense strand and antisense strand are separate strands and are not covalently linked. In some embodiments, the sense strand and the antisense strand are covalently linked. In some embodiments, the sense strand and the antisense strand form a duplex region, wherein the sense strand and the antisense strand, or a portion thereof, binds with one another in a complementary fashion (*e.g.*, by Watson-Crick base pairing).

[0080] In some embodiments, the sense strand has a first region (R1) and a second region (R2), wherein R2 comprises a first subregion (S1), a L (*e.g.*, tetraL or triL), and a second subregion (S2), wherein L is located between S1 and S2, and wherein S1 and S2 form a second duplex (D2). D2 may have various lengths. In some embodiments, D2 is about 1 to about 6 bp in length. In some embodiments, D2 is 2-6, 3-6, 4-6, 5-6, 1-5, 2-5, 3-5, or 4-5 bp in length. In some embodiments, D2 is 1, 2, 3, 4, 5, or 6 bp in length. In some embodiments, D2 is 6 bp in length.

[0081] In some embodiments, R1 of the sense strand and the antisense strand form a first duplex (D1). In some embodiments, D1 is at least about 15 (*e.g.*, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21) nucleotides in length. In some embodiments, D1 is in the range of about 12 to about 30 nucleotides in length (*e.g.*, 12 to 30, 12 to 27, 15 to 22, 18 to 22, 18 to 25, 18 to 27, 18 to 30, or 21 to 30 nucleotides in length). In some embodiments, D1 is at least 12 nucleotides in length (*e.g.*, at least 12, at least 15, at least 20, at least 25, or at least 30 nucleotides in length). In some embodiments, D1 is 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. In some embodiments, D1 is 19 nucleotides in length. In some embodiments, D1 is 20 nucleotides in length. In some embodiments, D1 comprising the

sense strand and the antisense strand does not span the entire length of the sense strand and/or the antisense strand. In some embodiments, D1 comprising the sense strand and the antisense strand spans the entire length of either the sense strand or the antisense strand or both. In certain embodiments, D1 comprising the sense strand and the antisense strand spans the entire length of both the sense strand and the antisense strand.

[0082] In some embodiments, a sense strand described here is 36 nucleotides in length and positions are numbered 1-36 from 5' to 3'. In some embodiments, an antisense strand described herein is 22 nucleotides in length and positions are numbered 1-22 from 5' to 3'. In some embodiments, position numbers described herein adhere to this numbering format.

[0083] In some embodiments, the RNAi oligonucleotide comprises a sense strand having a sequence of any one of SEQ ID NOs: 1-384 and an antisense strand comprising a complementary sequence of any one of SEQ ID NOs: 385-768. In some embodiments, the RNAi oligonucleotide comprises a sense strand having a sequence of SEQ ID NOs: 912-1295 and an antisense strand comprising a complementary sequence of any one of SEQ ID NOs: 1296-1679.

[0084] In some embodiments, the RNAi oligonucleotide comprises a sense strand having a sequence of any one of SEQ ID NOs: 769-803 and an antisense strand comprising a complementary sequence of any one of SEQ ID NOs: 804-838. In some embodiments, the RNAi oligonucleotide comprises a sense strand having a sequence of any one of SEQ ID NOs: 769-803 and 1681 and an antisense strand comprising a complementary sequence of any one of SEQ ID NOs: 804-838.

[0085] In some embodiments, the RNAi oligonucleotide comprises a sense strand and an antisense strand comprising nucleotide sequences selected from:

a) SEQ ID NOs: 769 and 804, respectively;

b) SEQ ID NOs: 770 and 805, respectively;

c) SEQ ID NOs: 771 and 806, respectively;

d) SEQ ID NOs: 772 and 807, respectively;

e) SEQ ID NOs: 773 and 808, respectively;

f) SEQ ID NOs: 774 and 809, respectively;

g) SEQ ID NOs: 775 and 810, respectively;

h) SEQ ID NOs: 776 and 811, respectively;
i) SEQ ID NOs: 777 and 812, respectively;
j) SEQ ID NOs: 778 and 813, respectively;
k) SEQ ID NOs: 779 and 814, respectively;
l) SEQ ID NOs: 780 and 815, respectively;
m) SEQ ID NOs: 781 and 816, respectively;
n) SEQ ID NOs: 782 and 817, respectively;
o) SEQ ID NOs: 783 and 818, respectively;
p) SEQ ID NOs: 784 and 819, respectively;
q) SEQ ID NOs: 785 and 820, respectively;
r) SEQ ID NOs: 786 and 821, respectively;
s) SEQ ID NOs: 787 and 822, respectively;
t) SEQ ID NOs: 788 and 823, respectively;
u) SEQ ID NOs: 789 and 824, respectively;
v) SEQ ID NOs: 790 and 825, respectively;
w) SEQ ID NOs: 791 and 826, respectively;
x) SEQ ID NOs: 792 and 827, respectively;
y) SEQ ID NOs: 793 and 828, respectively;
z) SEQ ID NOs: 794 and 829, respectively;
aa) SEQ ID NOs: 795 and 830, respectively;
bb) SEQ ID NOs: 796 and 831, respectively;
cc) SEQ ID NOs: 797 and 832, respectively;
dd) SEQ ID NOs: 798 and 833, respectively;
ee) SEQ ID NOs: 799 and 834, respectively;
ff) SEQ ID NOs: 800 and 835, respectively;
gg) SEQ ID NOs: 801 and 836, respectively;
hh) SEQ ID NOs: 802 and 837, respectively;
ii) SEQ ID NOs: 803 and 838, respectively; and
jj) SEQ ID NOs: 1681 and 815, respectively.

[0086] In some embodiments, the RNAi oligonucleotide comprises a sense strand and an antisense strand comprising nucleotide sequences selected from:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively;

j) SEQ ID NOs: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively.

[0087] In some embodiments, the RNAi oligonucleotide comprises a sense strand and an antisense strand comprising nucleotide sequences selected from:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

d) SEQ ID NOs: 798 and 833, respectively;

e) SEQ ID NOs: 799 and 834, respectively;

f) SEQ ID NOs: 803 and 838, respectively; and

g) SEQ ID NOs: 1681 and 815, respectively.

[0088] In some embodiments, the sense strand comprises the sequence of SEQ ID NO: 771, and the antisense strand comprises the sequence of SEQ ID NO: 806. In some embodiments, the sense strand comprises the sequence of SEQ ID NO: 780, and the antisense strand comprises the sequence of SEQ ID NO: 815. In some embodiments, the sense strand comprises the sequence of SEQ ID NO: 781, and the antisense strand comprises the sequence of SEQ ID NO: 816. In some embodiments, the sense strand comprises the sequence of SEQ ID NO: 798, and the antisense strand comprises the sequence of SEQ ID NO: 833. In some embodiments, the sense strand

comprises the sequence of SEQ ID NO: 799, and the antisense strand comprises the sequence of SEQ ID NO: 834. In some embodiments, the sense strand comprises the sequence of SEQ ID NO: 803, and the antisense strand comprises the sequence of SEQ ID NO: 838. In some embodiments, the sense strand comprises the sequence of SEQ ID NO: 1681, and the antisense strand comprises the sequence of SEQ ID NO: 815.

[0089] It should be appreciated that, in some embodiments, sequences presented in the Sequence Listing may be referred to in describing the structure of the oligonucleotide (*e.g.*, a RNAi oligonucleotide) or other nucleic acid. In such embodiments, the actual oligonucleotide or other nucleic acid may have one or more alternative nucleotides (*e.g.*, a RNA counterpart of a DNA nucleotide or a DNA counterpart of an RNA nucleotide) and/or one or more modified nucleotides and/or one or more modified internucleotide linkages and/or one or more other modification when compared with the specified sequence while retaining essentially same or similar complementary properties as the specified sequence.

[0090] In some embodiments, a RNAi oligonucleotide herein comprises a 25-nucleotide sense strand and a 27-nucleotide antisense strand that when acted upon by a Dicer enzyme results in an antisense strand that is incorporated into the mature RNA-induced silencing complex (RISC). In some embodiments, the 25-nucleotide sense strand comprises a sequence selected from SEQ ID NOs: 1-384. In some embodiments, the 27-nucleotide antisense strand comprises a sequence selected from SEQ ID NOs: 385-768. In some embodiments, the sense strand of the RNAi oligonucleotide is longer than 27 nucleotides (*e.g.*, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 nucleotides). In some embodiments, the sense strand of the RNAi oligonucleotide is longer than 25 nucleotides (*e.g.*, 26, 27, 28, 29 or 30 nucleotides). In some embodiments, the sense strand of the RNAi oligonucleotide comprises a nucleotide sequence selected from SEQ ID NOs: 912-1295, wherein the nucleotide sequence is longer than 27 nucleotides (*e.g.*, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 nucleotides). In some embodiments, the sense strand of the RNAi oligonucleotide comprises a nucleotide sequence selected from SEQ ID NOs: 912-1295, wherein the nucleotide sequence is longer than 25 nucleotides (*e.g.*, 26, 27, 28, 29, or 30 nucleotides).

[0091] In some embodiments, the RNAi oligonucleotide has one 5' end that is thermodynamically less stable when compared to the other 5' end. In some embodiments, an asymmetric RNAi oligonucleotide is provided that comprises a blunt end at the 3' end of a sense strand and a 3' overhang at the 3' end of an antisense strand. In some embodiments, the 3' overhang on the antisense strand is about 1-8 nucleotides in length (*e.g.*, 1, 2, 3, 4, 5, 6, 7, or 8 nucleotides in length). Typically, the RNAi oligonucleotide has a two-nucleotide overhang on the 3' end of the antisense (guide) strand; however, other overhangs are possible. In some embodiments, the overhang is a 3' overhang comprising a length of between about 1 to about 6 nucleotides, optionally 1 to 5, 1 to 4, 1 to 3, 1 to 2, 2 to 6, 2 to 5, 2 to 4, 2 to 3, 3 to 6, 3 to 5, 3 to 4, 4 to 6, 4 to 5, 5 to 6 nucleotides, or 1, 2, 3, 4, 5 or 6 nucleotides. However, in some embodiments, the overhang is a 5' overhang comprising a length of between about 1 to about 6 nucleotides, optionally 1 to 5, 1 to 4, 1 to 3, 1 to 2, 2 to 6, 2 to 5, 2 to 4, 2 to 3, 3 to 6, 3 to 5, 3 to 4, 4 to 6, 4 to 5, 5 to 6 nucleotides, or 1, 2, 3, 4, 5, or 6 nucleotides. In some embodiments, the RNAi oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 912-1295, and a 5' overhang comprising a length of between about 1 and about 6 nucleotides. In some embodiments, the RNAi oligonucleotide comprises a sense strand comprising a nucleotide sequence selected from SEQ ID NOs: 912-1295, wherein the RNAi oligonucleotide comprises a 5' overhang comprising a length of between about 1 and about 6 nucleotides. In some embodiments, the RNAi oligonucleotide comprises an antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 1296-1679, wherein the RNAi oligonucleotide comprises a 5' overhang comprising a length of between about 1 and about 6 nucleotides. In some embodiments, the RNAi oligonucleotide comprises a sense strand comprising a nucleotide sequence selected from SEQ ID NOs: 912-1295 and antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 1296-1679, wherein the RNAi oligonucleotide comprises a 5' overhang comprising a length of between about 1 and about 6 nucleotides.

[0092] In some embodiments, two terminal nucleotides on the 3' end of an antisense strand are modified. In some embodiments, the two terminal nucleotides on the 3' end of the antisense strand are complementary with the target mRNA (*e.g.*, MAPT mRNA). In some embodiments, the two

terminal nucleotides on the 3' end of the antisense strand are not complementary with the target mRNA. In some embodiments, the two terminal nucleotides on the 3' end of the antisense strand of a RNAi oligonucleotide herein are unpaired. In some embodiments, the two terminal nucleotides on the 3' end of the antisense strand of the RNAi oligonucleotide herein comprise an unpaired GG. In some embodiments, the two terminal nucleotides on the 3' end of the antisense strand of the RNAi oligonucleotide herein are not complementary to the target mRNA. In some embodiments, two terminal nucleotides on each 3' end of the RNAi oligonucleotide are GG. Typically, one or both of the two terminal GG nucleotides on each 3' end of the RNAi oligonucleotide is not complementary with the target mRNA. In some embodiments, two terminal nucleotides on each 3' end of the oligonucleotide are GG. In some embodiments, one or both of the two terminal GG nucleotides on each 3' end of the RNAi oligonucleotide is not complementary with the target mRNA. In some embodiments, the RNAi oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 912-1295, wherein the two terminal nucleotides on the 3' end of the antisense strand of the oligonucleotide herein comprises an unpaired GG. In some embodiments, the RNAi oligonucleotide comprises an antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 1296-1679, wherein the two terminal nucleotides on the 3' end of the antisense strand of the RNAi oligonucleotide comprises an unpaired GG. In some embodiments, the RNAi oligonucleotide comprises a sense strand comprising a nucleotide sequence selected from SEQ ID NOs: 912-1295 and antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 1296-1679, wherein the two terminal nucleotides on the 3' end of the antisense strand of the RNAi oligonucleotide comprises an unpaired GG.

[0093] In some embodiments, there is one or more (*e.g.*, 1, 2, 3, 4, or 5) mismatch(s) between a sense strand and an antisense strand comprising the RNAi oligonucleotide. If there is more than one mismatch between the sense and antisense strands, they may be positioned consecutively (*e.g.*, 2, 3, or more in a row), or interspersed throughout the region of complementarity. In some embodiments, the 3' end of the sense strand contains one or more mismatches. In one embodiment, two mismatches are incorporated at the 3' end of the sense strand. In some embodiments, base

mismatches, or destabilization of segments at the 3' end of the sense strand of the RNAi oligonucleotide improves or increases the potency of the oligonucleotide.

[0094] In some embodiments, the RNAi oligonucleotide comprises a sense strand and an antisense strand comprising nucleotide sequences selected from:

a) SEQ ID NOs: 769 and 804, respectively;
b) SEQ ID NOs: 770 and 805, respectively;
c) SEQ ID NOs: 771 and 806, respectively;
d) SEQ ID NOs: 772 and 807, respectively;
e) SEQ ID NOs: 773 and 808, respectively;
f) SEQ ID NOs: 774 and 809, respectively;
g) SEQ ID NOs: 775 and 810, respectively;
h) SEQ ID NOs: 776 and 811, respectively;
i) SEQ ID NOs: 777 and 812, respectively;
j) SEQ ID NOs: 778 and 813, respectively;
k) SEQ ID NOs: 779 and 814, respectively;
l) SEQ ID NOs: 780 and 815, respectively;
m) SEQ ID NOs: 781 and 816, respectively;
n) SEQ ID NOs: 782 and 817, respectively;
o) SEQ ID NOs: 783 and 818, respectively;
p) SEQ ID NOs: 784 and 819, respectively;
q) SEQ ID NOs: 785 and 820, respectively;
r) SEQ ID NOs: 786 and 821, respectively;
s) SEQ ID NOs: 787 and 822, respectively;
t) SEQ ID NOs: 788 and 823, respectively;
u) SEQ ID NOs: 789 and 824, respectively;
v) SEQ ID NOs: 790 and 825, respectively;
w) SEQ ID NOs: 791 and 826, respectively;
x) SEQ ID NOs: 792 and 827, respectively;
y) SEQ ID NOs: 793 and 828, respectively;

z) SEQ ID NOs: 794 and 829, respectively;

aa) SEQ ID NOs: 795 and 830, respectively;

bb) SEQ ID NOs: 796 and 831, respectively;

cc) SEQ ID NOs: 797 and 832, respectively;

dd) SEQ ID NOs: 798 and 833, respectively;

ee) SEQ ID NOs: 799 and 834, respectively;

ff) SEQ ID NOs: 800 and 835, respectively;

gg) SEQ ID NOs: 801 and 836, respectively;

hh) SEQ ID NOs: 802 and 837, respectively;

ii) SEQ ID NOs: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively, wherein there is one or more (*e.g.*, 1, 2, 3, 4, or 5) mismatch(s) between the sense and antisense strands.

[0095] In some embodiments, the RNAi oligonucleotide comprises a sense strand and an antisense strand comprising nucleotide sequences selected from:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively;

j) SEQ ID NOs: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively, wherein there is one or more (*e.g.*, 1, 2, 3, 4, or 5) mismatch(s) between the sense and antisense strands.

[0096] In some embodiments, the RNAi oligonucleotide comprises a sense strand and an antisense strand comprising sequence selected from:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

d) SEQ ID NOs: 798 and 833, respectively;

e) SEQ ID NOs: 799 and 834, respectively;

f) SEQ ID NOs: 803 and 838, respectively; and

g) SEQ ID NOs: 1681 and 815, respectively, wherein there is one or more (*e.g.*, 1, 2, 3, 4, or 5) mismatch(s) between the sense and antisense strands.

[0097] *Antisense Strands*

[0098] In some embodiments, an antisense strand of an oligonucleotide herein (*e.g.*, a RNAi oligonucleotide) is referred to as a "guide strand." The antisense strand engages with RISC and binds to an *Argonaute* protein such as Ago2, or engages with or binds to one or more similar factors, and directs silencing of a target gene. In some embodiments, a sense strand complementary to a guide strand is referred to as a "passenger strand."

[0099] In some embodiments, an oligonucleotide comprises an antisense strand of up to about 50 nucleotides in length (*e.g.*, up to 50, up to 40, up to 35, up to 30, up to 27, up to 25, up to 21, up to 19, up to 17, up to 15, or up to 12 nucleotides in length). In some embodiments, the oligonucleotide comprises an antisense strand of at least about 12 nucleotides in length (*e.g.*, at least 12, at least 15, at least 19, at least 21, at least 22, at least 25, at least 27, at least 30, at least 35, or at least 38 nucleotides in length). In some embodiments, the oligonucleotide comprises an antisense strand in a range of about 12 to about 40 (*e.g.*, 12 to 40, 12 to 36, 12 to 32, 12 to 28, 15 to 40, 15 to 36, 15 to 32, 15 to 30, 15 to 28, 17 to 22, 17 to 25, 19 to 27, 19 to 30, 20 to 40, 22 to 40, 25 to 40, or 32 to 40) nucleotides in length. In some embodiments, the oligonucleotide comprises an antisense of about 15 to about 30 nucleotides in length. In some embodiments, an antisense strand of any one of the oligonucleotides disclosed herein is 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40 nucleotides in length. In some embodiments, the oligonucleotide comprises an antisense strand of 22 nucleotides in length.

[00100] In some embodiments, an oligonucleotide for targeting *MAPT* comprises an antisense strand comprising or consisting of a sequence as set forth in any one of SEQ ID NOs: 1296-1679. In some embodiments, the oligonucleotide comprises an antisense strand comprising at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 1296-1679. In some embodiments, the oligonucleotide for targeting *MAPT* comprises an antisense strand comprising or consisting of a sequence as set forth in any one of SEQ ID NOs: 385-768. In some embodiments, the oligonucleotide comprises an antisense strand comprising at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 385-768. In some embodiments, the oligonucleotide for targeting *MAPT* comprises an antisense strand comprising or consisting of a sequence as set forth in any one of SEQ ID NOs: 804-838. In some embodiments, the oligonucleotide comprises an antisense strand comprising at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 804-838. In some embodiments, the oligonucleotide for targeting *MAPT* comprises an antisense strand comprising or consisting of a sequence as set forth in any one of SEQ ID NOs: 1509, 1511, 1514, 1403, 1415, 1428, 1448, 1449, 1451, 1467, 1299, 1479, 1480, 1486, 1494, 1307, 1309, 1409, 1423, 1433, 1445, 1454, 1456, 1459, 1465, 1492, 1495, 1498, 1503, 1504, 1505, 1506, 1507, 1508, and 1308. In some embodiments, the oligonucleotide comprises an antisense strand comprising at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 1509, 1511, 1514, 1403, 1415, 1428, 1448, 1449, 1451, 1467, 1299, 1479, 1480, 1486, 1494, 1307, 1309, 1409, 1423, 1433, 1445, 1454, 1456, 1459, 1465, 1492, 1495, 1498, 1503, 1504, 1505, 1506, 1507, 1508, and 1308. In some embodiments, the oligonucleotide for targeting *MAPT* comprises an antisense strand comprising or consisting of a sequence as set forth in any one of SEQ ID NOs: 806, 811, 815, 816, 817, 825, 830, 833, 834, and 838. In some embodiments, the oligonucleotide comprises an antisense strand

comprising at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 806, 811, 815, 816, 817, 825, 830, 833, 834, and 838. In some embodiments, the oligonucleotide for targeting *MAPT* comprises an antisense strand comprising or consisting of a sequence as set forth in any one of SEQ ID NOs: 806, 815, 816, 833, 834, and 838. In some embodiments, the oligonucleotide comprises an antisense strand comprising at least about 12 (*e.g.*, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 806, 815, 816, 833, 834, and 838.

Sense Strands

[00101] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for targeting MAPT mRNA comprises a sense strand comprising or consisting of a sequence as set forth in in any one of SEQ ID NOs: 912-1295. In some embodiments, the oligonucleotide has a sense strand that comprise at least about 12 (*e.g.*, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in in any one of SEQ ID NOs: 912-1295. In some embodiments, the oligonucleotide comprises a sense strand sequence a set forth in any one of SEQ ID NOs: 1-384. In some embodiments, the oligonucleotide has a sense strand that comprise at least about 12 (*e.g.*, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in in any one of SEQ ID NOs: 1-384. In some embodiments, the oligonucleotide comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 769-803. In some embodiments, the oligonucleotide comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 769-803 and 1681. In some embodiments, the oligonucleotide comprises the sense strand sequence as set forth in SEQ ID NO: 1681. In some embodiments, the oligonucleotide has a sense strand comprised of least about 12 (*e.g.*, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 769-803. In some embodiments, the oligonucleotide comprises a sense

strand sequence as set forth in any one of SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, 1124, and 924. In some embodiments, the oligonucleotide has a sense strand comprised of least about 12 (*e.g.*, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, 1124, and 924. In some embodiments, the oligonucleotide comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 771, 776, 780, 781, 782, 790, 795, 798, 799, and 803. In some embodiments, the oligonucleotide has a sense strand that comprise at least about 12 (*e.g.*, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 771, 776, 780, 781, 782, 790, 795, 798, 799, and 803. In some embodiments, the oligonucleotide comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 771, 780, 781, 798, 799, and 803. In some embodiments, the oligonucleotide has a sense strand that comprise at least about 12 (*e.g.*, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 771, 780, 781, 798, 799, and 803.

[00102] In some embodiments, the oligonucleotide comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 771, 776, 780, 781, 782, 790, 795, 798, 799, 803, and 1681. In some embodiments, the oligonucleotide has a sense strand that comprises at least about 12 (*e.g.*, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 771, 776, 780, 781, 782, 790, 795, 798, 799, 803, and 1681. In some embodiments, the oligonucleotide comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 771, 780, 781, 798, 799, 803, and 1681. In some embodiments, the oligonucleotide has a sense strand that comprise at least about 12 (*e.g.*, at least 13, at least 14, at least 15, at least 16, at least 17, at

least 18, at least 19, at least 20, at least 21, at least 22, or at least 23) contiguous nucleotides of a sequence as set forth in any one of SEQ ID NOs: 771, 780, 781, 798, 799, 803, and 1681.

[00103] In some embodiments, the oligonucleotide comprises a sense strand of up to about 50 nucleotides in length (*e.g.*, up to 50, up to 40, up to 36, up to 30, up to 27, up to 25, up to 21, up to 19, up to 17, or up to 12 nucleotides in length). In some embodiments, the oligonucleotide may have a sense strand of at least about 12 nucleotides in length (*e.g.*, at least 12, at least 15, at least 19, at least 21, at least 25, at least 27, at least 30, at least 36, or at least 38 nucleotides in length). In some embodiments, the oligonucleotide may have a sense strand in a range of about 12 to about 50 (*e.g.*, 12 to 50, 12 to 40, 12 to 36, 12 to 32, 12 to 28, 15 to 40, 15 to 36, 15 to 32, 15 to 28, 17 to 21, 17 to 25, 19 to 27, 19 to 30, 20 to 40, 22 to 40, 25 to 40, or 32 to 40) nucleotides in length. In some embodiments, the oligonucleotide comprises a sense strand about 15 to about 50 nucleotides in length. In some embodiments, the oligonucleotide comprises a sense strand 18 to 36 nucleotides in length. In some embodiments, the oligonucleotide may have a sense strand of 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 nucleotides in length. In some embodiments, the oligonucleotide comprises a sense strand of 36 nucleotides in length.

[00104] In some embodiments, the oligonucleotide comprises a sense strand comprising a stem-loop structure at the 3' end of the sense strand. In some embodiments, the stem-loop is formed by intrastrand base pairing. In some embodiments, the sense strand comprises a stem-loop structure at its 5' end. In some embodiments, the stem of the stem-loop comprises a duplex of 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 2 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 3 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 4 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 5 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 6 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 7 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 8 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 9 nucleotides in length. In some embodiments, the stem of the stem-

loop comprises a duplex of 10 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 11 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 12 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 13 nucleotides in length. In some embodiments, the stem of the stem-loop comprises a duplex of 14 nucleotides in length.

[00105] In some embodiments, a stem-loop provides oligonucleotide protection against degradation (*e.g.*, enzymatic degradation), facilitates or improves targeting and/or delivery to a target cell, tissue, or organ (*e.g.*, the liver or brain), or both. For example, in some embodiments, the loop of a stem-loop provides nucleotides comprising one or more modifications that facilitate, improve, or increase targeting to a target mRNA (*e.g.*, a MAPT mRNA), inhibition of target gene expression (*e.g.*, *MAPT* gene expression), and/or delivery to a target cell, tissue, or organ (*e.g.*, the CNS), or a combination thereof. In some embodiments, the stem-loop itself or modification(s) to the stem-loop do not substantially affect the inherent gene expression inhibition activity of the oligonucleotide, but facilitates, improves, or increases stability (*e.g.*, provides protection against degradation) and/or delivery of the oligonucleotide to a target cell, tissue, or organ (*e.g.*, the CNS). In certain embodiments, the oligonucleotide comprises a sense strand comprising (*e.g.*, at its 3' end) a stem-loop set forth as: S1-L-S2, in which S1 is complementary to S2, and in which loop (L) forms a ss loop between S1 and S2 of up to about 10 nucleotides in length (*e.g.*, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides in length). In some embodiments, the L is 3 nucleotides in length. In some embodiments, the L is 4 nucleotides in length. In some embodiments, the L is 5 nucleotides in length. In some embodiments, the L is 6 nucleotides in length. In some embodiments, the L is 7 nucleotides in length. In some embodiments, the L is 8 nucleotides in length. In some embodiments, the L is 9 nucleotides in length. In some embodiments, the L is 10 nucleotides in length.

[00106] In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 912-1295, and the oligonucleotide comprises a sense strand comprising (*e.g.*, at its 3' end) a stem-loop set forth as: S1-L-S2, in which S1 is complementary to S2, and in which L forms a ss loop between S1 and S2 of up to about 10 nucleotides in length (*e.g.*, 3, 4, 5, 6, 7, 8, 9, or 10

nucleotides in length). In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 912-1295, and the oligonucleotide comprises a sense strand comprising (*e.g.*, at its 3' end) a stem-loop set forth as: S1-L-S2, in which S1 is complementary to S2, and in which L forms a ss loop between S1 and S2 of 4 nucleotides in length (*i.e.*, a tetraL).

[00107] In some embodiments, the tetraL comprises the sequence 5'-GAAA-3'. In some embodiments, the stem-loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 1680).

[00108] In some embodiments, the L of a stem-loop having the structure S1-L-S2 as described above is a triL. In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 912-1295 and a triL. In some embodiments, the triL comprises ribonucleotides, deoxyribonucleotides, modified nucleotides, delivery ligands, and combinations thereof.

[00109] In some embodiments, the L of a stem-loop having the structure S1-L-S2 as described above is a tetraL as described in US Patent No. 10,131,912, incorporated herein by reference (*e.g.*, within a nicked tetraL structure). In some embodiments, the oligonucleotide comprises a targeting sequence or a region of complementary that is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 912-1295 and a tetraL. In some embodiments, the tetraL comprises ribonucleotides, deoxyribonucleotides, modified nucleotides, delivery ligands, and combinations thereof.

[00110] *Duplex Length*

[00111] In some embodiments, a duplex is formed between a sense and antisense strand and is at least about 12 (*e.g.,* at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or at least 21) nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is in the range of about 12 to about 30 nucleotides in length (*e.g.*, 12 to 30, 12 to 27, 12 to 22, 15 to 25, 18 to 30, 18 to 22, 18 to 25, 18 to 27, 18 to 30, 19 to 30, or 21 to 30 nucleotides in length). In some embodiments, the duplex formed between

the sense and antisense strands is 12, 13, 14, 15, 16, 17, 18, 19, 29, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 12 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 13 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 14 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 15 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 16 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 17 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 18 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 19 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 20 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 21 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 22 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 23 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 24 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 25 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 26 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 27 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 28 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 29 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands is 30 nucleotides in length. In some embodiments, the duplex formed between the sense and antisense strands does not span the entire length of the sense strand and/or antisense strand. In some embodiments, the duplex between the sense and antisense strand spans the entire length of either the sense or antisense strands. In some embodiments, the duplex between the sense and antisense strands spans the entire length of both the sense strand and the antisense strand.

[00112] In some embodiments, the duplex between the sense and antisense strands spans the entire length of both the sense strand and the antisense strand. In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 769 and 804, respectively;
b) SEQ ID NO: 770 and 805, respectively;
c) SEQ ID NO: 771 and 806, respectively;
d) SEQ ID NO: 772 and 807, respectively;
e) SEQ ID NO: 773 and 808, respectively;
f) SEQ ID NO: 774 and 809, respectively;
g) SEQ ID NO: 775 and 810, respectively;
h) SEQ ID NO: 776 and 811, respectively;
i) SEQ ID NO: 777 and 812, respectively;
j) SEQ ID NO: 778 and 813, respectively;
k) SEQ ID NO: 779 and 814, respectively;
l) SEQ ID NO: 780 and 815, respectively;
m) SEQ ID NO: 781 and 816, respectively;
n) SEQ ID NO: 782 and 817, respectively;
o) SEQ ID NO: 783 and 818, respectively;
p) SEQ ID NO: 784 and 819, respectively;
q) SEQ ID NO: 785 and 820, respectively;
r) SEQ ID NO: 786 and 821, respectively;
s) SEQ ID NO: 787 and 822, respectively;
t) SEQ ID NO: 788 and 823, respectively;
u) SEQ ID NO: 789 and 824, respectively;
v) SEQ ID NO: 790 and 825, respectively;
w) SEQ ID NO: 791 and 826, respectively;
x) SEQ ID NO: 792 and 827, respectively;
y) SEQ ID NO: 793 and 828, respectively;

z) SEQ ID NO: 794 and 829, respectively;

aa) SEQ ID NO: 795 and 830, respectively;

bb) SEQ ID NO: 796 and 831, respectively;

cc) SEQ ID NO: 797 and 832, respectively;

dd) SEQ ID NO: 798 and 833, respectively;

ee) SEQ ID NO: 799 and 834, respectively;

ff) SEQ ID NO: 800 and 835, respectively;

gg) SEQ ID NO: 801 and 836, respectively;

hh) SEQ ID NO: 802 and 837, respectively;

ii) SEQ ID NO: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively, wherein the duplex formed between the sense and antisense strand is in the range of about 12 to about 30 nucleotides in length (*e.g.*, 12 to 30, 12 to 27, 12 to 22, 15 to 25, 18 to 30, 18 to 22, 18 to 25, 18 to 27, 18 to 30, 19 to 30, or 21 to 30 nucleotides in length).

[00113] In some embodiments, the duplex between the sense and antisense strands spans the entire length of both the sense strand and the antisense strand. In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 771 and 806, respectively;

b) SEQ ID NO: 776 and 811, respectively;

c) SEQ ID NO: 780 and 815, respectively;

d) SEQ ID NO: 781 and 816, respectively;

e) SEQ ID NO: 782 and 817, respectively;

f) SEQ ID NO: 790 and 825, respectively;

g) SEQ ID NO: 795 and 830, respectively;\

h) SEQ ID NO: 798 and 833, respectively;

i) SEQ ID NO: 799 and 834, respectively;

j) SEQ ID NO: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively, wherein the duplex formed between the sense and antisense strand is in the range of about 12 to about 30 nucleotides in length (*e.g.*, 12 to 30, 12 to 27, 12 to 22, 15 to 25, 18 to 30, 18 to 22, 18 to 25, 18 to 27, 18 to 30, 19 to 30, or 21 to 30 nucleotides in length).

[00114] In some embodiments, the duplex between the sense and antisense strands spans the entire length of both the sense strand and the antisense strand. In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 771 and 806, respectively;

b) SEQ ID NO: 780 and 815, respectively;

c) SEQ ID NO: 781 and 816, respectively;

d) SEQ ID NO: 798 and 833, respectively;

e) SEQ ID NO: 799 and 834, respectively;

f) SEQ ID NO: 803 and 838, respectively; and

g) SEQ ID NOs: 1681 and 815, respectively, wherein the duplex formed between the sense and antisense strand is in the range of about 12 to about 30 nucleotides in length (*e.g.*, 12 to 30, 12 to 27, 12 to 22, 15 to 25, 18 to 30, 18 to 22, 18 to 25, 18 to 27, 18 to 30, 19 to 30, or 21 to 30 nucleotides in length).

[00115] ***Oligonucleotide Termini***

[00116] In some embodiments, an oligonucleotide herein (*e.g.*, a RNAi oligonucleotide) comprises a sense strand and an antisense strand, wherein termini of either or both strands comprise a blunt end. In some embodiments, the oligonucleotide comprises sense and antisense strands that are separate strands that form an asymmetric duplex region having an overhang at the 3' terminus of the antisense strand. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein termini of either or both strands comprise an overhang comprising one or more nucleotides. In some embodiments, the one or more nucleotides comprising the overhang are unpaired nucleotides. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein a 3' terminus of the sense strand and a 5' terminus of the

antisense strand comprise a blunt end. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein a 5' terminus of the sense strand and a 3' terminus of the antisense strand comprise a blunt end.

[00117] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein a 3' terminus of either or both strands comprises a 3' overhang comprising one or more nucleotides. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the sense strand comprises a 3' overhang comprising one or more nucleotides. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the antisense strand comprises a 3' overhang comprising one or more nucleotides. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein both the sense strand and the antisense strand comprise a 3' overhang comprising one or more nucleotides.

[00118] In some embodiments, the 3' overhang is about 1 to about 20 nucleotides in length (*e.g.*, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides in length). In some embodiments, the 3' overhang is 1 to 19, 1 to 18, 1 to 17, 1 to 16, 1 to 15, 1 to 14, 1 to 13, 1 to 12, 1 to 11, 1 to 10, 1 to 9, 1 to 8, 1 to 7, 1 to 6, 1 to 5, 1 to 4, 1 to 3, or 1 to 2 nucleotides in length). In some embodiments, the 3' overhang is 1 nucleotide in length. In some embodiments, the 3' overhang is 2 nucleotides in length. In some embodiments, the 3' overhang is 3 nucleotides in length. In some embodiments, the 3' overhang is 4 nucleotides in length. In some embodiments, the 3' overhang is 5 nucleotides in length. In some embodiments, the 3' overhang is 6 nucleotides in length. In some embodiments, the 3' overhang is 7 nucleotides in length. In some embodiments, the 3'-overhang is 8 nucleotides in length. In some embodiments, the 3' overhang is 9 nucleotides in length. In some embodiments, the 3' overhang is 10 nucleotides in length. In some embodiments, the 3' overhang is 11 nucleotides in length. In some embodiments, the 3' overhang is 12 nucleotides in length. In some embodiments, the 3' overhang is 13 nucleotides in length. In some embodiments, the 3' overhang is 14 nucleotides in length. In some embodiments, the 3' overhang is 15 nucleotides in length. In some embodiments, the 3' overhang is 16 nucleotides in length. In some embodiments, the 3' overhang is 17 nucleotides in length. In some embodiments, the 3' overhang is 18 nucleotides

in length. In some embodiments, the 3' overhang is 19 nucleotides in length. In some embodiments, the 3' overhang is 20 nucleotides in length.

[00119] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the antisense strand comprises a 3' overhang, wherein the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 769 and 804, respectively;
b) SEQ ID NO: 770 and 805, respectively;
c) SEQ ID NO: 771 and 806, respectively;
d) SEQ ID NO: 772 and 807, respectively;
e) SEQ ID NO: 773 and 808, respectively;
f) SEQ ID NO: 774 and 809, respectively;
g) SEQ ID NO: 775 and 810, respectively;
h) SEQ ID NO: 776 and 811, respectively;
i) SEQ ID NO: 777 and 812, respectively;
j) SEQ ID NO: 778 and 813, respectively;
k) SEQ ID NO: 779 and 814, respectively;
l) SEQ ID NO: 780 and 815, respectively;
m) SEQ ID NO: 781 and 816, respectively;
n) SEQ ID NO: 782 and 817, respectively;
o) SEQ ID NO: 783 and 818, respectively;
p) SEQ ID NO: 784 and 819, respectively;
q) SEQ ID NO: 785 and 820, respectively;
r) SEQ ID NO: 786 and 821, respectively;
s) SEQ ID NO: 787 and 822, respectively;
t) SEQ ID NO: 788 and 823, respectively;
u) SEQ ID NO: 789 and 824, respectively;
v) SEQ ID NO: 790 and 825, respectively;
w) SEQ ID NO: 791 and 826, respectively;

x) SEQ ID NO: 792 and 827, respectively;

y) SEQ ID NO: 793 and 828, respectively;

z) SEQ ID NO: 794 and 829, respectively;

aa) SEQ ID NO: 795 and 830, respectively;

bb) SEQ ID NO: 796 and 831, respectively;

cc) SEQ ID NO: 797 and 832, respectively;

dd) SEQ ID NO: 798 and 833, respectively;

ee) SEQ ID NO: 799 and 834, respectively;

ff) SEQ ID NO: 800 and 835, respectively;

gg) SEQ ID NO: 801 and 836, respectively;

hh) SEQ ID NO: 802 and 837, respectively;

ii) SEQ ID NO: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively, wherein the antisense strand comprises the 3' overhang about 1 to about 20 nucleotides in length (*e.g.*, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides in length), optionally wherein the 3' overhang is 2 nucleotides in length.

[00120] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the antisense strand comprises the 3' overhang, wherein the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 771 and 806, respectively;

b) SEQ ID NO: 776 and 811, respectively;

c) SEQ ID NO: 780 and 815, respectively;

d) SEQ ID NO: 781 and 816, respectively;

e) SEQ ID NO: 782 and 817, respectively;

f) SEQ ID NO: 790 and 825, respectively;

g) SEQ ID NO: 795 and 830, respectively;

h) SEQ ID NO: 798 and 833, respectively;

i) SEQ ID NO: 799 and 834, respectively;

j) SEQ ID NO: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively, wherein the antisense strand comprises the 3' overhang about 1 to about 20 nucleotides in length (*e.g.*, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides in length), optionally wherein the 3' overhang is 2 nucleotides in length.

[00121] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the antisense strand comprises the 3' overhang, wherein the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 771 and 806, respectively;

b) SEQ ID NO: 780 and 815, respectively;

c) SEQ ID NO: 781 and 816, respectively;

d) SEQ ID NO: 798 and 833, respectively;

e) SEQ ID NO: 799 and 834, respectively;

f) SEQ ID NO: 803 and 838, respectively; and

g) SEQ ID NOs: 1681 and 815, respectively, wherein the antisense strand comprises a 3' overhang about 1 to about 20 nucleotides in length (*e.g.*, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides in length), optionally wherein the 3' overhang is 2 nucleotides in length.

[00122] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the sense strand comprises a 5' overhang comprising one or more nucleotides.

[00123] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 769 and 804, respectively;

b) SEQ ID NOs: 770 and 805, respectively;

c) SEQ ID NOs: 771 and 806, respectively;

d) SEQ ID NOs: 772 and 807, respectively;

e) SEQ ID NOs: 773 and 808, respectively;

f) SEQ ID NOs: 774 and 809, respectively;
g) SEQ ID NOs: 775 and 810, respectively;
h) SEQ ID NOs: 776 and 811, respectively;
i) SEQ ID NOs: 777 and 812, respectively;
j) SEQ ID NOs: 778 and 813, respectively;
k) SEQ ID NOs: 779 and 814, respectively;
l) SEQ ID NOs: 780 and 815, respectively;
m) SEQ ID NOs: 781 and 816, respectively;
n) SEQ ID NOs: 782 and 817, respectively;
o) SEQ ID NOs: 783 and 818, respectively;
p) SEQ ID NOs: 784 and 819, respectively;
q) SEQ ID NOs: 785 and 820, respectively;
r) SEQ ID NOs: 786 and 821, respectively;
s) SEQ ID NOs: 787 and 822, respectively;
t) SEQ ID NOs: 788 and 823, respectively;
u) SEQ ID NOs: 789 and 824, respectively;
v) SEQ ID NOs: 790 and 825, respectively;
w) SEQ ID NOs: 791 and 826, respectively;
x) SEQ ID NOs: 792 and 827, respectively;
y) SEQ ID NOs: 793 and 828, respectively;
z) SEQ ID NOs: 794 and 829, respectively;
aa) SEQ ID NOs: 795 and 830, respectively;
bb) SEQ ID NOs: 796 and 831, respectively;
cc) SEQ ID NOs: 797 and 832, respectively;
dd) SEQ ID NOs: 798 and 833, respectively;
ee) SEQ ID NOs: 799 and 834, respectively;
ff) SEQ ID NOs: 800 and 835, respectively;
gg) SEQ ID NOs: 801 and 836, respectively;
hh) SEQ ID NOs: 802 and 837, respectively;

ii) SEQ ID NOs: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively, wherein the antisense strand comprises a 3' overhang about 1 to about 20 nucleotides in length (*e.g.*, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or about 20 nucleotides in length), optionally wherein the 3' overhang is 2 nucleotides in length.

[00124] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively;

j) SEQ ID NOs: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively, wherein the antisense strand comprises the 3' overhang about 1 to about 20 nucleotides in length (*e.g.*, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or about 20 nucleotides in length), optionally wherein the 3' overhang is 2 nucleotides in length.

[00125] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 771 and 806, respectively;

b) SEQ ID NO: 780 and 815, respectively;

c) SEQ ID NO: 781 and 816, respectively;

d) SEQ ID NO: 798 and 833, respectively;

e) SEQ ID NO: 799 and 834, respectively;

f) SEQ ID NO: 803 and 838, respectively; and

g) SEQ ID NOs: 1681 and 815, respectively, wherein the antisense strand comprises the 3' overhang about 1 to about 20 nucleotides in length (*e.g.*, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or about 20 nucleotides in length), optionally wherein the 3' overhang is 2 nucleotides in length.

[00126] In some embodiments, one or more (*e.g.*, 2, 3, 4, 5, or more) nucleotides comprising the 3' terminus or 5' terminus of the sense and/or antisense strand are modified. For example, in some embodiments, one or two terminal nucleotides of the 3' terminus of the antisense strand are modified. In some embodiments, the last nucleotide at the 3' terminus of an antisense strand is modified, for example, comprises 2' modification (*e.g.*, a 2'-OMe). In some embodiments, the last one or two terminal nucleotides at the 3' terminus of an antisense strand are complementary with the target. In some embodiments, the last one or two nucleotides at the 3' terminus of the antisense strand are not complementary with the target.

[00127] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the 3' terminus of the sense strand comprises a step-loop and the 3' terminus of the antisense strand comprises the 3' overhang. In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand that form a nicked tetraL structure, wherein the 3' terminus of the sense strand comprises the stem-loop, wherein the loop is a tetraL, and wherein the 3' terminus of the antisense strand comprises the 3' overhang described herein. In some embodiments, the 3' overhang is 2 nucleotides in length. In some embodiments, the 2 nucleotides comprising the 3' overhang both comprise guanine (G) nucleobases. Typically, one or both of the nucleotides comprising the 3' overhang of the antisense strand are not complementary with the target mRNA.

[00128] ***Oligonucleotide Modifications***

[00129] In some embodiments, the oligonucleotide (*e.g.*, a RNAi oligonucleotide) comprises a modification. Oligonucleotides may be modified in various ways to improve or control specificity, stability, delivery, bioavailability, resistance from nuclease degradation, immunogenicity, base-

pairing properties, RNA distribution and cellular uptake, and other features relevant to therapeutic research use.

[00130] In some embodiments, the modification is a modified sugar. In some embodiments, the modification is a 5' terminal phosphate group. In some embodiments, the modification is a modified internucleoside linkage. In some embodiments, the modification is a modified base. In some embodiments, the modification is a reversible modification. In some embodiments, the oligonucleotide may comprise any one of the modifications described herein or any combination thereof. For example, in some embodiments, the oligonucleotide comprises at least one modified sugar, a 5' terminal phosphate group, at least one modified internucleoside linkage, at least one modified base, and at least one reversible modification.

[00131] In some embodiments, the oligonucleotide comprises at least one modified sugar, a 5' terminal phosphate group, at least one modified internucleotide linkage, and at least one modified base. In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 769 and 804, respectively;

b) SEQ ID NO: 770 and 805, respectively;

c) SEQ ID NO: 771 and 806, respectively;

d) SEQ ID NO: 772 and 807, respectively;

e) SEQ ID NO: 773 and 808, respectively;

f) SEQ ID NO: 774 and 809, respectively;

g) SEQ ID NO: 775 and 810, respectively;

h) SEQ ID NO: 776 and 811, respectively;

i) SEQ ID NO: 777 and 812, respectively;

j) SEQ ID NO: 778 and 813, respectively;

k) SEQ ID NO: 779 and 814, respectively;

l) SEQ ID NO: 780 and 815, respectively;

m) SEQ ID NO: 781 and 816, respectively;

n) SEQ ID NO: 782 and 817, respectively;

o) SEQ ID NO: 783 and 818, respectively;

p) SEQ ID NO: 784 and 819, respectively;

q) SEQ ID NO: 785 and 820, respectively;

r) SEQ ID NO: 786 and 821, respectively;

s) SEQ ID NO: 787 and 822, respectively;

t) SEQ ID NO: 788 and 823, respectively;

u) SEQ ID NO: 789 and 824, respectively;

v) SEQ ID NO: 790 and 825, respectively;

w) SEQ ID NO: 791 and 826, respectively;

x) SEQ ID NO: 792 and 827, respectively;

y) SEQ ID NO: 793 and 828, respectively;

z) SEQ ID NO: 794 and 829, respectively;

aa) SEQ ID NO: 795 and 830, respectively;

bb) SEQ ID NO: 796 and 831, respectively;

cc) SEQ ID NO: 797 and 832, respectively;

dd) SEQ ID NO: 798 and 833, respectively;

ee) SEQ ID NO: 799 and 834, respectively;

ff) SEQ ID NO: 800 and 835, respectively;

gg) SEQ ID NO: 801 and 836, respectively;

hh) SEQ ID NO: 802 and 837, respectively;

ii) SEQ ID NO: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises at least one modified sugar, a 5' terminal phosphate group, at least one modified internucleotide linkage, and at least one modified base.

[00132] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 771 and 806, respectively;

b) SEQ ID NO: 776 and 811, respectively;

c) SEQ ID NO: 780 and 815, respectively;

d) SEQ ID NO: 781 and 816, respectively;

e) SEQ ID NO: 782 and 817, respectively;

f) SEQ ID NO: 790 and 825, respectively;

g) SEQ ID NO: 795 and 830, respectively;

h) SEQ ID NO: 798 and 833, respectively;

i) SEQ ID NO: 799 and 834, respectively;

j) SEQ ID NO: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises at least one modified sugar, a 5' terminal phosphate group, at least one modified internucleotide linkage, and at least one modified base.

[00133] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 771 and 806, respectively;

b) SEQ ID NO: 780 and 815, respectively;

c) SEQ ID NO: 781 and 816, respectively;

d) SEQ ID NO: 798 and 833, respectively;

e) SEQ ID NO: 799 and 834, respectively;

f) SEQ ID NO: 803 and 838, respectively; and

g) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises at least one modified sugar, a 5' terminal phosphate group, at least one modified internucleotide linkage, and at least one modified base.

[00134] The number of modifications on the oligonucleotide and the position of those nucleotide modifications may influence the properties of an oligonucleotide. For example, oligonucleotides may be delivered *in vivo* by conjugating them to encompassing them in a lipid nanoparticle (LNP) or similar carrier. However, when an oligonucleotide is not protected by an LNP or similar carrier, it may be advantageous for at least some of the nucleotides to be modified. Accordingly, in some embodiments, all or substantially all of the nucleotides of the oligonucleotides are modified. In some embodiments, more than half of the nucleotides are modified. In some embodiments, less than half of the nucleotides are modified. In some embodiments, the sugar moiety of all nucleotides comprising the oligonucleotide is modified at the 2' position. The modifications may be reversible

or irreversible. In some embodiments, an oligonucleotide as disclosed herein has a number and type of modified nucleotides sufficient to cause the desired characteristics (*e.g.,* protection from enzymatic degradation, capacity to target a desired cell after *in vivo* administration, and/or thermodynamic stability).

[00135] *Sugar Modifications*

[00136] In some embodiments, the oligonucleotide comprises a modified sugar. In some embodiments, the modified sugar (also referred herein to a sugar analog) includes a modified deoxyribose or ribose moiety in which, for example, one or more modifications occur at the 2', 3', 4', and/or 5' carbon position of the sugar. In some embodiments, the modified sugar may also include non-natural alternative carbon structures such as those present in locked nucleic acids ("LNA"; *see, e.g.*, Koshkin *et al.* (1998) TETRAHEDON 54:3607-30), unlocked nucleic acids ("UNA"; *see, e.g.*, Snead *et al.* (2013) MOL. THER-NUCL. ACIDS 2:e103), and bridged nucleic acids ("BNA"; *see, e.g.*, Imanishi & Obika (2002) CHEM COMMUN. (CAMB) 21:1653-59).

[00137] In some embodiments, a nucleotide modification in a sugar comprises a 2'-modification. In some embodiments, the 2'-modification may be 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, 2'-F, EA, 2'-OMe, 2'-MOE, 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA) or 2'-FANA. In some embodiments, the modification is 2'-F, 2'-OMe or 2'-MOE. In some embodiments, the modification in a sugar comprises a modification of the sugar ring, which may comprise modification of one or more carbons of the sugar ring. For example, the modification of a sugar of a nucleotide may comprise a 2'-oxygen of a sugar is linked to a 1'-carbon or 4'-carbon of the sugar, or a 2'-oxygen is linked to the 1'-carbon or 4'-carbon *via* an ethylene or methylene bridge. In some embodiments, the modified nucleotide has an acyclic sugar that lacks a 2'-carbon to 3'-carbon bond. In some embodiments, the modified nucleotide has a thiol group, for example, in the 4' position of the sugar.

[00138] In some embodiments, the oligonucleotide described herein comprises at least about 1 modified nucleotide (*e.g.*, at least 1, at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, or more). In some embodiments, the sense strand of the RNAi oligonucleotide comprises at least about 1 modified

nucleotide (*e.g.*, at least 1, at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, or more). In some embodiments, the antisense strand of the oligonucleotide comprises at least about 1 modified nucleotide (*e.g.*, at least 1, at least 5, at least 10, at least 15, at least 20, or more).

[00139] In some embodiments, all the nucleotides of the sense strand of the oligonucleotide are modified. In some embodiments, all the nucleotides of the antisense strand of the oligonucleotide are modified. In some embodiments, all the nucleotides of the oligonucleotide (*i.e.*, both the sense strand and the antisense strand) are modified. In some embodiments, the modified nucleotide comprises a 2'-modification (*e.g.*, a 2'-F or 2'-OMe, 2'-MOE, and 2'-FANA). In some embodiments, the modified nucleotide comprises a 2'-modification (*e.g.*, a 2'-F or 2'-OMe)

[00140] In some embodiments, the disclosure provides oligonucleotides having different modification patterns. In some embodiments, the modified oligonucleotides comprise a sense strand sequence having a modification pattern as set forth in the Examples and Sequence Listing and an antisense strand having a modification pattern as set forth in the Examples and Sequence Listing.

[00141] In some embodiments, the oligonucleotide comprises an antisense strand having nucleotides that are modified with 2'-F. In some embodiments, the oligonucleotide comprises an antisense strand comprises nucleotides that are modified with 2'-F and 2'-OMe. In some embodiments, the oligonucleotide comprises a sense strand having nucleotides that are modified with 2'-F. In some embodiments, the oligonucleotide comprises a sense strand comprising nucleotides that are modified with 2'-F and 2'-OMe.

[00142] In some embodiments, the oligonucleotide comprises a sense strand with about 10-15%, 10%, 11%, 12%, 13%, 14%, or 15% of the nucleotides of the sense strand comprising a 2'-F modification. In some embodiments, the oligonucleotide comprises a sense strand with about 18-23% (*e.g.*, 18%, 19%, 20%, 21%, 22%, or 23%) of the nucleotides of the sense strand comprising a 2'-F modification. In some embodiments, the oligonucleotide comprises a sense strand with about 38-43% (*e.g.*, 38%, 39%, 40%, 41%, 42%, or 43%) of the nucleotides of the sense strand comprising a 2'-F modification. In some embodiments, about 11% of the nucleotides of the sense strand comprise a 2'-F modification. In some embodiments, about 22% of the nucleotides of the

sense strand comprise a 2'-F modification. In some embodiments, about 40% of the nucleotides of the sense strand comprise a 2'-F modification. In some embodiments, the oligonucleotide comprises an antisense strand with about 25% to about 35% (*e.g.*, 25%, 26%, 27%, 28%, 29%, 30%, 31%, 32%, 33%, 34%, or 35%) of the nucleotides of the antisense strand comprising a 2'-F modification. In some embodiments, about 32% of the nucleotides of the antisense strand comprise a 2'-F modification. In some embodiments, the oligonucleotide has about 15% to about 25% (*e.g.*, 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, or 25%) of its nucleotides comprising a 2'-F modification. In some embodiments, the oligonucleotide has about 35-45% (*e.g.*, 35%, 36%, 37%, 38%, 39%, 40%, 41%, 42%, 43%, 44% or 45%) of its nucleotides comprising a 2'-F modification. In some embodiments, about 19% of the nucleotides in the oligonucleotide comprise a 2'-F modification. In some embodiments, about 29% of the nucleotides in the oligonucleotide comprise a 2'-F modification. In some embodiments, about 40% of the nucleotides in the oligonucleotide comprise a 2'-F modification.

[00143] In some embodiments, one or more of positions 8, 9, 10, or 11 of a 36-nucleotide sense strand are modified with a 2'-F group. In some embodiments, one or more of positions 8, 9, 10, or 11 of a sense strand comprising a stem-loop are modified with a 2'-F group. In some embodiments, the sugar moiety at each of nucleotides at positions 1-7 and 12-20 of a 36-nucleotide sense strand is modified with a 2'-OMe. In some embodiments, the sugar moiety at each of nucleotides at positions 1-7 and 12-20 of a sense strand comprising a stem-loop is modified with a 2'-OMe. In some embodiments, the sugar moiety at each of nucleotides at positions 1-7 and 12-36 in the sense strand is modified with a 2'-OMe.

[00144] In some embodiments, one or more of positions 3, 5, 8, 10, 12, 13, 15, and 17 of the sense strand are modified with a 2'-F .

[00145] In some embodiments, the antisense strand has 3 nucleotides that are modified at the 2'-position of the sugar moiety with a 2'-F. In some embodiments, the sugar moiety at positions 2, 5 and 14 and optionally up to 3 of the nucleotides at positions 1, 3, 7, and 10 of the antisense strand are modified with a 2'-F. In some embodiments, the sugar moiety at positions 2, 5, and 14 and optionally up to 3 of the nucleotides at positions 3, 4, 7, and 10 of the antisense strand are modified with a 2'-F. In other embodiments, the sugar moiety at each of the positions at positions 2, 5, and

14 of the antisense strand is modified with the 2'-F. In other embodiments, the sugar moiety at each of the positions at positions 1, 2, 5, and 14 of the antisense strand is modified with the 2'-F. In other embodiments, the sugar moiety at each of the positions at positions 2, 4, 5, and 14 of the antisense strand is modified with the 2'-F. In still other embodiments, the sugar moiety at each of the positions at positions 1, 2, 3, 5, 7, and 14 of the antisense strand is modified with the 2'-F. In other embodiments, the sugar moiety at each of the positions at positions 2, 3, 4, 5, 7, and 14 of the antisense strand is modified with the 2'-F. In yet another embodiment, the sugar moiety at each of the positions at positions 1, 2, 3, 5, 10, and 14 of the antisense strand is modified with the 2'-F. In other embodiments, the sugar moiety at each of the positions at positions 2, 3, 4, 5, 10, and 14 of the antisense strand is modified with the 2'-F. In another embodiment, the sugar moiety at each of the positions at positions 2, 3, 5, 7, 10, and 14 of the antisense strand is modified with the 2'-F. In other embodiments, the sugar moiety at each of the positions at positions 2, 3, 4, 5, 7, 10, and 14 of an antisense strand duplexed with a 36-nucleotide sense strand is modified with the 2'-F. In other embodiments, the sugar moiety at each of the positions at positions 2, 3, 4, 5, 7, 10, and 14 of an antisense strand duplexed with a sense strand comprising a stem-loop is modified with the 2'-F.

[00146] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at positions 2 and 14 modified with 2'-F. In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at positions 2, 5, and 14 modified with 2'-F. In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at positions 1, 2, 5, and 14 modified with 2'-F. In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at positions 2, 4, 5, and 14 modified with 2'-F. In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at positions 1, 2, 3, 5, 7, and 14 modified with 2'-F. In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at positions 2, 3, 4, 5, 7, and 14 modified with 2'-F. In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at positions 1, 2, 3, 5, 10, and 14 modified with 2'-F. In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at positions 2, 3, 4, 5, 10, and 14 modified with 2'-F. In some embodiments, the oligonucleotide

comprises a 36-nucleotide sense strand and an antisense strand, wherein the antisense strand comprises a sugar moiety at positions 2, 3, 4, 5, 7, 10, and 14 modified with 2'-F. In some embodiments, the oligonucleotide comprises a sense strand comprising a stem-loop and an antisense strand, wherein the antisense strand comprises a sugar moiety at positions 2, 3, 4, 5, 7, 10, and 14 modified with 2'-F. In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at positions 2, 3, 4, 5, 7, 10, 14, 16, and 19 modified with 2'-F.

[00147] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 2, 5, and 14 of the antisense strand modified with 2'-F and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00148] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 1, 2, 5, and 14 of the antisense strand modified with 2'-F and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00149] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 2, 4, 5, and 14 of the antisense strand modified with 2'-F and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00150] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 1, 2, 3, 5, 7, and 14 of the antisense strand modified with 2'-F and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00151] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 2, 3, 4, 5, 7, and 14 of the antisense strand modified with 2'-F and the sugar moiety of each of the remaining nucleotides of the antisense

strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00152] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 1, 2, 3, 5, 10, and 14 of the antisense strand modified with 2'-F and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00153] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 2, 3, 4, 5, 10, and 14 of the antisense strand modified with 2'-F and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00154] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 2, 3, 5, 7, 10, and 14 of the antisense strand modified with 2'-F and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00155] In some embodiments, the oligonucleotide comprises a 36-nucleotide sense strand and an antisense strand, wherein the antisense strand comprising a sugar moiety at positions 2, 3, 4, 5, 7, 10, and 14 of the antisense strand modified with 2'-F and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA. In some embodiments, the oligonucleotide comprises a sense strand comprising a stem-loop and an antisense strand, wherein the antisense strand comprising a sugar moiety at positions 2, 3, 4, 5, 7, 10, and 14 of the antisense strand modified with 2'-F and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00156] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 2, 3, 4, 5, 7, 10, 14, 16, and 19 of the antisense strand modified with 2′-F and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00157] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at position 1, position 2, position 3, position 4, position 5, position 6, position 7, position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, position 16, position 17, position 18, position 19, position 20, position 21, or position 22 modified with 2'-F.

[00158] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at position 1, position 2, position 3, position 4, position 5, position 6, position 7, position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, position 16, position 17, position 18, position 19, position 20, position 21, or position 22 modified with 2'-OMe.

[00159] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety at position 1, position 2, position 3, position 4, position 5, position 6, position 7, position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, position 16, position 17, position 18, position 19, position 20, position 21, or position 22 modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00160] In some embodiments, the oligonucleotide comprises a 36-nucleotide sense strand having the sugar moiety at positions 8-11 modified with 2'-F. In some embodiments, the oligonucleotide comprises a sense strand comprising a stem-loop and the sugar moiety at positions 8-11 modified with 2'-F. In some embodiments, the oligonucleotide comprises a 36-nucleotide sense strand having the sugar moiety at positions 1-7 and 12-17 or 12-20 modified with 2'-OMe. In some embodiments, the oligonucleotide comprises a sense strand comprising a stem loop and the sugar moiety at positions 1-7 and 12-17 or 12-20 modified with 2'-OMe. In some embodiments, the oligonucleotide comprises a 36-nucleotide sense strand having the sugar moiety at positions 1-7

and 12-17, 12-20 or 12-22 modified with 2'-OMe. In some embodiments, the oligonucleotide comprises a sense strand comprising a stem-loop and the sugar moiety at positions 1-7 and 12-17, 12-20, or 12-22 modified with 2'-OMe. In some embodiments, the oligonucleotide comprises a 36-nucleotide sense strand having the sugar moiety of each of the nucleotides at positions 1-7 and 12-17 or 12-20 of the sense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA. In some embodiments, the oligonucleotide comprises a sense strand comprising and stem-loop and having the sugar moiety of each of the nucleotides at positions 1-7 and 12-17 or 12-20 of the sense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA. In some embodiments, the oligonucleotide comprises a 36-nucleotide sense strand having the sugar moiety of each of the nucleotides at positions 1-7 and 12-17, 12-20, or 12-22 of the sense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA. In some embodiments, the oligonucleotide comprises a sense strand comprising a stem-loop and the sugar moiety of each of the nucleotides at positions 1-7 and 12-17, 12-20, or 12-22 of the sense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00161] In some embodiments, the oligonucleotide comprises a sense strand having the sugar moiety at positions 3, 5, 8, 10, 12, 13, 15, and 17 modified with 2'-F. In some embodiments, the oligonucleotide comprises a sense strand having the sugar moiety at positions 1, 2, 4, 6, 7, 9, 11, 14, 16, and 18-20 modified with 2'-OMe. In some embodiments, the oligonucleotide comprises a sense strand having the sugar moiety of each of the nucleotides at positions 1, 2, 4, 6, 7, 9, 11, 14, 16, and 18-20 of the sense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA. In some embodiments, the oligonucleotide comprises a sense strand having the sugar moiety of each of the nucleotides at positions 1-7 and 12-17, 12-20, or 12-22 of the sense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00162] In some embodiments, the oligonucleotide comprises a sense strand having the sugar moiety at position 1, position 2, position 3, position 4, position 5, position 6, position 7, position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, position 16, position 17, position 18, position 19, position 20, position 21, position 22, position 23, position 24, position 25, position 26, position 27, position 28, position 29, position 30, position 31, position 32, position 33, position 34, position 35, or position 36 modified with 2'-F.

[00163] In some embodiments, the oligonucleotide comprises a sense strand having the sugar moiety at position 1, position 2, position 3, position 4, position 5, position 6, position 7, position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, position 16, position 17, position 18, position 19, position 20, position 21, position 22, position 23, position 24, position 25, position 26, position 27, position 28, position 29, position 30, position 31, position 32, position 33, position 34, position 35, or position 36 modified with 2'-OMe.

[00164] In some embodiments, the oligonucleotide comprises a sense strand having the sugar moiety at position 1, position 2, position 3, position 4, position 5, position 6, position 7, position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, position 16, position 17, position 18, position 19, position 20, position 21, position 22, position 23, position 24, position 25, position 26, position 27, position 28, position 29, position 30, position 31, position 32, position 33, position 34, position 35, or position 36 modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00165] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 2, 3, 4, 5, 7, 10, and 14 of the antisense strand modified with 2'-F, and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2′-deoxy-2′-fluoro-β-d-arabinonucleic acid (2'-FANA); and a 36-nucleotide sense strand having the sugar moiety at each of the nucleotides at positions 8-11 of the sense strand modified with 2'-F, and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-

MOE, 2'-O-NMA, and 2′-deoxy-2′-fluoro-β-d-arabinonucleic acid (2'-FANA). In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 2, 3, 4, 5, 7, 10, and 14 of the antisense strand modified with 2'-F, and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA; and a sense strand comprising a stem-loop and the sugar moiety at each of the nucleotides at positions 8-11 of the sense strand modified with 2'-F, and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, 2'-EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00166] In some embodiments, the oligonucleotide comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 2, 3, 4, 5, 7, 10, 14, 16, and 19 of the antisense strand modified with 2'-F, and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA; and a sense strand having the sugar moiety at each of the nucleotides at positions 3, 5, 8, 10, 12, 13, 15, and 17 of the sense strand modified with 2'-F, and the sugar moiety of each of the remaining nucleotides of the antisense strand modified with a modification selected from the group consisting of 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, EA, 2'-OMe, 2'-MOE, 2'-O-NMA, and 2'-FANA.

[00167] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NO: 769 and 804, respectively;

b) SEQ ID NO: 770 and 805, respectively;

c) SEQ ID NO: 771 and 806, respectively;

d) SEQ ID NO: 772 and 807, respectively;

e) SEQ ID NO: 773 and 808, respectively;

f) SEQ ID NO: 774 and 809, respectively;

g) SEQ ID NO: 775 and 810, respectively;

h) SEQ ID NO: 776 and 811, respectively;
i) SEQ ID NO: 777 and 812, respectively;
j) SEQ ID NO: 778 and 813, respectively;
k) SEQ ID NO: 779 and 814, respectively;
l) SEQ ID NO: 780 and 815, respectively;
m) SEQ ID NO: 781 and 816, respectively;
n) SEQ ID NO: 782 and 817, respectively;
o) SEQ ID NO: 783 and 818, respectively;
p) SEQ ID NO: 784 and 819, respectively;
q) SEQ ID NO: 785 and 820, respectively;
r) SEQ ID NO: 786 and 821, respectively;
s) SEQ ID NO: 787 and 822, respectively;
t) SEQ ID NO: 788 and 823, respectively;
u) SEQ ID NO: 789 and 824, respectively;
v) SEQ ID NO: 790 and 825, respectively;
w) SEQ ID NO: 791 and 826, respectively;
x) SEQ ID NO: 792 and 827, respectively;
y) SEQ ID NO: 793 and 828, respectively;
z) SEQ ID NO: 794 and 829, respectively;
aa) SEQ ID NO: 795 and 830, respectively;
bb) SEQ ID NO: 796 and 831, respectively;
cc) SEQ ID NO: 797 and 832, respectively;
dd) SEQ ID NO: 798 and 833, respectively;
ee) SEQ ID NO: 799 and 834, respectively;
ff) SEQ ID NO: 800 and 835, respectively;
gg) SEQ ID NO: 801 and 836, respectively;
hh) SEQ ID NO: 802 and 837, respectively;
ii) SEQ ID NO: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively, wherein one or more of positions 3, 5, 8, 10, 12, 13, 15, or 17 of the sense strand are modified with a 2'-F group.

[00168] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively;

j) SEQ ID NOs: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively, wherein one or more of positions 3, 5, 8, 10, 12, 13, 15, or 17 of the sense strand is modified with a 2'-F group.

[00169] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

d) SEQ ID NOs: 798 and 833, respectively;

e) SEQ ID NOs: 799 and 834, respectively;

f) SEQ ID NOs: 803 and 838, respectively; and

g) SEQ ID NOs: 1681 and 815, respectively, wherein one or more of positions 3, 5, 8, 10, 12, 13, 15, or 17 of the sense strand is modified with a 2'-F group.

[00170] *5' Terminal Phosphate*

[00171] In some embodiments, the oligonucleotide comprises a sense strand and an antisense strand, wherein the antisense strand comprises a 5' terminal phosphate. In some embodiments, 5' terminal phosphate groups of the oligonucleotide enhance the interaction with Ago2. However, oligonucleotides comprising a 5'-phosphate group may be susceptible to degradation *via* phosphatases or other enzymes, which can limit their bioavailability *in vivo*. In some embodiments, the oligonucleotide includes analogs of 5' phosphates that are resistant to such degradation. In some embodiments, the phosphate analog is oxymethyl phosphonate, vinyl phosphonate or malonyl phosphonate, or a combination thereof. In certain embodiments, the 5' end of the oligonucleotide strand is attached to chemical moiety that mimics the electrostatic and steric properties of a natural 5'-phosphate group ("phosphate mimic").

[00172] In some embodiments, the oligonucleotide has a phosphate analog at a 4'-carbon position of the sugar (referred to as a "4'-phosphate analog"). *See*, *e.g.*, Intl. Patent Application Publication No. WO 2018/045317. In some embodiments, the oligonucleotide comprises a 4'-phosphate analog at a 5' terminal nucleotide. In some embodiments, the phosphate analog is an oxymethyl phosphonate, in which the oxygen atom of the oxymethyl group is bound to the sugar moiety (*e.g.*, at its 4'-carbon) or analog thereof. In other embodiments, the 4'-phosphate analog is a thiomethylphosphonate or an aminomethylphosphonate, in which the sulfur atom of the thiomethyl group or the nitrogen atom of the amino methyl group is bound to the 4'-carbon of the sugar moiety or analog thereof. In certain embodiments, the 4'-phosphate analog is an oxymethyl phosphonate. In some embodiments, the oxymethyl phosphonate is represented by the formula $–O–CH_2–PO(OH)_2$,$–O–CH_2–PO(OR)_2$, or -O-CH2-POOH(R), in which R is independently selected from H, CH_3, an alkyl group, CH_2CH_2CN, $CH_2OCOC(CH_3)_3$, $CH_2OCH_2CH_2Si(CH_3)_3$ or a protecting group. In certain embodiments, the alkyl group is CH_2CH_3. More typically, R is independently selected from H, CH_3 or CH_2CH_3. In some embodiment, R is CH_3. In some embodiments, the 4'-phosphate analog is 4'-oxymethylphosphonate. In some embodiments, the modified nucleotide having the 4'-phosphonate analog is a uridine. In some embodiments, the modified nucleotide is 4'-O-monomethylphosphonate-2'-O-methyl uridine.

[00173] In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 769 and 804, respectively;

b) SEQ ID NOs: 770 and 805, respectively;

c) SEQ ID NOs: 771 and 806, respectively;

d) SEQ ID NOs: 772 and 807, respectively;

e) SEQ ID NOs: 773 and 808, respectively;

f) SEQ ID NOs: 774 and 809, respectively;

g) SEQ ID NOs: 775 and 810, respectively;

h) SEQ ID NOs: 776 and 811, respectively;

i) SEQ ID NOs: 777 and 812, respectively;

j) SEQ ID NOs: 778 and 813, respectively;

k) SEQ ID NOs: 779 and 814, respectively;

l) SEQ ID NOs: 780 and 815, respectively;

m) SEQ ID NOs: 781 and 816, respectively;

n) SEQ ID NOs: 782 and 817, respectively;

o) SEQ ID NOs: 783 and 818, respectively;

p) SEQ ID NOs: 784 and 819, respectively;

q) SEQ ID NOs: 785 and 820, respectively;

r) SEQ ID NOs: 786 and 821, respectively;

s) SEQ ID NOs: 787 and 822, respectively;

t) SEQ ID NOs: 788 and 823, respectively;

u) SEQ ID NOs: 789 and 824, respectively;

v) SEQ ID NOs: 790 and 825, respectively;

w) SEQ ID NOs: 791 and 826, respectively;

x) SEQ ID NOs: 792 and 827, respectively;

y) SEQ ID NOs: 793 and 828, respectively;

z) SEQ ID NOs: 794 and 829, respectively;

aa) SEQ ID NOs: 795 and 830, respectively;

bb) SEQ ID NOs: 796 and 831, respectively;

cc) SEQ ID NOs: 797 and 832, respectively;

dd) SEQ ID NOs: 798 and 833, respectively;

ee) SEQ ID NOs: 799 and 834, respectively;

ff) SEQ ID NOs: 800 and 835, respectively;

gg) SEQ ID NOs: 801 and 836, respectively;

hh) SEQ ID NOs: 802 and 837, respectively;

ii) SEQ ID NOs: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises a 5' terminal phosphate, optionally a 5' terminal phosphate analog.

[00174] In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively;

j) SEQ ID NOs: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises a 5' terminal phosphate, optionally a 5' terminal phosphate analog.

[00175] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

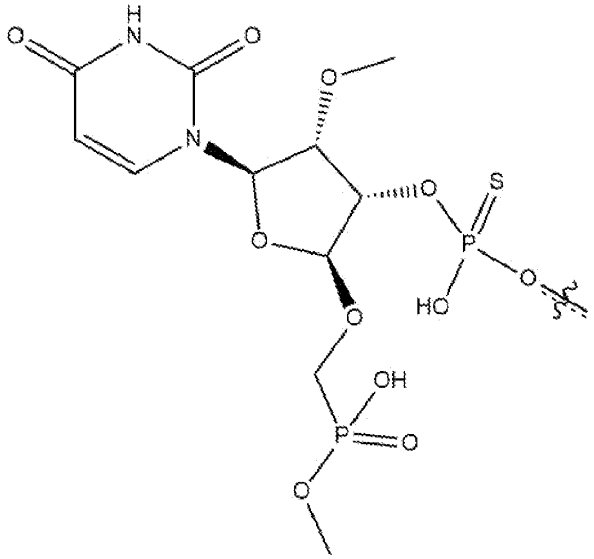
d) SEQ ID NOs: 798 and 833, respectively;

e) SEQ ID NOs: 799 and 834, respectively;

f) SEQ ID NOs: 803 and 838, respectively; and

g) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises a 5' terminal phosphate, optionally a 5' terminal phosphate analog.

[00176] In some embodiments, the oligonucleotide comprises an antisense strand comprising a 4'-phosphate analog at the 5' terminal nucleotide, wherein 5' terminal nucleotide comprises the following structure:



4'-O-monomethylphosphonate-2'-O-methyl uridine phosphorothioate [MePhosphonate-4O-mUs].

[00177] *Modified Internucleotide Linkage*

[00178] In some embodiments, an oligonucleotide herein (*e.g.*, a RNAi oligonucleotide) comprises a modified internucleotide linkage. In some embodiments, phosphate modifications or substitutions result in an oligonucleotide that comprises at least about 1 (*e.g.*, at least 1, at least 2, at least 3, or at least 5) modified internucleotide linkage. In some embodiments, the oligonucleotide comprises about 1 to about 10 (*e.g.*, 1 to 10, 2 to 8, 4 to 6, 3 to 10, 5 to 10, 1 to 5, 1 to 3, or 1 to 2) modified internucleotide linkages. In some embodiments, the oligonucleotide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified internucleotide linkages.

[00179] A modified internucleotide linkage may be a phosphorodithioate linkage, a phosphorothioate linkage, a phosphotriester linkage, a thionoalkylphosphonate linkage, a thionalkylphosphotriester linkage, a phosphoramidite linkage, a phosphonate linkage or a boranophosphate linkage. In some embodiments, at least one modified internucleotide linkage of the oligonucleotide is a phosphorothioate linkage.

[00180] In some embodiments, the oligonucleotide has a phosphorothioate linkage between one or more of positions 1 and 2 of the sense strand, positions 1 and 2 of the antisense strand, positions 2 and 3 of the antisense strand, positions 3 and 4 of the antisense strand, positions 20 and 21 of the antisense strand, and positions 21 and 22 of the antisense strand. In some embodiments, the oligonucleotide described herein has a phosphorothioate linkage between each of positions 1 and 2 of the sense strand, positions 1 and 2 of the antisense strand, positions 2 and 3 of the antisense strand, positions 20 and 21 of the antisense strand, and positions 21 and 22 of the antisense strand. In some embodiments, the oligonucleotide described herein has a phosphorothioate linkage between each of (i) positions 1 and 2 of the sense strand; and (ii) positions 1 and 2, positions 2 and 3, positions 3 and 4, positions 20 and 21, and positions 21 and 22 of the antisense strand.

[00181] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 769 and 804, respectively;

b) SEQ ID NOs: 770 and 805, respectively;

c) SEQ ID NOs: 771 and 806, respectively;

d) SEQ ID NOs: 772 and 807, respectively;

e) SEQ ID NOs: 773 and 808, respectively;

f) SEQ ID NOs: 774 and 809, respectively;

g) SEQ ID NOs: 775 and 810, respectively;

h) SEQ ID NOs: 776 and 811, respectively;

i) SEQ ID NOs: 777 and 812, respectively;

j) SEQ ID NOs: 778 and 813, respectively;

k) SEQ ID NOs: 779 and 814, respectively;

l) SEQ ID NOs: 780 and 815, respectively;

m) SEQ ID NOs: 781 and 816, respectively;

n) SEQ ID NOs: 782 and 817, respectively;

o) SEQ ID NOs: 783 and 818, respectively;

p) SEQ ID NOs: 784 and 819, respectively;

q) SEQ ID NOs: 785 and 820, respectively;

r) SEQ ID NOs: 786 and 821, respectively;

s) SEQ ID NOs: 787 and 822, respectively;

t) SEQ ID NOs: 788 and 823, respectively;

u) SEQ ID NOs: 789 and 824, respectively;

v) SEQ ID NOs: 790 and 825, respectively;

w) SEQ ID NOs: 791 and 826, respectively;

x) SEQ ID NOs: 792 and 827, respectively;

y) SEQ ID NOs: 793 and 828, respectively;

z) SEQ ID NOs: 794 and 829, respectively;

aa) SEQ ID NOs: 795 and 830, respectively;

bb) SEQ ID NOs: 796 and 831, respectively;

cc) SEQ ID NOs: 797 and 832, respectively;

dd) SEQ ID NOs: 798 and 833, respectively;

ee) SEQ ID NOs: 799 and 834, respectively;

ff) SEQ ID NOs: 800 and 835, respectively;

gg) SEQ ID NOs: 801 and 836, respectively;

hh) SEQ ID NOs: 802 and 837, respectively;

ii) SEQ ID NOs: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises a modified internucleotide linkage.

[00182] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively;

j) SEQ ID NOs: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises a modified internucleotide linkage.

[00183] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

d) SEQ ID NOs: 798 and 833, respectively;

e) SEQ ID NOs: 799 and 834, respectively;

f) SEQ ID NOs: 803 and 838, respectively; and

g) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises a modified internucleotide linkage.

[00184] *Base Modifications*

[00185] In some embodiments, an oligonucleotide herein (*e.g.*, a RNAi oligonucleotide) has one or more modified nucleobases. In some embodiments, modified nucleobases (also referred to herein as base analogs) are linked at the 1' position of a nucleotide sugar moiety. In certain embodiments, a modified nucleobase is a nitrogenous base. In certain embodiments, a modified nucleobase does not contain nitrogen atom. *See*, *e.g.*, US Patent Application Publication No. 2008/0274462. In some embodiments, a modified nucleotide comprises a universal base. In some embodiments, a modified nucleotide does not contain a nucleobase (abasic).

[00186] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 769 and 804, respectively;

b) SEQ ID NOs: 770 and 805, respectively;

c) SEQ ID NOs: 771 and 806, respectively;

d) SEQ ID NOs: 772 and 807, respectively;

e) SEQ ID NOs: 773 and 808, respectively;

f) SEQ ID NOs: 774 and 809, respectively;

g) SEQ ID NOs: 775 and 810, respectively;

h) SEQ ID NOs: 776 and 811, respectively;

i) SEQ ID NOs: 777 and 812, respectively;

j) SEQ ID NOs: 778 and 813, respectively;

k) SEQ ID NOs: 779 and 814, respectively;

l) SEQ ID NOs: 780 and 815, respectively;

m) SEQ ID NOs: 781 and 816, respectively;

n) SEQ ID NOs: 782 and 817, respectively;

o) SEQ ID NOs: 783 and 818, respectively;

p) SEQ ID NOs: 784 and 819, respectively;

q) SEQ ID NOs: 785 and 820, respectively;

r) SEQ ID NOs: 786 and 821, respectively;

s) SEQ ID NOs: 787 and 822, respectively;

t) SEQ ID NOs: 788 and 823, respectively;

u) SEQ ID NOs: 789 and 824, respectively;

v) SEQ ID NOs: 790 and 825, respectively;

w) SEQ ID NOs: 791 and 826, respectively;

x) SEQ ID NOs: 792 and 827, respectively;

y) SEQ ID NOs: 793 and 828, respectively;

z) SEQ ID NOs: 794 and 829, respectively;

aa) SEQ ID NOs: 795 and 830, respectively;

bb) SEQ ID NOs: 796 and 831, respectively;

cc) SEQ ID NOs: 797 and 832, respectively;

dd) SEQ ID NOs: 798 and 833, respectively;

ee) SEQ ID NOs: 799 and 834, respectively;

ff) SEQ ID NOs: 800 and 835, respectively;

gg) SEQ ID NOs: 801 and 836, respectively;

hh) SEQ ID NOs: 802 and 837, respectively;

ii) SEQ ID NOs: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises one or more modified nucleobases.

[00187] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively;

j) SEQ ID NOs: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises one or more modified nucleobases.

[00188] In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

d) SEQ ID NOs: 798 and 833, respectively;

e) SEQ ID NOs: 799 and 834, respectively;

f) SEQ ID NOs: 803 and 838, respectively;

g) SEQ ID NOs: 1681 and 815, respectively, wherein the oligonucleotide comprises one or more modified nucleobases.

[00189] In some embodiments, a universal base is a heterocyclic moiety located at the 1' position of a nucleotide sugar moiety in a modified nucleotide, or the equivalent position in a nucleotide sugar moiety substitution, that, when present in a duplex, can be positioned opposite more than one type of base without substantially altering structure of the duplex. In some embodiments, compared to a reference ss nucleic acid (*e.g.*, an oligonucleotide) that is fully complementary to a target nucleic acid, a ss nucleic acid containing a universal base forms a duplex with the target nucleic acid that has a lower T_m than a duplex formed with the complementary nucleic acid. In some embodiments, when compared to a reference ss nucleic acid in which the universal base has been replaced with a base to generate a single mismatch, the ss nucleic acid containing the universal base forms a duplex with the target nucleic acid that has a higher T_m than a duplex formed with the nucleic acid comprising the mismatched base.

[00190] Non-limiting examples of universal-binding nucleotides include, but are not limited to, inosine, 1-β-D-ribofuranosyl-5-nitroindole and/or 1-β-D-ribofuranosyl-3-nitropyrrole (*see*, US Patent Application Publication No. 2007/0254362; Van Aerschot *et al.* (1995) NUCLEIC ACIDS RES. 23:4363-4370; Loakes *et al.* (1995) NUCLEIC ACIDS RES. 23:2361-66; and Loakes & Brown (1994) NUCLEIC ACIDS RES. 22:4039-43).

[00191] ***Targeting Ligands***

[00192] In some embodiments, it is desirable to target the oligonucleotide (*e.g.*, a RNAi oligonucleotide) to one or more cells or one or more organs. Such a strategy can help to avoid undesirable effects in other organs or avoid undue loss of the oligonucleotide to cells, tissue, or organs that would not benefit from the oligonucleotide. Accordingly, in some embodiments, the oligonucleotide is modified to facilitate targeting and/or delivery to a particular tissue, cell, or organ (*e.g.*, to facilitate delivery of the oligonucleotide to the CNS). In some embodiments, the

oligonucleotide comprises at least one nucleotide (*e.g.*, 1, 2, 3, 4, 5, 6, or more nucleotides) conjugated to one or more targeting ligand(s). In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 769 and 804, respectively;
b) SEQ ID NOs: 770 and 805, respectively;
c) SEQ ID NOs: 771 and 806, respectively;
d) SEQ ID NOs: 772 and 807, respectively;
e) SEQ ID NOs: 773 and 808, respectively;
f) SEQ ID NOs: 774 and 809, respectively;
g) SEQ ID NOs: 775 and 810, respectively;
h) SEQ ID NOs: 776 and 811, respectively;
i) SEQ ID NOs: 777 and 812, respectively;
j) SEQ ID NOs: 778 and 813, respectively;
k) SEQ ID NOs: 779 and 814, respectively;
l) SEQ ID NOs: 780 and 815, respectively;
m) SEQ ID NOs: 781 and 816, respectively;
n) SEQ ID NOs: 782 and 817, respectively;
o) SEQ ID NOs: 783 and 818, respectively;
p) SEQ ID NOs: 784 and 819, respectively;
q) SEQ ID NOs: 785 and 820, respectively;
r) SEQ ID NOs: 786 and 821, respectively;
s) SEQ ID NOs: 787 and 822, respectively;
t) SEQ ID NOs: 788 and 823, respectively;
u) SEQ ID NOs: 789 and 824, respectively;
v) SEQ ID NOs: 790 and 825, respectively;
w) SEQ ID NOs: 791 and 826, respectively;
x) SEQ ID NOs: 792 and 827, respectively;
y) SEQ ID NOs: 793 and 828, respectively;

z) SEQ ID NOs: 794 and 829, respectively;

aa) SEQ ID NOs: 795 and 830, respectively;

bb) SEQ ID NOs: 796 and 831, respectively;

cc) SEQ ID NOs: 797 and 832, respectively;

dd) SEQ ID NOs: 798 and 833, respectively;

ee) SEQ ID NOs: 799 and 834, respectively;

ff) SEQ ID NOs: 800 and 835, respectively;

gg) SEQ ID NOs: 801 and 836, respectively;

hh) SEQ ID NOs: 802 and 837, respectively; and

ii) SEQ ID NOs: 803 and 838, respectively, wherein the oligonucleotide comprises a targeting ligand conjugated to at least one nucleotide.

[00193] In some embodiments, the oligonucleotide comprises at least one nucleotide (*e.g.*, 1, 2, 3, 4, 5, 6, or more nucleotides) conjugated to one or more targeting ligand(s). In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively; and

j) SEQ ID NOs: 803 and 838, respectively, wherein the oligonucleotide comprises a targeting ligand conjugated to at least one nucleotide.

[00194] In some embodiments, the oligonucleotide comprises at least one nucleotide (*e.g.*, 1, 2, 3, 4, 5, 6, or more nucleotides) conjugated to one or more targeting ligand(s). In some

embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

d) SEQ ID NOs: 798 and 833, respectively;

e) SEQ ID NOs: 799 and 834, respectively; and

f) SEQ ID NOs: 803 and 838, respectively, wherein the oligonucleotide comprises a targeting ligand conjugated to at least one nucleotide.

[00195] In some embodiments, the targeting ligand comprises a carbohydrate, amino sugar, cholesterol, peptide, polypeptide, or protein or part of a protein (*e.g.*, an antibody or antibody fragment). In some embodiments, the targeting ligand is an aptamer. For example, the targeting ligand may be an RGD peptide that is used to target tumor vasculature or glioma cells, CREKA peptide to target tumor vasculature or stoma, transferring, lactoferrin, or an aptamer to target transferrin receptors expressed on CNS vasculature, or an anti-EGFR antibody to target EGFR on glioma cells. In certain embodiments, the targeting ligand is one or more GalNAc moieties. In some embodiments, the targeting ligand is one or more lipid moieties.

[00196] In some embodiments, 1 or more (*e.g.*, 1, 2, 3, 4, 5, or 6) nucleotides of the oligonucleotide are each conjugated to a separate targeting ligand. In some embodiments, 2 to 4 nucleotides of the oligonucleotide are each conjugated to a separate targeting ligand. In some embodiments, targeting ligands are conjugated to 2 to 4 nucleotides at either ends of the sense or antisense strand (*e.g.*, targeting ligands are conjugated to a 2 to 4 nucleotide overhang or extension on the 5' or 3' end of the sense or antisense strand) such that the targeting ligands resemble bristles of a toothbrush and the oligonucleotide resembles a toothbrush. For example, the oligonucleotide may comprise a stem-loop at either the 5' or 3' end of the sense strand and 1, 2, 3, or 4 nucleotides of the loop of the stem may be individually conjugated to a targeting ligand. In some embodiments, the oligonucleotide comprises a stem-loop at the 3' end of the sense strand, wherein the loop of the stem-loop comprises a triL or a tetraL, and wherein the 3 or 4 nucleotides comprising the triL or tetraL, respectfully, are individually conjugated to a targeting ligand. In some embodiments, the

oligonucleotide comprises a blunt end at the 3' end of the oligonucleotide and one or more targeting ligands conjugated to at least one nucleotide. In some embodiments, the oligonucleotide comprises a blunt end at the 3' end of the oligonucleotide and one or more targeting ligands conjugated to the 5' terminal nucleotide of the sense strand.

[00197] *GalNAc Conjugation*

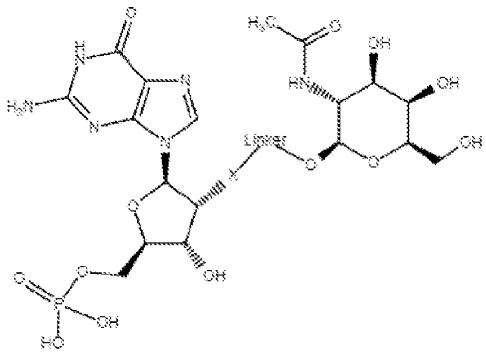
[00198] GalNAc is a high affinity ligand for the asialoglycoprotein receptor (ASGPR), which is primarily expressed on the sinusoidal surface of hepatocyte cells and has a major role in binding, internalizing and subsequent clearing circulating glycoproteins that contain terminal galactose or GalNAc residues (asialoglycoproteins). Conjugation (either indirect or direct) of GalNAc moieties to the oligonucleotides herein can be used to target them to ASGPR expressed on cells. In some embodiments, the oligonucleotide is conjugated to at least one or more GalNAc moieties, wherein the GalNAc moieties target the oligonucleotide to ASGPR expressed on human liver cells (*e.g.*, human hepatocytes). In some embodiments, the GalNAc moiety target the oligonucleotide to the liver.

[00199] In some embodiments, the oligonucleotide is conjugated directly or indirectly to a monovalent GalNAc. In some embodiments, the oligonucleotide is conjugated directly or indirectly to more than one monovalent GalNAc (*i.e.*, is conjugated to 2, 3, or 4 monovalent GalNAc moieties, and is typically conjugated to 3 or 4 monovalent GalNAc moieties). In some embodiments, the oligonucleotide is conjugated to one or more bivalent GalNAc, trivalent GalNAc, or tetravalent GalNAc moieties. In some embodiments, the bivalent, trivalent, or tetravalent GalNAc moiety is conjugated to the oligonucleotide via a branched linker. In some embodiments, the monovalent GalNAc moiety is conjugated to a first nucleotide and the bivalent, trivalent, or tetravalent GalNAc moiety is conjugated to a second nucleotide via a branched linker.

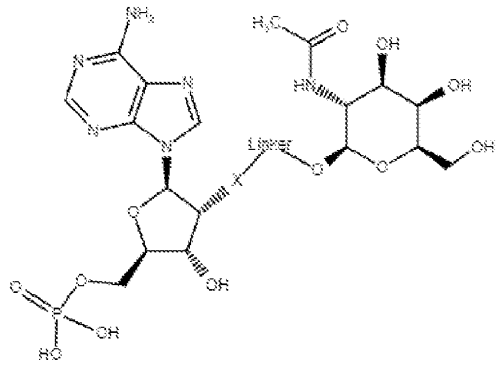
[00200] In some embodiments, 1 or more (*e.g.*, 1, 2, 3, 4, 5, or 6) nucleotides of the oligonucleotide are each conjugated to a GalNAc moiety. In some embodiments, 2 to 4 nucleotides of a tetraL are each conjugated to a separate GalNAc. In some embodiments, 1 to 3 nucleotides of a triL are each conjugated to a separate GalNAc. In some embodiments, targeting ligands are conjugated to 2 to 4 nucleotides at either ends of the sense or antisense strand (*e.g.*, ligands are

conjugated to a 2 to 4 nucleotide overhang or extension on the 5' or 3' end of the sense or antisense strand) such that the GalNAc moieties resemble bristles of a toothbrush and the oligonucleotide resembles a toothbrush. In some embodiments, GalNAc moieties are conjugated to a nucleotide of the sense strand. For example, 4 GalNAc moieties can be conjugated to nucleotides in the tetraL of the sense strand where each GalNAc moiety is conjugated to 1 nucleotide.

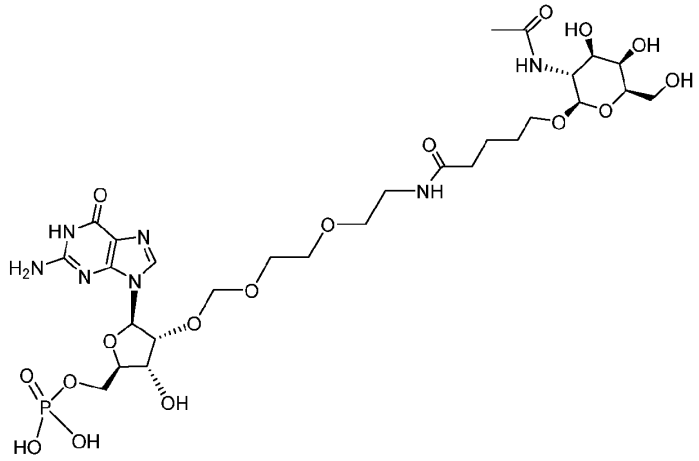
[00201] In some embodiments, the oligonucleotide comprises a tetraL, wherein the tetraL is any combination of adenine (A) and guanine (G) nucleotides. In some embodiments, the tetraL comprises a monovalent GalNAc moiety attached to any one or more guanine (G) nucleotides of the tetraloop *via* any linker described herein, as depicted below (X=heteroatom):



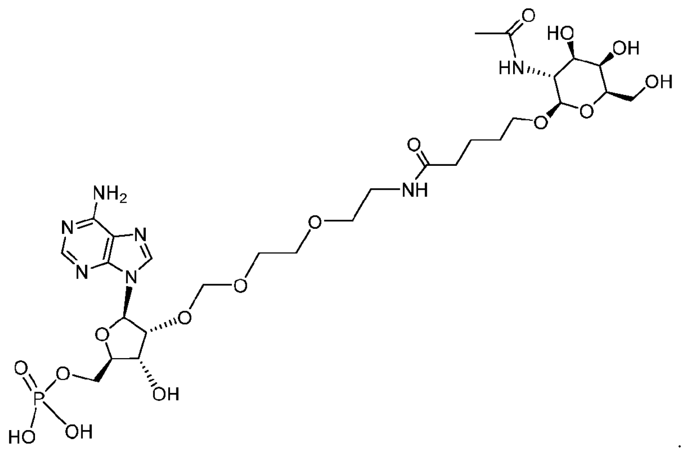
[00202] In some embodiments, the tetraL has a monovalent GalNAc attached to any one or more adenine nucleotides of the tetraloop via any linker described herein, as depicted below (X=heteroatom):



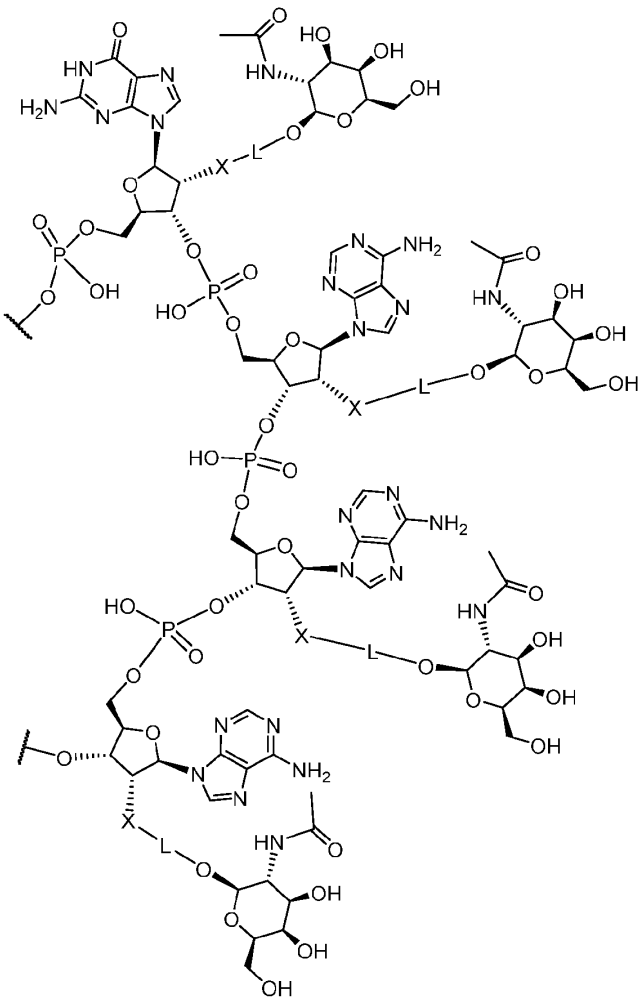
[00203] In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) comprises a monovalent GalNAc attached to a guanine nucleotide referred to as [ademG-GalNAc] or 2′-aminodiethoxymethanol-Guanine-GalNAc, as depicted below:



[00204] In some embodiments, an oligonucleotide herein comprises a monovalent GalNAc attached to an adenine nucleotide, referred to as [ademA-GalNAc] or 2'-aminodiethoxymethanol-Adenine-GalNAc, as depicted below:

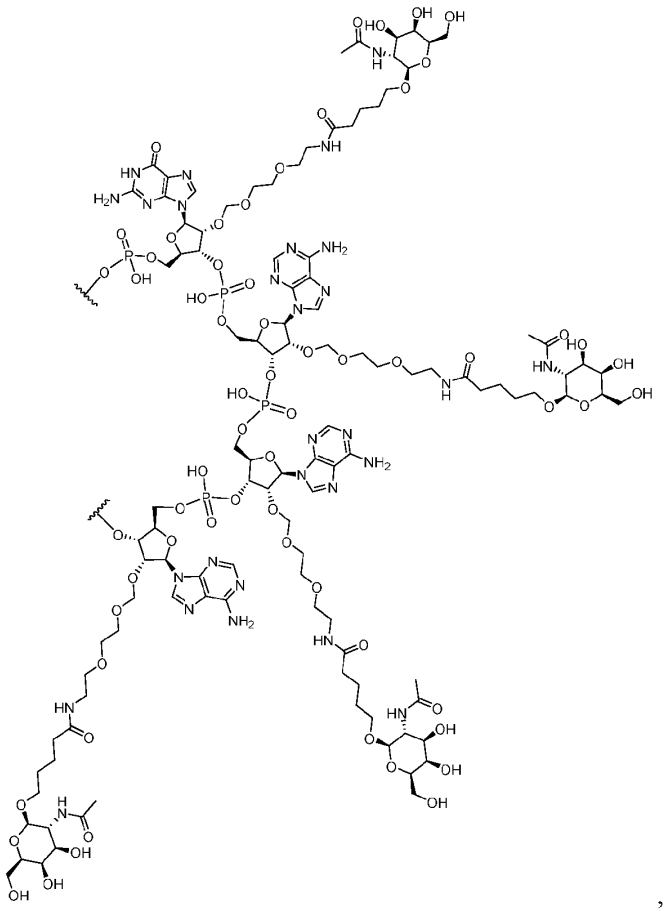


[00205] An example of such conjugation is shown below for a loop comprising from 5' to 3' the nucleotide sequence GAAA (L = linker, X = heteroatom) stem attachment points are shown. Such a loop may be present, for example, at positions 27-30 of the sense strand of any one of the sense strands listed in Tables 4 and 5. In the chemical formula, is used to describe an attachment point to the oligonucleotide strand:

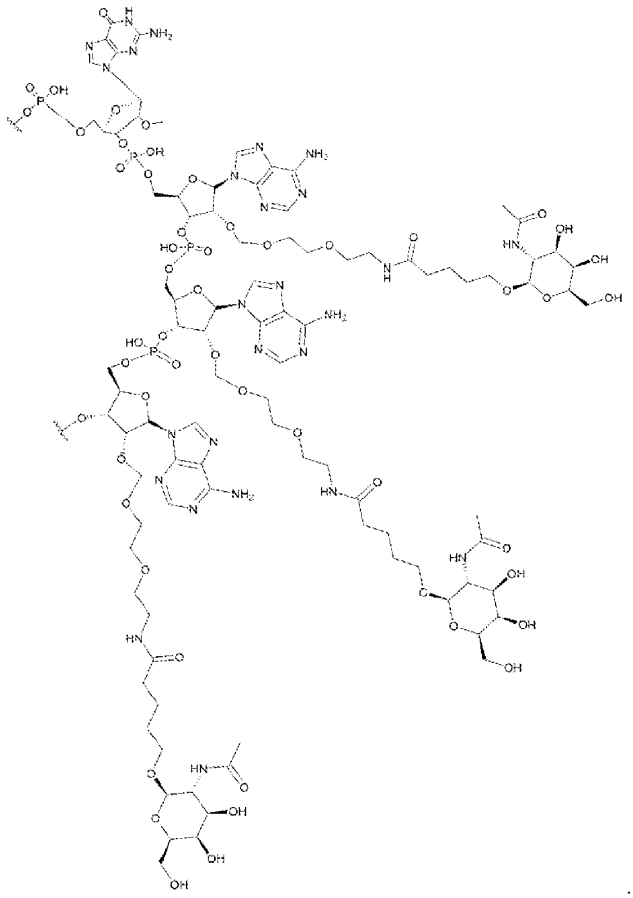


[00206] Appropriate methods or chemistry (*e.g.*, click chemistry) can be used to link a targeting ligand to a nucleotide. In some embodiments, a targeting ligand is conjugated to a nucleotide using a click linker. In some embodiments, an acetal-based linker is used to conjugate a targeting ligand to a nucleotide of any one of the oligonucleotides described herein. Acetal-based linkers are disclosed, for example, in Intl. Patent Application Publication No. WO 2016/100401. In some embodiments, the linker is a labile linker. However, in other embodiments, the linker is stable. Examples are shown below for a loop comprising from 5' to 3' the nucleotides GAAA, in which GalNAc moieties are attached to 3 or 4 nucleotides of the loop using an acetal linker. Such a loop

may be present, for example, at positions 27-30 of the any one of the sense strands listed in Tables 4 and 5. In the chemical formula,  is an attachment point to the oligonucleotide strand:



,



[00207] As mentioned, various appropriate methods or chemistry synthetic techniques (*e.g.*, click chemistry) can be used to link a targeting ligand to a nucleotide. In some embodiments, a targeting ligand is conjugated to a nucleotide using a click linker. In some embodiments, an acetal-based linker is used to conjugate a targeting ligand to a nucleotide of any one of the oligonucleotides described herein. Acetal-based linkers are disclosed, for example, in Intl. Patent Application Publication No. WO 2016/100401. In some embodiments, the linker is a labile linker. However, in other embodiments, the linker is a stable linker.

[00208] In some embodiments, a duplex extension (*e.g.*, of up to 3, 4, 5, or 6 bp in length) is provided between a targeting ligand (*e.g.*, a GalNAc moiety) and a RNAi oligonucleotide. In some embodiments, the oligonucleotides herein do not have a GalNAc conjugated thereto.

[00209] In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 769 and 804, respectively;

b) SEQ ID NOs: 770 and 805, respectively;

c) SEQ ID NOs: 771 and 806, respectively;

d) SEQ ID NOs: 772 and 807, respectively;

e) SEQ ID NOs: 773 and 808, respectively;

f) SEQ ID NOs: 774 and 809, respectively;

g) SEQ ID NOs: 775 and 810, respectively;

h) SEQ ID NOs: 776 and 811, respectively;

i) SEQ ID NOs: 777 and 812, respectively;

j) SEQ ID NOs: 778 and 813, respectively;

k) SEQ ID NOs: 779 and 814, respectively;

l) SEQ ID NOs: 780 and 815, respectively;

m) SEQ ID NOs: 781 and 816, respectively;

n) SEQ ID NOs: 782 and 817, respectively;

o) SEQ ID NOs: 783 and 818, respectively;

p) SEQ ID NOs: 784 and 819, respectively;

q) SEQ ID NOs: 785 and 820, respectively;

r) SEQ ID NOs: 786 and 821, respectively;

s) SEQ ID NOs: 787 and 822, respectively;

t) SEQ ID NOs: 788 and 823, respectively;

u) SEQ ID NOs: 789 and 824, respectively;

v) SEQ ID NOs: 790 and 825, respectively;

w) SEQ ID NOs: 791 and 826, respectively;

x) SEQ ID NOs: 792 and 827, respectively;

y) SEQ ID NOs: 793 and 828, respectively;

z) SEQ ID NOs: 794 and 829, respectively;

aa) SEQ ID NOs: 795 and 830, respectively;

bb) SEQ ID NOs: 796 and 831, respectively;

cc) SEQ ID NOs: 797 and 832, respectively;

dd) SEQ ID NOs: 798 and 833, respectively;

ee) SEQ ID NOs: 799 and 834, respectively;

ff) SEQ ID NOs: 800 and 835, respectively;

gg) SEQ ID NOs: 801 and 836, respectively;

hh) SEQ ID NOs: 802 and 837, respectively; and

ii) SEQ ID NOs: 803 and 838, respectively, wherein the oligonucleotide comprises at least one GalNAc moiety conjugated to a nucleotide.

[00210] In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively; and

j) SEQ ID NOs: 803 and 838, respectively, wherein the oligonucleotide comprises at least one GalNAc moiety conjugated to a nucleotide.

[00211] In some embodiments, the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

d) SEQ ID NOs: 798 and 833, respectively;

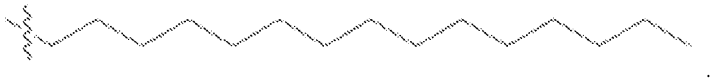
e) SEQ ID NOs: 799 and 834, respectively; and

f) SEQ ID NOs: 803 and 838, respectively, wherein the oligonucleotide comprises at least one GalNAc moiety conjugated to a nucleotide.

Lipid Conjugation

[00212] In some embodiments, one or more lipid moieties are conjugated to a 5' terminal nucleotide of a sense strand. In some embodiments, one or more lipid moieties are conjugated to an adenine nucleotide. In some embodiments, one or more lipid moieties are conjugated to a guanine nucleotide. In some embodiments, one or more lipid moieties are conjugated to a cytosine nucleotide. In some embodiments, one or more lipid moieties are conjugated to a thymine nucleotide. In some embodiments, one or more lipid moieties are conjugated to a uracil nucleotide.

[00213] In some embodiments, the lipid moiety is a hydrocarbon chain. In some embodiments, the hydrocarbon chain is saturated. In some embodiments, the hydrocarbon chain is unsaturated. In some embodiments, the hydrocarbon chain is branched. In some embodiments, the hydrocarbon chain is straight. In some embodiments, the lipid moiety is a C_8-C_{30} hydrocarbon chain. In some embodiments, the lipid moiety is a C_8:0, C_{10}:0, C_{11}:0, C_{12}:0, C_{14}:0, C_{16}:0, C_{17}:0, C_{18}:0, C_{18}:1, C_{18}:2, C_{22}:5, C_{22}:0, C_{24}:0, C_{26}:0, C_{22}:6, C_{24}:1, diacyl C_{16}:0 or diacyl C_{18}:1. In some embodiments, the lipid moiety is a C_{16} hydrocarbon chain. In some embodiments, the C_{16} hydrocarbon chain is represented as:



[00214] In some embodiments, the sense strand is 20-22 nucleotides in length and the lipid moiety is a hydrocarbon chain that is conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the sense strand is 20-22 nucleotides in length and the hydrocarbon chain is conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the sense strand is 20-22 nucleotides in length and a C_{14}-C_{22} hydrocarbon chain is conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the sense strand is 20-22 nucleotides in length and a C_{16} hydrocarbon chain is conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the sense strand is 20 nucleotides in length and the lipid moiety is conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the sense strand

is 20 nucleotides in length and the lipid moiety is a hydrocarbon chain is conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the sense strand is 20 nucleotides in length and a C_{14}-C_{22} hydrocarbon chain is conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the sense strand is 20 nucleotides in length and a C_{16} hydrocarbon chain is conjugated to the 5' terminal nucleotide of the sense strand.

[00215] In some embodiments, the oligonucleotide comprises (i) a sense strand of 20-22 nucleotides in length; (ii) an antisense strand comprising a 3' overhang sequence of one or more nucleotides in length; (iii) a blunt end comprising the 3' end of the sense strand; and (iv) a lipid moiety conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) a sense strand of 20-22 nucleotides in length; (ii) an antisense strand comprising a 3' overhang sequence of one or more nucleotides in length; (iii) a blunt end comprising the 3' end of the sense strand; and (iv) a hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) a sense strand of 20-22 nucleotides in length; (ii) an antisense strand comprising a 3' overhang sequence of one or more nucleotides in length; (iii) a blunt end comprising the 3' end of the sense strand; and (iv) a C_{14}-C_{22} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) a sense strand of 20-22 nucleotides in length; (ii) an antisense strand comprising a 3' overhang sequence of one or more nucleotides in length; (iii) a blunt end comprising the 3' end of the sense strand; and (iv) a C_{16} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand.

[00216] In some embodiments, the oligonucleotide comprises (i) a sense strand of 20 nucleotides in length; (ii) an antisense strand of 22 nucleotides in length comprising a 3' overhang sequence of two nucleotides in length; (iii) a blunt end comprising the 3' end of the sense strand; and (iv) a lipid moiety conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) a sense strand of 20 nucleotides in length; (ii) an antisense strand of 22 nucleotides in length comprising a 3' overhang sequence of two nucleotides in length; (iii) a blunt end comprising the 3' end of the sense strand; and (iv) a hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) a sense strand of 20 nucleotides in length; (ii) an antisense strand of 22 nucleotides in length

comprising a 3' overhang sequence of two nucleotides in length; (iii) a blunt end comprising the 3' end of the sense strand; and (iv) a C_{14}-C_{22} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) a sense strand of 20 nucleotides in length; (ii) an antisense strand of 22 nucleotides in length comprising a 3' overhang sequence of two nucleotides in length; (iii) a blunt end comprising the 3' end of the sense strand; and (iv) a C_{16} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand.

[00217] In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, and 1124; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a lipid moiety conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1061, 1108, 1119, 1120, 1124, 1130, 1065, 1095, 1096, and 1102; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a lipid moiety conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1130, 1095, 1096, 1119, 1120, and 1124; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a lipid moiety conjugated to the 5' terminal nucleotide of the sense strand.

[00218] In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, and 1124; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a hydrocarbon chain conjugated to the 5' terminal

nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1061, 1108, 1119, 1120, 1124, 1130, 1065, 1095, 1096, and 1102; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1130, 1095, 1096, 1119, 1120, and 1124; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand.

[00219] In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096, 1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, and 1124; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a C_{14}-C_{22} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1061, 1108, 1119, 1120, 1124, 1130, 1065, 1095, 1096, and 1102; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a C_{14}-C_{22} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1130, 1095, 1096, 1119, 1120, and 1124; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a C_{14}-C_{22} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand.

[00220] In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1125, 1127, 1130, 1019, 1031, 1044, 1064, 1065, 1067, 1083, 915, 1095, 1096,

1102, 1110, 923, 925, 1025, 1039, 1049, 1061, 1070, 1072, 1075, 1081, 1108, 1111, 1114, 1119, 1120, 1121, 1122, 1123, and 1124; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a C_{16} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1061, 1108, 1119, 1120, 1124, 1130, 1065, 1095, 1096, and 1102; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a C_{16} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises (i) an antisense strand of 19-30 nucleotides comprising a region of complementarity to a MAPT mRNA target sequence selected from SEQ ID NOs: 1130, 1095, 1096, 1119, 1120, and 1124; (ii) a sense strand of 19-25 nucleotides that forms a duplex region with the antisense strand; and (iii) a C_{16} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand.

[00221] In some embodiments, the oligonucleotide comprises a sense strand comprising the nucleotide sequence of SEQ ID NO: 1681 and an antisense strand comprising the nucleotide sequence of SEQ ID NO: 815, wherein the sense strand comprises a lipid moiety conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises a sense strand comprising the nucleotide sequence of SEQ ID NO: 1681 and an antisense strand comprising the nucleotide sequence of SEQ ID NO: 815, wherein the sense strand comprises a hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises a sense strand comprising the nucleotide sequence of SEQ ID NO: 1681 and an antisense strand comprising the nucleotide sequence of SEQ ID NO: 815, wherein the sense strand comprises a C_{14}-C_{22} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand. In some embodiments, the oligonucleotide comprises a sense strand comprising the nucleotide sequence of SEQ ID NO: 1681 and an antisense strand comprising the nucleotide sequence of SEQ ID NO: 815, wherein the sense strand comprises a C_{16} hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand.

[00222] ***Exemplary MAPT-Targeting RNAi Oligonucleotides***

[00223] In some embodiments, the *MAPT*-targeting RNAi oligonucleotide for reducing *MAPT* gene expression provided by the current disclosure comprises a sense strand and an antisense strand, wherein all nucleotides comprising the sense strand and the antisense strand are modified, wherein the antisense strand comprises a region of complementarity to a MAPT mRNA target sequence of any one of SEQ ID NOs: 912-1295, and wherein the region of complementarity is at least 15 contiguous nucleotides in length. In some embodiments, the 5' terminal nucleotide of the antisense strand comprises 4'-O-monomethylphosphonate-2'-O-methyluridine [MePhosphonate-4O-mU], as described herein. In some embodiments, the 5' terminal nucleotide of the antisense strand comprises a phosphorothioate linkage. In some embodiments, the antisense strand and the sense strand comprise one or more 2'-F- and 2'-OMe-modified nucleotides and at least one phosphorothioate linkage. In some embodiments, the antisense strand comprises 4 phosphorothioate linkages and the sense strand comprises 1 phosphorothioate linkage. In some embodiments, the antisense strand comprises 5 phosphorothioate linkages and the sense strand comprises 1 phosphorothioate linkage.

[00224] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) comprises a sense strand having a sequence of any one of SEQ ID NOs: 912-1295 and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 1296-1679.

[00225] In some embodiments, the oligonucleotide comprises a sense strand having a sequence of any one of SEQ ID NOs: 1-384 and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 385-768.

[00226] In some embodiments, the oligonucleotide pcomprises a sense strand having a sequence of any one of SEQ ID NOs: 769-803 and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 804-838.

[00227] In some embodiments, the oligonucleotide comprises a sense strand having a sequence of any one of SEQ ID NOs: 769-803 and 1681, and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 804-838.

[00228] In some embodiments, the oligonucleotide comprises a sense strand having a sequence of any one of SEQ ID NOs: 839-873 and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 874-908.

[00229] In some embodiments, the oligonucleotide comprises a sense strand having a sequence of any one of SEQ ID NOs: 839-873 and 1681, and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 874-908.

[00230] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises:

a sense strand of 36 nucleotides comprising a 2'-F-modified nucleotide at positions 3, 5, 8, 10, 12, 13, 15, and 17; a 2'-OMe-modified nucleotide at positions 1, 2, 4, 6, 7, 9, 11, 14, 16, 18-27, and 31-36; a GalNAc-conjugated nucleotide at position 28, 29, and 30; and a phosphorothioate linkage between positions 1 and 2; and

an antisense strand of 22 nucleotides comprising a 2'-F-modified nucleotide at positions 2, 3, 4, 5, 7, 10, 14, 16, and 19; a 2'-OMe-modified nucleotide at positions 1, 6, 8, 9, 11, 12, 13, 15, 17, 18, and 20-22; a phosphorothioate linkage between positions 1 and 2, positions 2 and 3, positions 20 and 21, and positions 21 and 22; and a 5' terminal nucleotide at position 1 comprising a 4'-phosphate analog, optionally wherein the 5' terminal nucleotide comprises 4'-O-monomethylphosphonate-2'-O-methyluridine [MePhosphonate-4O-mU]; wherein positions 1-20 of the antisense strand form a duplex region with positions 1-20 of the sense strand, wherein positions 21-36 of the sense strand form a stem-loop, wherein positions 27-30 form the loop of the stem-loop, optionally wherein positions 27-30 comprise a tetraL, wherein positions 21 and 22 of the antisense strand comprise an overhang, and wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 769 and 804, respectively;

b) SEQ ID NOs: 770 and 805, respectively;

c) SEQ ID NOs: 771 and 806, respectively;

d) SEQ ID NOs: 772 and 807, respectively;

e) SEQ ID NOs: 773 and 808, respectively;

f) SEQ ID NOs: 774 and 809, respectively;

g) SEQ ID NOs: 775 and 810, respectively;
h) SEQ ID NOs: 776 and 811, respectively;
i) SEQ ID NOs: 777 and 812, respectively;
j) SEQ ID NOs: 778 and 813, respectively;
k) SEQ ID NOs: 779 and 814, respectively;
l) SEQ ID NOs: 780 and 815, respectively;
m) SEQ ID NOs: 781 and 816, respectively;
n) SEQ ID NOs: 782 and 817, respectively;
o) SEQ ID NOs: 783 and 818, respectively;
p) SEQ ID NOs: 784 and 819, respectively;
q) SEQ ID NOs: 785 and 820, respectively;
r) SEQ ID NOs: 786 and 821, respectively;
s) SEQ ID NOs: 787 and 822, respectively;
t) SEQ ID NOs: 788 and 823, respectively;
u) SEQ ID NOs: 789 and 824, respectively;
v) SEQ ID NOs: 790 and 825, respectively;
w) SEQ ID NOs: 791 and 826, respectively;
x) SEQ ID NOs: 792 and 827, respectively;
y) SEQ ID NOs: 793 and 828, respectively;
z) SEQ ID NOs: 794 and 829, respectively;
aa) SEQ ID NOs: 795 and 830, respectively;
bb) SEQ ID NOs: 796 and 831, respectively;
cc) SEQ ID NOs: 797 and 832, respectively;
dd) SEQ ID NOs: 798 and 833, respectively;
ee) SEQ ID NOs: 799 and 834, respectively;
ff) SEQ ID NOs: 800 and 835, respectively;
gg) SEQ ID NOs: 801 and 836, respectively;
hh) SEQ ID NOs: 802 and 837, respectively; and
ii) SEQ ID NOs: 803 and 838, respectively.

[00231] In some embodiments, an oligonucleotide (*e.g.*, and RNAi oligonucleotide) for reducing *MAPT* gene expression comprises:

a sense strand of 36 nucleotides comprising a 2'-F-modified nucleotide at positions 3, 5, 8, 10, 12, 13, 15, and 17; a 2'-OMe-modified nucleotide at positions 1, 2, 4, 6, 7, 9, 11, 14, 16, 18-27, and 31-36; a GalNAc-conjugated nucleotide at position 28, 29, and 30; and a phosphorothioate linkage between positions 1 and 2; and

an antisense strand of 22 nucleotides comprising a 2'-F-modified nucleotide at positions 2, 3, 4, 5, 7, 10, 14, 16, and 19; a 2'-OMe-modified nucleotide at positions 1, 6, 8, 9, 11, 12, 13, 15, 17, 18, and 20-22; a phosphorothioate linkage between positions 1 and 2, positions 2 and 3, positions 20 and 21, and positions 21 and 22; and a 5' terminal nucleotide at position 1 comprising a 4'-phosphate analog, optionally wherein the 5' terminal nucleotide comprises 4'-O-monomethylphosphonate-2'-O-methyluridine [MePhosphonate-4O-mU]; wherein positions 1-20 of the antisense strand form a duplex region with positions 1-20 of the sense strand, wherein positions 21-36 of the sense strand form a stem-loop, wherein positions 27-30 form the loop of the stem-loop, optionally wherein positions 27-30 comprise a tetraloop, wherein positions 21 and 22 of the antisense strand comprise an overhang, and wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively; and

j) SEQ ID NOs: 803 and 838, respectively.

[00232] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises:

a sense strand of 36 nucleotides comprising a 2'-F-modified nucleotide at positions 3, 5, 8, 10, 12, 13, 15, and 17; a 2'-OMe-modified nucleotide at positions 1, 2, 4, 6, 7, 9, 11, 14, 16, 18-27, and 31-36; a GalNAc-conjugated nucleotide at position 28, 29, and 30; and a phosphorothioate linkage between positions 1 and 2; and

an antisense strand of 22 nucleotides comprising a 2'-F-modified nucleotide at positions 2, 3, 4, 5, 7, 10, 14, 16, and 19; a 2'-OMe-modified nucleotide at positions 1, 6, 8, 9, 11, 12, 13, 15, 17, 18, and 20-22; a phosphorothioate linkage between positions 1 and 2, positions 2 and 3, positions 20 and 21, and positions 21 and 22; and a 5' terminal nucleotide at position 1 comprising a 4'-phosphate analog, optionally wherein the 5' terminal nucleotide comprises 4'-O-monomethylphosphonate-2'-O-methyluridine [MePhosphonate-4O-mU]; wherein positions 1-20 of the antisense strand form a duplex region with positions 1-20 of the sense strand, wherein positions 21-36 of the sense strand form a stem-loop, wherein positions 27-30 form the loop of the stem-loop, optionally wherein positions 27-30 comprise a tetraloop, wherein positions 21 and 22 of the antisense strand comprise an overhang, and wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

d) SEQ ID NOs: 798 and 833, respectively;

e) SEQ ID NOs: 799 and 834, respectively; and

f) SEQ ID NOs: 803 and 838, respectively.

[00233] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises:

a sense strand of 20 nucleotides comprising a 2'-F-modified nucleotide at positions 3, 5, 8, 10, 12, 13, 15, and 17; a 2'-OMe-modified nucleotide at positions 2, 4, 6, 7, 9, 11, 14, 16, and 18-20; a C_{16} hydrocarbon chain conjugated to a nucleotide at position 1; and a phosphorothioate linkage between positions 1 and 2, between positions 18 and 19, and between positions 19 and 20; and

an antisense strand of 22 nucleotides comprising a 2'-F-modified nucleotide at positions 2, 3, 4, 5, 7, 10, 14, 16, and 19; a 2'-OMe modified-nucleotide at positions 1, 6, 8, 9, 11, 12, 13, 15, 17, 18, and 20-22; a phosphorothioate linkage between positions 1 and 2, positions 2 and 3, positions 20 and 21, and positions 21 and 22; and a 5' terminal nucleotide at position 1 comprising a 4'-phosphate analog, optionally wherein the 5' terminal nucleotide comprises 4'-O-monomethylphosphonate-2'-O-methyluridine [MePhosphonate-4O-mU]; wherein positions 1-20 of the antisense strand form a duplex region with positions 1-20 of the sense strand, wherein positions 21 and 22 of the antisense strand comprise an overhang, and wherein the sense strand and antisense strands comprise nucleotide sequences of SEQ ID NOs: 1681 and 815, respectively.

[00234] In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 771 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 806. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 780 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 815. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 781 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 816. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 798 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 833. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 799 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 834. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 803 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 838. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 1681 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 815.

[00235] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1514; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00236] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1479; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00237] In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1480; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00238] In some embodiments, a *MAPT*-targeting RNAi oligonucleotide for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1503; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the antisense and sense strands are separate strands that form an

asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00239] In some embodiments an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1504; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00240] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1508; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00241] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1514; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00242] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1479; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00243] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1480; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00244] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1503; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an

asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00245] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1504; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00246] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1508; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00247] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1479; and (ii) a sense strand of 19-25 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the oligonucleotide comprises a blunt end comprising the 3' end of the sense strand, wherein the antisense and sense strands are separate strands that form an

asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00248] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1514; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1130, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00249] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1479; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1095, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00250] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1480; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1096, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00251] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1503; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1119, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00252] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1504; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1120, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00253] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1508; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1124, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00254] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein

the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1514; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1130, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00255] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1479; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1095, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00256] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1480; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1096, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an

asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00257] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1503; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1119, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00258] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1504; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand and a stem-loop at the 3' terminus, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1120, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00259] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1508; and (ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity

to the antisense strand and a stem-loop at the 3' terminus, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1124, wherein the stem-loop is set forth as S1-L-S2, wherein S1 is complementary to S2 and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00260] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises (i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a *MAPT* mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1479; and (ii) a sense strand of 19-25 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the region of complementarity to the antisense strand is set forth in SEQ ID NO: 1095, wherein the oligonucleotide comprises a blunt end comprising the 3' end of the sense strand, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

[00261] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises a sense strand and an antisense strand according to:

Sense Strand: 5'-mX-*S*-mX-fX-mX-fX-mX-mX-fX-mX-fX-mX-fX-fX-mX-fX-mX-fX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-[ademX-GalNAc]-[ademX-GalNAc]-[ademX-GalNAc]-mX-mX-mX-mX-mX-mX-3' hybridized to:

Antisense Strand: 5'-[MePhosphonate-4O-mX]-*S*-fX-*S*-fX-fX-fX-mX-fX-mX-mX-fX-mX-mX-mX-fX-mX-fX-mX-mX-fX-mX-*S*-mX-*S*-mX-3', wherein mX = 2'-OMe-modified nucleotide, fX = 2'-F-modified nucleotide, -*S*- = phosphorothioate linkage, - = phosphodiester linkage, [MePhosphonate-4O-mX] = 4'-O-monomethylphosphonate-2'-O-methyl-modified nucleotide, and ademX-GalNAc = GalNAc attached to a nucleotide.

[00262] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises a sense strand and an antisense strand according to:

Sense Strand: 5'-mX-*S*-mX-mX-mX-mX-mX-mX-fX-fX-fX-fX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-[ademX-GalNAc]-[ademX-GalNAc]-[ademX-GalNAc]-mX-mX-mX-mX-mG-mX-3' hybridized to:

Antisense Strand: 5'-[MePhosphonate-4O-mX]-*S*-fX-*S*-fX-*S*-fX-fX-mX-fX-mX-mX-fX-mX-mX-mX-fX-mX-mX-mX-mX-mX-mX-mX-*S*-mX-*S*-mX-3', wherein mX = 2'-OMe-modified nucleotide, fX = 2'-F-modified nucleotide, -*S*- = phosphorothioate linkage, - = phosphodiester linkage, [MePhosphonate-4O-mX] = 4'-O-monomethylphosphonate-2'-O-methyl modified nucleotide, and ademX-GalNAc = GalNAc attached to a nucleotide.

[00263] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises a sense strand and an antisense strand according to:

Sense Strand: 5'-[AdemX-L]-*S*-mX-fX-mX-fX-mX-mX-fX-mX-fX-mX-fX-fX-mX-fX-mX-fX-mX- *S*-mX-*S*-mX-3' hybridized to:

Antisense Strand: 5'-[MePhosphonate-4O-mX]-*S*-fX-*S*-fX-fX-fX-mX-fX-mX-mX-fX-mX-mX-mX-fX-mX-fX-mX-mX-fX-mX-*S*-mX-*S*-mX-3', wherein mX = 2'-OMe-modified nucleotide, fX = 2'-F-modified nucleotide, -*S*- = phosphorothioate linkage, - = phosphodiester linkage, [MePhosphonate-4O-mX] = 4'-O-monomethylphosphonate-2'-O-methyl modified nucleotide, and ademX-L = lipid moiety attached to a nucleotide.

[00264] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises a sense strand and an antisense strand according to:

Sense Strand: 5'-[AdemX-C16]-*S*-mX-fX-mX-fX-mX-mX-fX-mX-fX-mX-fX-fX-mX-fX-mX-fX-mX- *S*-mX-*S*-mX-3' hybridized to:

Antisense Strand: 5'-[MePhosphonate-4O-mX]-*S*-fX-*S*-fX-fX-fX-mX-fX-mX-mX-fX-mX-mX-mX-fX-mX-fX-mX-mX-fX-mX-*S*-mX-*S*-mX-3', wherein mX = 2'-OMe-modified nucleotide, fX = 2'-F-modified nucleotide, -*S*- = phosphorothioate linkage, - = phosphodiester linkage, [MePhosphonate-4O-mX] = 4'-O-monomethylphosphonate-2'-O-methyl modified nucleotide, and ademX-C16 = C_{16} hydrocarbon chain attached to a nucleotide.

[00265] In some embodiments, the current disclosure provides an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression, wherein the oligonucleotide comprises a

sense strand and an antisense strand comprising nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 839 and 874, respectively;

b) SEQ ID NOs: 840 and 875, respectively;

c) SEQ ID NOs: 841 and 876, respectively;

d) SEQ ID NOs: 842 and 877, respectively;

e) SEQ ID NOs: 843 and 878, respectively;

f) SEQ ID NOs: 844 and 879, respectively;

g) SEQ ID NOs: 845 and 880, respectively;

h) SEQ ID NOs: 846 and 881, respectively;

i) SEQ ID NOs: 847 and 882, respectively;

j) SEQ ID NOs: 848 and 883, respectively;

k) SEQ ID NOs: 849 and 884, respectively;

l) SEQ ID NOs: 850 and 885, respectively;

m) SEQ ID NOs: 851 and 886, respectively;

n) SEQ ID NOs: 852 and 887, respectively;

o) SEQ ID NOs: 853 and 888, respectively;

p) SEQ ID NOs: 854 and 889, respectively;

q) SEQ ID NOs: 855 and 890, respectively;

r) SEQ ID NOs: 856 and 891, respectively;

s) SEQ ID NOs: 857 and 892, respectively;

t) SEQ ID NOs: 858 and 893, respectively;

u) SEQ ID NOs: 859 and 894, respectively;

v) SEQ ID NOs: 860 and 895, respectively;

w) SEQ ID NOs: 861 and 896, respectively;

x) SEQ ID NOs: 862 and 897, respectively;

y) SEQ ID NOs: 863 and 898, respectively;

z) SEQ ID NOs: 864 and 899, respectively;

aa) SEQ ID NOs: 865 and 900, respectively;

bb) SEQ ID NOs: 866 and 901, respectively;

cc) SEQ ID NOs: 867 and 902, respectively;

dd) SEQ ID NOs: 868 and 903, respectively;

ee) SEQ ID NOs: 869 and 904, respectively;

ff) SEQ ID NOs: 870 and 905, respectively;

gg) SEQ ID NOs: 871 and 906, respectively;

hh) SEQ ID NOs: 872 and 907, respectively;

ii) SEQ ID NOs: 873 and 908, respectively; and

jj) SEQ ID NOs: 1682 and 885, respectively.

[00266] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises a sense strand and an antisense strand comprising nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 860 and 895, respectively;

b) SEQ ID NOs: 865 and 900, respectively;

c) SEQ ID NOs: 868 and 903, respectively;

d) SEQ ID NOs: 869 and 904, respectively;

e) SEQ ID NOs: 873 and 908, respectively;

f) SEQ ID NOs: 841 and 876, respectively;

g) SEQ ID NOs: 846 and 881, respectively;

h) SEQ ID NOs: 850 and 885, respectively;

i) SEQ ID NOs: 851 and 886, respectively;

j) SEQ ID NOs: 852 and 887, respectively; and

k) SEQ ID NOs: 1682 and 885, respectively.

[00267] In some embodiments, an oligonucleotide (*e.g.*, a RNAi oligonucleotide) for reducing *MAPT* gene expression comprises a sense strand and an antisense strand comprising nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 841 and 876, respectively;

b) SEQ ID NOs: 850 and 885, respectively;

c) SEQ ID NOs: 851 and 886, respectively;

d) SEQ ID NOs: 868 and 903, respectively;

e) SEQ ID NOs: 869 and 904, respectively;

f) SEQ ID NOs: 873 and 908, respectively; and

g) SEQ ID NOs: 1682 and 885, respectively.

[00268] In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 841 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 876. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 850 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 885. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 851 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 886. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 868 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 903. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 869 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 904. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 873 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 908. In some embodiments, an oligonucleotide for reducing *MAPT* gene expression comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 1682 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 885.

[00269] Formulations

[00270] Various formulations have been developed to facilitate oligonucleotide use. For example, oligonucleotides (*e.g.*, RNAi oligonucleotides) can be delivered to a subject or a cellular environment using a formulation that minimizes degradation, facilitates delivery and/or uptake, or

provides another beneficial property to the oligonucleotides in the formulation. In some embodiments, provided herein are compositions comprising oligonucleotides reduce *MAPT* gene expression. Such compositions can be suitably formulated such that when administered to a subject, either into the immediate environment of a target cell or systemically, a sufficient portion of the oligonucleotides enter the cell to reduce *MAPT* gene expression. Any variety of suitable oligonucleotide formulations can be used to deliver oligonucleotides for the reduction of *MAPT* gene expression as disclosed herein. In some embodiments, an oligonucleotide is formulated in buffer solutions such as phosphate buffered saline solutions, liposomes, micellar structures, and capsids. In some embodiments, an oligonucleotide is formulated in buffer solutions such as phosphate buffered saline solutions.

[00271] Formulations of oligonucleotides with cationic lipids can be used to facilitate transfection of the oligonucleotides into cells. For example, cationic lipids, such as lipofectin, cationic glycerol derivatives, and polycationic molecules (*e.g.*, polylysine, can be used. Suitable lipids include Oligofectamine, Lipofectamine (Life Technologies), NC388 (Ribozyme Pharmaceuticals, Inc., Boulder, Colo.), or FuGene 6 (Roche) all of which can be used according to the manufacturer's instructions. In some embodiments, an oligonucleotide is not formulated with a component to facilitate transfection into cells.

[00272] Accordingly, in some embodiments, a formulation comprises a lipid nanoparticle. In some embodiments, an excipient comprises a liposome, a lipid, a lipid complex, a microsphere, a microparticle, a nanosphere or a nanoparticle, or may be otherwise formulated for administration to the cells, tissues, organs, or body of a subject in need thereof (*see*, *e.g.*, Remington: THE SCIENCE AND PRACTICE OF PHARMACY , 22nd edition, Pharmaceutical Press, 2013).

[00273] In some embodiments, the formulations herein comprise an excipient. In some embodiments, an excipient confers to a composition improved stability, improved absorption, improved solubility and/or therapeutic enhancement of the active ingredient. In some embodiments, an excipient is a buffering agent (*e.g.*, sodium citrate, sodium phosphate, a tris base, or sodium hydroxide) or a vehicle (*e.g.*, a buffered solution, petrolatum, dimethyl sulfoxide, or mineral oil). In some embodiments, an oligonucleotide is lyophilized for extending its shelf-life and then made into a solution before use (*e.g.*, administration to a subject). Accordingly, an

excipient in a composition comprising any one of the oligonucleotides described herein may be a lyoprotectant (*e.g.*, mannitol, lactose, polyethylene glycol, or polyvinylpyrrolidone) or a collapse temperature modifier (*e.g.*, dextran, Ficoll™, or gelatin).

[00274] In some embodiments, a pharmaceutical composition is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral (*e.g.*, intravenous, intramuscular, intraperitoneal, intradermal, subcutaneous), oral (*e.g.*, inhalation), transdermal (*e.g.*, topical), transmucosal, and rectal administration.

[00275] In some embodiments, a pharmaceutical composition is formulated for administration into the central nervous system. In some embodiments, a pharmaceutical composition is formulated for administration into the cerebral spinal fluid. In some embodiments, a pharmaceutical composition is formulated for administration to the spinal cord. In some embodiments, a pharmaceutical composition is formulated for intrathecal administration. In some embodiments, a pharmaceutical composition is formulated for administration to the brain. In some embodiments, a pharmaceutical composition is formulated for intracerebroventricular administration. In some embodiments, a pharmaceutical composition is formulated for the brain stem. In some embodiments, a pharmaceutical composition is formulated for intracisternal magna administration.

[00276] Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF), or phosphate buffered saline (PBS). The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (*e.g.*, glycerol, propylene glycol, liquid polyethylene glycol, and the like), and suitable mixtures thereof. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, and/or sodium chloride in the composition. Sterile injectable solutions can be prepared by incorporating the oligonucleotides in a required amount in a selected solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization.

[00277] In some embodiments, a composition may contain at least about 0.1% of the therapeutic agent (*e.g.*, a RNAi oligonucleotide for reducing *MAPT* gene expression) or more, although the percentage of the active ingredient(s) may be between about 1% to about 80% or more of the weight or volume of the total composition. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.

[00278] Methods of Use

[00279] ***Reducing MAPT Gene Expression***

[00280] In some embodiments, the disclosure provides methods for contacting or delivering to a cell or population of cells an effective amount of any of the oligonucleotides (*e.g.*, RNAi oligonucleotides) herein to reduce *MAPT* gene expression. In some embodiments, a reduction of *MAPT* gene expression is determined by measuring a reduction in the amount or level of MAPT mRNA, Tau protein, or Tau activity in a cell. The methods include those described herein and known to one of ordinary skill in the art.

[00281] In some embodiments, the disclosure provides methods for reducing *MAPT* gene expression in the CNS. In some embodiments, the CNS comprises the brain and spinal cord. In some embodiments, *MAPT* gene expression is reduced in at least one region of the brain. In some embodiments, regions of the brain cervical spinal cord, thoracic spinal cord, lumbar spinal cord, frontal cortex, temporal cortex, cerebellum, midbrain, occipital cortex, parietal cortex, hippocampus, caudate nucleus, thalamus, and brainstem. In some embodiments, *MAPT* gene expression is reduced in at least one region of the spinal cord. In some embodiments, regions of the spinal cord include the cervical spinal cord, thoracic spinal cord, and lumbar spinal cord. In some embodiments, *MAPT* gene expression is reduced in at least one region of the brain and at least one region of the spinal cord. In some embodiments, *MAPT* gene expression is reduced in at least one of the cervical spinal cord, thoracic spinal cord, lumbar spinal cord, frontal cortex, temporal cortex, cerebellum, midbrain, occipital cortex, parietal cortex, hippocampus, caudate nucleus, thalamus, brainstem, motor cortex, globus pallidus, midbrain tegmentum, substantia

nigra, pons, cerebellar white matter, and cerebellar dentate nucleus. In some embodiments, *MAPT* gene expression is reduced in at least one of the lumbar spinal cord, thoracic spinal cord, and cervical spinal cord. In some embodiments, *MAPT* gene expression is reduced in tissue of the brain and/or spinal cord associated with Alzheimer's disease. In some embodiments, tissue associated with AD includes, but is not limited to, prefrontal cortex, motor cortex, temporal cortex, parietal cortex, and hippocampus. In some embodiments, *MAPT* gene expression is reduced in tissue of the brain and/or spinal cord associated with progressive supranuclear palsy. In some embodiments, tissue associated with AD includes, but is not limited to caudate nucleus, globus pallidus, thalamus, midbrain tegmentum, substantia nigra, pons, cerebellar white matter, cerebellar dentate nucleus, medulla, cervical spinal cord, thoracic spinal cord, and lumbar spinal cord.

[00282] In some embodiments, *MAPT* gene expression is reduced for about 1 week to about 12 weeks after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 weeks after administration of an oligonucleotide described herein. In some embodiments, *MAPT* expression is reduced for about 1 to about 4 months after administration of an oligonucleotide described herein. In some embodiments, *MAPT* expression is reduced for about 1 to about 6 months after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced for 1, 2, 3, or 4 months after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced for 1, 2, 3 4, 5, or 6 months after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced for about 7 to about 91 days after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced for 7, 14, 21, 28, 35, 42, 49, 56, 63, 70, 77, 84, or 91 days after administration of an oligonucleotide described herein.

[00283] In some embodiments, *MAPT* gene expression is reduced in at least one region of the brain and/or at least one region of the spinal cord for about 1 to about 12 weeks after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced in at least one region of the brain and/or at least one region of the spinal cord for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 weeks after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced in at least one region of the brain and/or at least

one region of the spinal cord for about 1 to about 4 months after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced in at least one region of the brain and/or at least one region of the spinal cord for about 1 to about 6 months after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced in at least one region of the brain and/or at least one region of the spinal cord for 1, 2, 3, or 4 months after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced in at least one region of the brain and/or at least one region of the spinal cord for 1, 2, 3 4, 5, or 6 months after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced in at least one region of the brain and/or at least one region of the spinal cord for about 7 to about 91 days after administration of an oligonucleotide described herein. In some embodiments, *MAPT* gene expression is reduced in at least one region of the brain and/or at least one region of the spinal cord for 7, 14, 21, 28, 35, 42, 49, 56, 63, 70, 77, 84, or 91 days after administration of an oligonucleotide described herein.

[00284] Methods provided herein are useful in any appropriate cell type. In some embodiments, a cell is any cell that expresses MAPT mRNA (*e.g.*, oligodendrocyte). In some embodiments, the cell is a primary cell obtained from a subject. In some embodiments, the primary cell has undergone a limited number of passages such that the cell substantially maintains is natural phenotypic properties. In some embodiments, a cell to which the oligonucleotide is delivered is *ex vivo* or *in vitro* (*i.e.*, can be delivered to a cell in culture or to an organism in which the cell resides).

[00285] In some embodiments, the oligonucleotides disclosed herein are delivered to a cell or population of cells using a nucleic acid delivery method known in the art including, but not limited to, injection of a solution or pharmaceutical composition containing the oligonucleotide, bombardment by particles covered by the oligonucleotide, exposing the cell or population of cells to a solution containing the oligonucleotide, or electroporation of cell membranes in the presence of the oligonucleotide. Other methods known in the art for delivering oligonucleotides to cells may be used, such as lipid-mediated carrier transport, chemical-mediated transport, and cationic liposome transfection such as calcium phosphate, and others.

[00286] In some embodiments, reduction of *MAPT* gene expression is determined by an assay or technique that evaluates one or more molecules, properties or characteristics of a cell or population of cells associated with *MAPT* gene expression, or by an assay or technique that evaluates molecules that are directly indicative of *MAPT* gene expression in a cell or population of cells (*e.g.*, MAPT mRNA or Tau protein). In some embodiments, the extent to which an oligonucleotide reduces *MAPT* gene expression is evaluated by comparing *MAPT* gene expression in a cell or population of cells contacted with the oligonucleotide to a control cell or population of cells (*e.g.*, a cell or population of cells not contacted with the oligonucleotide or contacted with a control oligonucleotide). In some embodiments, a control amount or level of *MAPT* gene expression in a control cell or population of cells is predetermined, such that the control amount or level need not be measured in every instance the assay or technique is performed. The predetermined level or value can take a variety of forms. In some embodiments, a predetermined level or value can be single cut-off value, such as a median or mean.

[00287] In some embodiments, contacting or delivering an oligonucleotide to a cell or a population of cells results in a reduction in *MAPT* gene expression. In some embodiments, the reduction in *MAPT* gene expression is relative to a control amount or level of *MAPT* gene expression in cell or population of cells not contacted with the oligonucleotide or contacted with a control oligonucleotide. In some embodiments, the reduction in *MAPT* gene expression is about 1% or lower, about 5% or lower, about 10% or lower, about 15% or lower, about 20% or lower, about 25% or lower, about 30% or lower, about 35% or lower, about 40% or lower, about 45% or lower, about 50% or lower, about 55% or lower, about 60% or lower, about 70% or lower, about 80% or lower, or about 90% or lower relative to a control amount or level of *MAPT* gene expression. In some embodiments, the control amount or level of *MAPT* gene expression is an amount or level of MAPT mRNA and/or Tau protein in a cell or population of cells that has not been contacted with an oligonucleotide herein. In some embodiments, the effect of delivery of an oligonucleotide to a cell or population of cells according to a method herein is assessed after any finite period or amount of time (*e.g.*, minutes, hours, days, weeks, months). For example, in some embodiments, *MAPT* gene expression is determined in a cell or population of cells at least about 4 hours, about 8 hours, about 12 hours, about 18 hours, about 24 hours; or at least about 1 day,

about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 11 days, about 12 days, about 13 days, about 14 days, about 21 days, about 28 days, about 35 days, about 42 days, about 49 days, about 56 days, about 63 days, about 70 days, about 77 days, about 84 days, or more after contacting or delivering the oligonucleotide to the cell or population of cells. In some embodiments, *MAPT* gene expression is determined in a cell or population of cells at least about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, or more after contacting or delivering the oligonucleotide to the cell or population of cells.

[00288] In some embodiments, the oligonucleotide is delivered in the form of a transgene that is engineered to express in a cell the oligonucleotide or strands comprising the oligonucleotide (*e.g.*, its sense and antisense strands). In some embodiments, the oligonucleotide is delivered using a transgene engineered to express any oligonucleotide disclosed herein. Transgenes may be delivered using viral vectors (*e.g.*, adenovirus, retrovirus, vaccinia virus, poxvirus, adeno-associated virus, or herpes simplex virus) or non-viral vectors (*e.g.*, plasmids or synthetic mRNAs). In some embodiments, transgenes can be injected directly to a subject.

[00289] ***Treatment Methods***

[00290] The disclosure also provides oligonucleotides (*e.g.*, RNAi oligonucleotides) for use, or adaptable for use, to treat a subject (*e.g.*, a human having a disease, disorder, or condition associated with *MAPT* gene expression) that would benefit from reducing *MAPT* gene expression. In some aspects, the disclosure provides oligonucleotides for use, or adapted for use, to treat a subject having a disease, disorder, or condition associated with *MAPT* gene expression. The disclosure also provides oligonucleotides for use, or adaptable for use, in the manufacture of a medicament or pharmaceutical composition for treating a disease, disorder, or condition associated with *MAPT* gene expression. In some embodiments, the oligonucleotides for use, or adaptable for use, target MAPT mRNA and reduce *MAPT* gene expression (*e.g.*, *via* the RNAi pathway). In some embodiments, the oligonucleotides for use, or adaptable for use, target MAPT mRNA and reduce the amount or level of MAPT mRNA, Tau protein, and/or Tau activity.

[00291] In addition, in some embodiments of the methods herein, a subject having a disease, disorder or condition associated with *MAPT* gene expression or is predisposed to the same is selected for treatment with an oligonucleotide (*e.g.*, a ds oligonucleotide) herein. In some embodiments, the method comprises selecting an individual having a marker (*e.g.*, a biomarker) for a disease, disorder, or condition associated with *MAPT* gene expression, or predisposed to the same, such as, but not limited to, MAPT mRNA, Tau protein, or a combination thereof. Likewise, and as detailed below, some embodiments of the methods provided by the disclosure include steps such as measuring or obtaining a baseline value for a marker of *MAPT* gene expression (*e.g.*, Tau protein or Tau activity), and then comparing such obtained value to one or more other baseline values or values obtained after the subject is administered the oligonucleotide to assess the effectiveness of treatment.

[00292] The disclosure also provides methods of treating a subject having, suspected of having, or at risk of developing a disease, disorder, or condition associated with *MAPT* gene expression with an oligonucleotide provided herein. In some aspects, the disclosure provides methods of treating or attenuating the onset or progression of a disease, disorder, or condition associated with *MAPT* gene expression using the oligonucleotides provided herein. In other aspects, the disclosure provides methods to achieve one or more therapeutic benefits in a subject having a disease, disorder, or condition associated with *MAPT* gene expression using the oligonucleotides provided herein. In some embodiments of the methods herein, the subject is treated by administering a therapeutically effective amount of any one or more of the oligonucleotides provided herein. In some embodiments, treatment comprises reducing *MAPT* gene expression. In some embodiments, the subject is treated therapeutically. In some embodiments, the subject is treated prophylactically.

[00293] In some embodiments of the methods herein, an oligonucleotide (*e.g.*, a RNAi oligonucleotide), or a pharmaceutical composition comprising the oligonucleotide, is administered to a subject having a disease, disorder, or condition associated with *MAPT* gene expression such that *MAPT* gene expression is reduced in the subject, thereby treating the subject. In some embodiments, an amount or level of MAPT mRNA is reduced in the subject. In some embodiments, an amount or level of Tau protein is reduced in the subject.

[00294] In some embodiments of the methods herein, the oligonucleotide, or a pharmaceutical composition comprising the oligonucleotide, is administered to a subject having a disease, disorder, or condition associated with *MAPT* gene expression such that *MAPT* gene expression is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to *MAPT* gene expression prior to administration of the oligonucleotide or pharmaceutical composition. In some embodiments of the methods herein, the oligonucleotide, or the pharmaceutical composition comprising the oligonucleotide, is administered to a subject having a disease, disorder, or condition associated with *MAPT* gene expression such that *MAPT* gene expression is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% for about 1 week to about 12 weeks, about 1 month to about 6 months, or about 7 days to about 91 days when compared to *MAPT* gene expression prior to administration of the oligonucleotide or pharmaceutical composition. In some embodiments, *MAPT* gene expression is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to *MAPT* gene expression in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or pharmaceutical composition or receiving a control oligonucleotide, pharmaceutical composition or treatment. In some embodiments, *MAPT* gene expression is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% for about 1 week to about 12 weeks, about 1 month to about 6 months, or about 7 days to about 91 days when compared to *MAPT* gene expression in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or pharmaceutical composition or receiving a control oligonucleotide, pharmaceutical composition or treatment.

[00295] In some embodiments of the methods herein, the oligonucleotide or the pharmaceutical composition is administered to a subject having a disease, disorder, or condition associated with

MAPT gene expression such that an amount or level of MAPT mRNA is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to the amount or level of MAPT mRNA prior to administration of the oligonucleotide or pharmaceutical composition. In some embodiments of the methods, the oligonucleotide or the pharmaceutical composition is administered to a subject having a disease, disorder, or condition associated with *MAPT* gene expression such that an amount or level of MAPT mRNA is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% for about 1 week to about 12 weeks, about 1 month to about 6 months, or about 7 days to about 91 days when compared to the amount or level of MAPT mRNA prior to administration of the oligonucleotide or pharmaceutical composition. In some embodiments, an amount or level of MAPT mRNA is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of MAPT mRNA in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or pharmaceutical composition or receiving a control oligonucleotide, pharmaceutical composition or treatment. In some embodiments, an amount or level of MAPT mRNA is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% for about 1 week to about 12 weeks, about 1 month to about 6 months, or about 7 days to about 91 days when compared to an amount or level of MAPT mRNA in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or pharmaceutical composition or receiving a control oligonucleotide, pharmaceutical composition or treatment.

[00296] In some embodiments of the methods, the oligonucleotide or the pharmaceutical composition is administered to a subject having a disease, disorder, or condition associated with *MAPT* gene expression such that an amount or level of Tau protein is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about

65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to the amount or level of Tau protein prior to administration of the oligonucleotide or pharmaceutical composition. In some embodiments of the methods herein, an oligonucleotide herein, or a pharmaceutical composition comprising the oligonucleotide, is administered to a subject having a disease, disorder, or condition associated with *MAPT* gene expression such that an amount or level of Tau protein is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% for about 1 week to about 12 weeks, about 1 month to about 6 months, or about 7 days to about 91 days when compared to the amount or level of Tau protein prior to administration of the oligonucleotide or pharmaceutical composition. In some embodiments, an amount or level of Tau protein is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of Tau protein in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or pharmaceutical composition or receiving a control oligonucleotide, pharmaceutical composition or treatment. In some embodiments, an amount or level of Tau protein is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% for about 1 week to about 12 weeks, about 1 month to about 6 months, or about 7 days to about 91 days when compared to an amount or level of Tau protein in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or pharmaceutical composition or receiving a control oligonucleotide, pharmaceutical composition or treatment.

[00297] In some embodiments of the methods, the oligonucleotide or the pharmaceutical composition is administered to a subject having a disease, disorder, or condition associated with *MAPT* gene expression such that an amount or level of Tau activity is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to the amount or level of Tau activity prior to administration of the

oligonucleotide or pharmaceutical composition. In some embodiments, the oligonucleotide or the pharmaceutical composition is administered to a subject having a disease, disorder, or condition associated with *MAPT* gene expression such that an amount or level of Tau activity is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% for about 1 week to about 12 weeks, about 1 month to about 6 months, or about 7 days to about 91 days when compared to the amount or level of Tau activity prior to administration of the oligonucleotide or pharmaceutical composition. In some embodiments, an amount or level of Tau activity is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% when compared to an amount or level of Tau activity in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or pharmaceutical composition or receiving a control oligonucleotide, pharmaceutical composition or treatment. In some embodiments, an amount or level of Tau activity is reduced in the subject by at least about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or greater than 99% for about 1 week to about 12 weeks, about 1 month to about 6 months, or about 7 days to about 91 days when compared to an amount or level of Tau activity in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or pharmaceutical composition or receiving a control oligonucleotide, pharmaceutical composition or treatment.

[00298] Suitable methods for determining *MAPT* gene expression, an amount or level of MAPT mRNA, an amount or level of Tau protein, and/or an amount or level of Tau activity, in the subject, or in a sample from the subject, are known in the art. Further, the Examples set forth herein illustrate exemplary methods for determining *MAPT* gene expression.

[00299] In some embodiments, *MAPT* gene expression, an amount or level of MAPT mRNA, an amount or level of Tau protein, an amount or level of Tau activity, or any combination thereof, is reduced in a cell (*e.g.*, an oligodendrocyte), a population or a group of cells (*e.g.*, an organoid), an organ (*e.g.*, frontal cortex), blood or a fraction thereof (*e.g.*, plasma), a tissue (*e.g.*, brain tissue), a

sample (*e.g.*, a brain biopsy sample), or any other biological material obtained or isolated from the subject. In some embodiments, *MAPT* gene expression, an amount or level of MAPT mRNA, an amount or level of Tau protein, an amount or level of Tau activity, or any combination thereof, is reduced in more than one type of cell (*e.g.*, an oligodendrocyte and one or more other type(s) of cell), more than one groups of cells, more than one organ (*e.g.*, brain and one or more other organ(s)), more than one fraction of blood (*e.g.*, plasma and one or more other blood fraction(s)), more than one type of tissue (*e.g.*, brain tissue and one or more other type(s) of tissue), more than one type of sample (*e.g.*, a brain biopsy sample and one or more other type(s) of biopsy sample) obtained or isolated from the subject. In some embodiments, *MAPT* gene expression, an amount or level of MAPT mRNA, an amount or level of Tau protein, an amount or level of Tau activity, or any combination thereof is reduced in one or more of the cervical spinal cord, thoracic spinal cord, lumbar spinal cord, frontal cortex, temporal cortex, cerebellum, midbrain, occipital cortex, parietal cortex, hippocampus, caudate nucleus, thalamus, brainstem, motor cortex, globus pallidus, midbrain tegmentum, substantia nigra, pons, cerebellar white matter, and cerebellar dentate nucleus. In some embodiments, *MAPT* gene expression, an amount or level of MAPT mRNA, an amount or level of Tau protein, an amount or level of Tau activity, or any combination thereof is reduced in tissue of the brain and/or spinal cord associated with AD. In some embodiments, tissue associated with AD includes, but is not limited to, prefrontal cortex, motor cortex, temporal cortex, parietal cortex, and hippocampus. In some embodiments, *MAPT* gene expression, an amount or level of MAPT mRNA, an amount or level of Tau protein, an amount or level of Tau activity, or any combination thereof is reduced in tissue of the brain and/or spinal cord associated with PSP. In some embodiments, tissue associated with AD includes, but is not limited to caudate nucleus, globus pallidus, thalamus, midbrain tegmentum, substantia nigra, pons, cerebellar white matter, cerebellar dentate nucleus, medulla, cervical spinal cord, thoracic spinal cord, and lumbar spinal cord.

[00300] Examples of a disease, disorder, or condition associated with *MAPT* gene expression include, but are not limited to, AD, FTD, PD, PSP, and Tau protein associated diseases (*e.g.*, primary age-related tauopathy, chronic traumatic encephalopathy, corticobasal degeneration, lytico-bodig disease, ganglioglioma, meningioangiomatosis, postencephalitic parkinsonism, and

subacute sclerosing panencephalitis), which have aberrant *MAPT* gene expression that results in pathology of these diseases. Over 50 missense, silencing, and intronic mutations are known in *MAPT* (Ghetti *et al.* (2015) NEUROPATHOL. APPL. NEUROBIOL. 41:24-46) that lead to these diseases.

[00301] Because of their high specificity, the oligonucleotides herein (*e.g.*, RNAi oligonucleotides) specifically target mRNAs of target genes of cells, tissue(s), or organ(s) (*e.g.*, brain). In preventing disease, the target gene may be one that is required for initiation or maintenance of the disease or that has been identified as being associated with a higher risk of contracting the disease. In treating disease, the oligonucleotide can be brought into contact with the cells, tissue(s), or organ(s) (*e.g.*, brain) exhibiting or responsible for mediating the disease. For example, an oligonucleotide substantially identical to all or part of a wild-type (*i.e.*, native) or mutated gene associated with a disorder or condition associated with *MAPT* gene expression may be brought into contact with or introduced into a cell or tissue type of interest such as an oligodendrocyte or other brain cell.

[00302] In some embodiments, the target gene may be a target gene from any mammal, such as a human. Any gene may be silenced according to the method described herein.

[00303] Methods described herein are typically involve administering to a subject a therapeutically effective amount of an oligonucleotide (*e.g.*, a RNAi oligonucleotide), that is, an amount capable of producing a desirable therapeutic result. A therapeutically acceptable amount may be an amount that can therapeutically treat a disease or disorder. The appropriate dosage for any one subject will depend on certain factors, including the subject's size, body surface area, age, the particular composition to be administered, the active ingredient(s) in the composition, time and route of administration, general health, and other drugs being administered concurrently.

[00304] In some embodiments, a subject is administered any one of the compositions herein either enterally (*e.g.*, orally, by gastric feeding tube, by duodenal feeding tube, *via* gastrostomy or rectally), parenterally (*e.g.*, subcutaneous injection, intravenous injection or infusion, intra-arterial injection or infusion, intraosseous infusion, intramuscular injection, intracerebral injection, intracerebroventricular injection, or intrathecal), topically (*e.g.*, epicutaneous, inhalational, *via* eye drops, or through a mucous membrane), or by direct injection into a target organ (*e.g.*, the brain of

a subject). Typically, the oligonucleotides are administered intravenously or subcutaneously. In some embodiments, the oligonucleotides are administered to the cerebral spinal fluid. In some embodiments, the oligonucleotides described herein are administered intrathecally. In some embodiments, the oligonucleotides are administered intracerebroventricularly. In some embodiments, the oligonucleotides are administered by intracisternal magna injection.

[00305] As a non-limiting set of examples, the oligonucleotides would typically be administered quarterly (once every three months), bi-monthly (once every two months), monthly or weekly. For example, the oligonucleotides may be administered every week or at intervals of two, or three weeks. Alternatively, the oligonucleotides may be administered daily. In some embodiments, a subject is administered one or more loading doses of the oligonucleotide followed by one or more maintenance doses of the oligonucleotide.

[00306] In some embodiments, the subject to be treated is a human or NHP or other mammalian subject. Other exemplary subjects include domesticated animals such as dogs and cats; livestock such as horses, cattle, pigs, sheep, goats, and chickens; and animals such as mice, rats, guinea pigs, and hamsters.

[00307] Kits

[00308] In some embodiments, the disclosure provides a kit comprising an oligonucleotide herein (*e.g.*, a RNAi oligonucleotide), and instructions for use. In some embodiments, the kit comprises the oligonucleotide and a package insert containing instructions for use of the kit and/or any component thereof. In some embodiments, the kit comprises, in a suitable container, the oligonucleotide, one or more controls, and various buffers, reagents, enzymes and other standard ingredients well known in the art. In some embodiments, the container comprises at least one vial, well, test tube, flask, bottle, syringe, or other container means, into which the oligonucleotide is placed, and in some instances, suitably aliquoted. In some embodiments where an additional component is provided, the kit contains additional containers into which this component is placed. The kits can also include a means for containing the oligonucleotide and any other reagent in close confinement for commercial sale. Such containers may include injection or blow-molded plastic

containers into which the desired vials are retained. Containers and/or kits can include labeling with instructions for use and/or warnings.

[00309] In some embodiments, the kit comprises the oligonucleotide and a pharmaceutically acceptable carrier, or a pharmaceutical composition comprising the oligonucleotide and instructions for treating or delaying progression of a disease, disorder or condition associated with *MAPT* gene expression in a subject in need thereof.

[00310] In some embodiments, the kit comprises the oligonucleotide and a pharmaceutically acceptable carrier or a pharmaceutical composition comprising the oligonucleotide, and instructions for administering the oligonucleotide or pharmaceutical composition to the cerebral spinal fluid to reduce *MAPT* gene expression in at least one region of the brain and/or at least one region of the spinal cord in a subject in need thereof.

[00311] Definitions

[00312] As used herein, "approximately" or "about," as applied to one or more values of interest, refers to a value that is similar to a stated reference value. In certain embodiments, "about" refers to a range of values that fall within 25%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1% or less in either direction (greater than or less than) of the stated reference value unless otherwise stated or otherwise evident from the context (except where such number would exceed 100% of a possible value).

[00313] As used herein, "administer," "administering," "administration" and the like refers to providing a substance (*e.g.*, an oligonucleotide) to a subject in a manner that is pharmacologically useful (*e.g.*, to treat a condition in the subject).

[00314] As used herein, "asialoglycoprotein receptor" or "ASGPR" refers to a bipartite C-type lectin formed by a major 48 kDa subunit (ASGPR-1) and minor 40 kDa subunit (ASGPR-2). ASGPR is primarily expressed on the sinusoidal surface of hepatocyte cells and has a major role in binding, internalizing and subsequent clearing of circulating glycoproteins that contain terminal galactose or GalNAc residues (asialoglycoproteins).

[00315] As used herein, "attenuate," "attenuating," "attenuation" and the like refers to reducing or effectively halting. As a non-limiting example, one or more of the treatments herein may reduce

or effectively halt the onset or progression of a disease associated with *MAPT* gene expression (*e.g.*, Tau-associated diseases) in a subject. This attenuation may be exemplified by, for example, a decrease in one or more aspects (*e.g.*, symptoms, tissue characteristics, and cellular, inflammatory or immunological activity, *etc.*) of a disease associated with *MAPT* gene expression (*e.g.*, Tau-associated diseases), no detectable progression (worsening) of one or more aspects of the disease, or no detectable aspects of the disease in a subject when they might otherwise be expected.

[00316] As used herein, "complementary" refers to a structural relationship between two nucleotides (*e.g.*, on two opposing nucleic acids or on opposing regions of a single nucleic acid strand) that permits the two nucleotides to form base pairs with one another. For example, a purine nucleotide of one nucleic acid that is complementary to a pyrimidine nucleotide of an opposing nucleic acid may base pair together by forming hydrogen bonds with one another. In some embodiments, complementary nucleotides can base pair in the Watson-Crick manner or in any other manner that allows for the formation of stable duplexes. In some embodiments, two nucleic acids may have regions of multiple nucleotides that are complementary with each other to form regions of complementarity, as described herein.

[00317] As used herein, "deoxyribonucleotide" refers to a nucleotide having a hydrogen in place of a hydroxyl at the 2' position of its pentose sugar when compared with a ribonucleotide. A modified deoxyribonucleotide is a deoxyribonucleotide having one or more modifications or substitutions of atoms other than at the 2' position, including modifications or substitutions in or of the sugar, phosphate group or base.

[00318] As used herein, "double-stranded oligonucleotide" or "ds oligonucleotide" refers to an oligonucleotide that is substantially in a duplex form. In some embodiments, the complementary base-pairing of duplex region(s) of a ds oligonucleotide is formed between antiparallel sequences of nucleotides of covalently separate nucleic acid strands. In some embodiments, complementary base-pairing of duplex region(s) of a ds oligonucleotide is formed between antiparallel sequences of nucleotides of nucleic acid strands that are covalently linked. In some embodiments, complementary base-pairing of duplex region(s) of a ds oligonucleotide is formed from single nucleic acid strand that is folded (*e.g.*, *via* a hairpin) to provide complementary antiparallel

sequences of nucleotides that base pair together. In some embodiments, a ds oligonucleotide comprises two covalently separate nucleic acid strands that are fully duplexed with one another. However, in some embodiments, a ds oligonucleotide comprises two covalently separate nucleic acid strands that are partially duplexed (*e.g.*, having overhangs at one or both ends). In some embodiments, a ds oligonucleotide comprises antiparallel sequence of nucleotides that are partially complementary, and thus, may have one or more mismatches, which may include internal mismatches or end mismatches.

[00319] As used herein, "duplex," in reference to nucleic acids (*e.g.*, oligonucleotides), refers to a structure formed through complementary base pairing of two antiparallel sequences of nucleotides.

[00320] As used herein, "excipient" refers to a non-therapeutic agent that may be included in a composition, for example, to provide or contribute to a desired consistency or stabilizing effect.

[00321] As used herein, "labile linker" refers to a linker that can be cleaved (*e.g.*, by acidic pH). A "fairly stable linker" refers to a linker that cannot be cleaved.

[00322] As used herein, "loop" refers to an unpaired region of a nucleic acid (*e.g.*, oligonucleotide) that is flanked by two antiparallel regions of the nucleic acid that are sufficiently complementary to one another, such that under appropriate hybridization conditions (*e.g.*, in a phosphate buffer, in a cells), the two antiparallel regions, which flank the unpaired region, hybridize to form a duplex (referred to as a "stem").

[00323] As used herein, "modified internucleotide linkage" refers to an internucleotide linkage having one or more chemical modifications when compared with a reference internucleotide linkage comprising a phosphodiester bond. In some embodiments, a modified nucleotide is a non-naturally occurring linkage. Typically, a modified internucleotide linkage confers one or more desirable properties to a nucleic acid in which the modified internucleotide linkage is present. For example, a modified nucleotide may improve thermal stability, resistance to degradation, nuclease resistance, solubility, bioavailability, bioactivity, reduced immunogenicity, *etc*.

[00324] As used herein, "modified nucleotide" refers to a nucleotide having one or more chemical modifications when compared with a corresponding reference nucleotide selected from: adenine ribonucleotide, guanine ribonucleotide, cytosine ribonucleotide, uracil ribonucleotide, adenine

deoxyribonucleotide, guanine deoxyribonucleotide, cytosine deoxyribonucleotide and thymidine deoxyribonucleotide. In some embodiments, a modified nucleotide is a non-naturally occurring nucleotide. In some embodiments, a modified nucleotide has one or more chemical modification in its sugar, nucleobase and/or phosphate group. In some embodiments, a modified nucleotide has one or more chemical moieties conjugated to a corresponding reference nucleotide. Typically, a modified nucleotide confers one or more desirable properties to a nucleic acid in which the modified nucleotide is present. For example, a modified nucleotide may improve thermal stability, resistance to degradation, nuclease resistance, solubility, bioavailability, bioactivity, reduced immunogenicity, *etc.*

[00325] As used herein, "nicked tetraloop structure" refers to a structure of an RNAi oligonucleotide that is characterized by separate sense (passenger) and antisense (guide) strands, in which the sense strand has a region of complementarity with the antisense strand, and in which at least one of the strands, generally the sense strand, has a tetraL configured to stabilize an adjacent stem region formed within the at least one strand.

[00326] As used herein, "oligonucleotide" refers to a short nucleic acid (*e.g.*, less than about 100 nucleotides in length). An oligonucleotide may be ss or ds. An oligonucleotide may or may not have duplex regions. As a set of non-limiting examples, an oligonucleotide may be, but is not limited to, a small interfering RNA (siRNA), microRNA (miRNA), short hairpin RNA (shRNA), dicer substrate interfering RNA (dsiRNA), antisense oligonucleotide, short siRNA, or ss siRNA. In some embodiments, a ds oligonucleotide is an RNAi oligonucleotide.

[00327] As used herein, "overhang" refers to terminal non-base pairing nucleotide(s) resulting from one strand or region extending beyond the terminus of a complementary strand with which the one strand or region forms a duplex. In some embodiments, an overhang comprises one or more unpaired nucleotides extending from a duplex region at the 5' terminus or 3′ terminus of a ds oligonucleotide. In certain embodiments, the overhang is a 3' or 5' overhang on the antisense strand or sense strand of a ds oligonucleotides.

[00328] As used herein, "phosphate analog" refers to a chemical moiety that mimics the electrostatic and/or steric properties of a phosphate group. In some embodiments, a phosphate analog is positioned at the 5' terminal nucleotide of an oligonucleotide in place of a 5'-phosphate,

which is often susceptible to enzymatic removal. In some embodiments, a 5'-phosphate analog contains a phosphatase-resistant linkage. Examples of phosphate analogs include, but are not limited to, 5' phosphonates, such as 5' methylenephosphonate (5'-MP) and 5'-(E)-vinylphosphonate (5'-VP). In some embodiments, an oligonucleotide has a phosphate analog at a 4'-carbon position of the sugar (referred to as a "4'-phosphate analog") at a 5' terminal nucleotide. An example of a 4'-phosphate analog is oxymethylphosphonate, in which the oxygen atom of the oxymethyl group is bound to the sugar moiety (*e.g.*, at its 4'-carbon) or analog thereof. *See*, *e.g.*, US Provisional Patent Application Nos. 62/383,207 (filed on 2 September 2016) and 62/393,401 (filed on 12 September 2016). Other modifications have been developed for the 5' end of oligonucleotides (*see*, *e.g.*, Intl. Patent Application Publication No. WO 2011/133871; US Patent No. 8,927,513; and Prakash *et al.* (2015) NUCLEIC ACIDS RES. 43:2993-3011).

[00329] As used herein, "MAPT" refers to Microtubule-Associated Protein Tau. The MAPT transcript undergoes several types of alternative splicing to produce different mRNA species and Tau proteins. There are six known Tau isoforms produced by the splicing of MAPT mRNA. *MAPT* gene expression is found primarily in the axons of neurons in the CNS. Tau protein interacts with tubulin to generate microtubules which are involved in several cellular processes. The MAPT mRNA encoding wild-type human Tau protein is set forth in SEQ ID NO: 909. The MAPT mRNA encoding mouse Tau protein is set forth in SEQ ID NO: 910. The MAPT mRNA encoding monkey Tau protein is set forth in SEQ ID NO: 911. One of skill in the art, however, understands that additional examples of MAPT mRNA sequences are readily available using publicly available databases such as, for example, GenBank and UniProt.

[00330] As used herein, "reduced expression" of a gene (*e.g.*, *MAPT*) refers to a decrease in the amount or level of RNA transcript (*e.g.*, MAPT mRNA) or protein encoded by the gene and/or a decrease in the amount or level of activity of the gene in a cell, a population of cells, a sample or a subject, when compared to an appropriate reference (*e.g.*, a reference cell, population of cells, sample, or subject). For example, the act of contacting a cell with an oligonucleotide herein (*e.g.*, an oligonucleotide comprising an antisense strand having a nucleotide sequence that is complementary to a nucleotide sequence comprising MAPT mRNA) may result in a decrease in the amount or level of MAPT mRNA, Tau protein, and/or Tau activity (*e.g.*, *via* inactivation and/or

degradation of MAPT mRNA by the RNAi pathway) when compared to a cell that is not treated with the ds oligonucleotide. Similarly, and as used herein, "reducing expression" refers to an act that results in reduced expression of a gene (*e.g.*, *MAPT*).

[00331] As used herein, "reduction of *MAPT* gene expression" refers to a decrease in the amount or level of MAPT mRNA, Tau protein, and/or Tau activity in a cell, a population of cells, a sample, or a subject when compared to an appropriate reference (*e.g.*, a reference cell, population of cells, sample, or subject).

[00332] As used herein, "region of complementarity" refers to a sequence of nucleotides of a nucleic acid (*e.g.*, a ds oligonucleotide) that is sufficiently complementary to an antiparallel sequence of nucleotides to permit hybridization between the two sequences of nucleotides under appropriate hybridization conditions (*e.g.*, in a phosphate buffer, in a cell, *etc.*). In some embodiments, an oligonucleotide herein comprises a targeting sequence having a region of complementary to a mRNA target sequence.

[00333] As used herein, "ribonucleotide" refers to a nucleotide having a ribose as its pentose sugar, which contains a hydroxyl group at its 2' position. A modified ribonucleotide is a ribonucleotide having one or more modifications or substitutions of atoms other than at the 2' position, including modifications or substitutions in or of the ribose, phosphate group or base.

[00334] As used herein, "RNAi oligonucleotide" refers to either (a) a ds oligonucleotide having a sense strand (passenger) and antisense strand (guide), in which the antisense strand or part of the antisense strand is used by the *Argonaute* 2 (Ago2) endonuclease in the cleavage of a target mRNA (*e.g.*, MAPT mRNA) or (b) a ss oligonucleotide having a single antisense strand, where that antisense strand (or part of that antisense strand) is used by the Ago2 endonuclease in the cleavage of a target mRNA (*e.g.*, MAPT mRNA).

[00335] As used herein, "strand" refers to a single, contiguous sequence of nucleotides linked together through internucleotide linkages (*e.g.*, phosphodiester linkages or phosphorothioate linkages). In some embodiments, a strand has two free ends (*e.g.*, a 5' end and a 3' end).

[00336] As used herein, "subject" means any mammal, including mice, rabbits, and humans. In one embodiment, the subject is a human or NHP. Moreover, "individual" or "patient" may be used interchangeably with "subject."

[00337] As used herein, "synthetic" refers to a nucleic acid or other molecule that is artificially synthesized (*e.g.*, using a machine (*e.g.*, a solid-state nucleic acid synthesizer)) or that is otherwise not derived from a natural source (*e.g.*, a cell or organism) that normally produces the molecule.

[00338] As used herein, "targeting ligand" refers to a molecule (*e.g.*, a carbohydrate, amino sugar, cholesterol, or polypeptide) that selectively binds to a cognate molecule (*e.g.*, a receptor) of a tissue or cell of interest and that is conjugatable to another substance for purposes of targeting the other substance to the tissue or cell of interest. For example, in some embodiments, a targeting ligand may be conjugated to an oligonucleotide for purposes of targeting the oligonucleotide to a specific tissue or cell of interest. In some embodiments, a targeting ligand selectively binds to a cell surface receptor. Accordingly, in some embodiments, a targeting ligand when conjugated to an oligonucleotide facilitates delivery of the oligonucleotide into a particular cell through selective binding to a receptor expressed on the surface of the cell and endosomal internalization by the cell of the complex comprising the oligonucleotide, targeting ligand and receptor. In some embodiments, a targeting ligand is conjugated to an oligonucleotide *via* a linker that is cleaved following or during cellular internalization such that the oligonucleotide is released from the targeting ligand in the cell.

[00339] As used herein, "tetraloop" or "tetraL" refers to a loop that increases stability of an adjacent duplex formed by hybridization of flanking sequences of nucleotides. The increase in stability is detectable as an increase in melting temperature (T_m) of an adjacent stem duplex that is higher than the T_m of the adjacent stem duplex expected, on average, from a set of loops of comparable length consisting of randomly selected sequences of nucleotides. For example, a tetraL can confer a T_m of at least about 50°C, at least about 55°C, at least about 56°C, at least about 58°C, at least about 60°C, at least about 65°C or at least about 75°C in 10 mM $NaHPO_4$ to a hairpin comprising a duplex of at least 2 base pairs (bp) in length. In some embodiments, a tetraL may stabilize a bp in an adjacent stem duplex by stacking interactions. In addition, interactions among the nucleotides in a tetraL include, but are not limited to, non-Watson-Crick base pairing, stacking interactions, hydrogen bonding and contact interactions (Cheong *et al.* (1990) NATURE 346:680-682; Heus & Pardi (1991) SCIENCE 253:191-94). In some embodiments, a tetraL comprises or consists of 3 to 6 nucleotides and is typically 4 to 5 nucleotides. In certain embodiments, a tetraL

comprises or consists of 3, 4, 5, or 6 nucleotides, which may or may not be modified (*e.g.*, which may or may not be conjugated to a targeting moiety). In certain embodiments, a tetraL comprises or consists of 3, 4, 5, or 6 nucleotides, which may or may not be modified (*e.g.*, which may or may not be conjugated to a targeting ligand). In one embodiment, a tetraL consists of 4 nucleotides. Any nucleotide may be used in the tetraloop and standard IUPAC-IUB symbols for such nucleotides may be used as described in Cornish-Bowden (1985) NUCLEIC ACIDS RES. 13:3021-30. For example, the letter "N" may be used to mean that any base may be in that position, the letter "R" may be used to show that A (adenine) or G (guanine) may be in that position, and "B" may be used to show that C (cytosine), G (guanine), T (thymine) or U (uracil) may be in that position. Examples of tetraLs include the UNCG family of tetraLs (*e.g.*, UUCG), the GNRA family of tetraLs (*e.g.*, GAAA), and the CUUG tetraloop (Woese *et al.* (1990) PROC. NATL. ACAD. SCI. *USA* 87:8467-71; Antao *et al.* (1991) NUCLEIC ACIDS RES. 19:5901-05). Examples of DNA tetraLs include the d(GNNA) family of tetraLs (*e.g.*, d(GTTA), the d(GNRA)) family of tetraLs, the d(GNAB) family of tetraLs, the d(CNNG) family of tetraLs, and the d(TNCG) family of tetraLs (*e.g.*, d(TTCG)). *See*, *e.g.*, Nakano *et al.* (2002) BIOCHEM. 41:4281-92; Shinji *et al.* (2000) NIPPON KAGAKKAI KOEN YOKOSHU 78:731. In some embodiments, the tetraloop is contained within a nicked tetraL structure.

[00340] As used herein, "treat" or "treating" refers to the act of providing care to a subject in need thereof, for example, by administering a therapeutic agent (*e.g.*, an oligonucleotide herein) to the subject, for purposes of improving the health and/or well-being of the subject with respect to an existing condition (*e.g.*, a disease, disorder) or to prevent or decrease the likelihood of the occurrence of a condition. In some embodiments, treatment involves reducing the frequency or severity of at least one sign, symptom, or contributing factor of a condition (*e.g.*, disease or disorder) experienced by a subject.

EXAMPLES

[00341] The following non-limiting examples are offered for purposes of illustration, not limitation.

[00342] Example 1: Preparation of RNAi Oligonucleotides

[00343] *Oligonucleotide Synthesis and Purification*

[00344] The oligonucleotides (RNAi oligonucleotides) described in the foregoing Examples are chemically synthesized using methods described herein. Generally, RNAi oligonucleotides are synthesized using solid phase oligonucleotide synthesis methods as described for 19-23mer siRNAs (*see, e.g.*, Scaringe *et al.* (1990) NUCLEIC ACIDS RES. 18:5433-5441 and Usman *et al.* (1987) J. AM. CHEM. SOC. 109:7845-45; *see also*, US Patent Nos. 5,804,683; 5,831,071; 5,998,203; 6,008,400; 6,111,086; 6,117,657; 6,353,098; 6,362,323; 6,437,117 and 6,469,158) in addition to using known phosphoramidite synthesis (*see, e.g.* Hughes & Ellington (2017) COLD SPRING HARB. PERSPECT. BIOL. 9(1):a023812; Beaucage & Caruthers (1981) TETRAHEDRON LETT. 22:1859-62). dsRNAi oligonucleotides have a 19mer core sequence were formatted into constructs having a 25mer sense strand and a 27mer antisense strand to allow for processing by the RNAi machinery. The 19mer core sequence is complementary to a region in the MAPT mRNA.

[00345] Individual RNA strands were synthesized and HPLC purified according to standard methods (Integrated DNA Technologies). For example, RNA oligonucleotides were synthesized using solid phase phosphoramidite chemistry, deprotected, and desalted on NAP-5 columns (Amersham Pharmacia Biotech) using standard techniques (Damha & Olgivie (1993) METHODS MOL. BIOL. 20:81-114; Wincott *et al.* (1995) NUCLEIC ACIDS RES. 23:2677-84). The oligomers were purified using ion-exchange high performance liquid chromatography (IE-HPLC) on an Amersham Source 15Q column (1.0 cm×25 cm; Amersham Pharmacia Biotech) using a 15 min step-linear gradient. The gradient varied from 90:10 Buffers A:B to 52:48 Buffers A:B, where Buffer A is 100 mM Tris pH 8.5 and Buffer B is 100 mM Tris pH 8.5, 1 M NaCl. Samples were monitored at 260 nm and peaks corresponding to the full-length oligonucleotide species were collected, pooled, desalted on NAP-5 columns, and lyophilized.

[00346] The purity of each oligomer was determined by capillary electrophoresis (CE) on a Beckman PACE 5000 (Beckman Coulter, Inc.). The CE capillaries have a 100 μm inner diameter and contain ssDNA 100R Gel (Beckman-Coulter). Typically, about 0.6 nmole of oligonucleotide was injected into a capillary, run in an electric field of 444 V/cm, and was detected by UV absorbance at 260 nm. Denaturing Tris-Borate-7 M-urea running buffer was purchased from Beckman-Coulter. Oligoribonucleotides were obtained that were at least 90% pure as assessed by

CE for use in experiments described below. Compound identity was verified by matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectroscopy on a Voyager DE™ Biospectometry Work Station (Applied Biosystems) following the manufacturer's recommended protocol. Relative molecular masses of all oligomers were obtained, often within 0.2% of expected molecular mass.

[00347] *Preparation of Duplexes*

[00348] ss RNA oligomers were resuspended (*e.g.*, at 100 µM concentration) in duplex buffer consisting of 100 mM potassium acetate, 30 mM HEPES, pH 7.5. Complementary sense and antisense strands were mixed in equal molar amounts to yield a final solution of, for example, 50 µM duplex. Samples were heated to 100°C for 5 min in RNA buffer (IDT) and were allowed to cool to room temperature before use. The RNAi oligonucleotides were stored at −20° C. ss RNA oligomers were stored lyophilized or in nuclease-free water at −80° C.

[00349] Example 2: Generation of *MAPT*-Targeting ds RNAi Oligonucleotides

[00350] *Identification of MAPT mRNA Target Sequences*

[00351] To generate *MAPT*-targeting RNAi oligonucleotides, a computer-based algorithm was used to computationally identify MAPT mRNA target sequences suitable for assaying inhibition of *MAPT* gene expression by the RNAi pathway. The algorithm provided RNAi oligonucleotide antisense (guide) strand sequences each having a region of complementarity to a suitable MAPT mRNA target sequence of human (Hs) or murine (Mm) mRNA (*e.g.*, SEQ ID NOs: 909 and 910, respectively; Table 1). Due to sequence conservation across species, some of the MAPT mRNA target sequences identified for human MAPT mRNA are homologous to the corresponding MAPT mRNA target sequence of murine (mM) MAPT mRNA (SEQ ID NO: 910; Table 1) and/or monkey (Mf) MAPT mRNA (SEQ ID NO: 911; Table 1). *MAPT*-targeting RNAi oligonucleotides comprising a region of complementarity to homologous MAPT mRNA target sequences with nucleotide sequence similarity are predicted to have the ability to target homologous MAPT mRNAs (*e.g.*, human and monkey MAPT mRNAs).

[00352] Table 1: Exemplary Human, Monkey, and Mouse MAPT mRNA Sequences.

Species	GenBank Ref Seq #	SEQ ID NO

Human (Hs)	NM_001123066.3	909
Mouse (Mm)	NM_001038609.02	910
Cynomolgus monkey (Mf)	XM_005584531.2	911

[00353] RNAi oligonucleotides (formatted as DsiRNA oligonucleotides) were generated as described in Example 1 for evaluation *in vitro*. Each DsiRNA was generated with the same modification pattern, and each with a unique guide strand having a region of complementarity to a *MAPT* target sequence identified by the algorithm. Modifications for the sense and antisense DsiRNA included the following (*X*- any nucleotide; *m*- 2'-OMe-modified nucleotide; *r*- ribosyl-modified nucleotide):

Sense Strand: *rXmXrXmXrXrXrXrXrXrXrXrXrXmXrXmXrXrXrXrXrXrXXX*

Anti-sense Strand: *mXmXmXmXrXrXrXrXrXrXrXmXrXmXrXrXrXrXrXrXrXrXrXmXrXmXmXmX*

[00354] *In Vitro Cell-Based* Assays

[00355] The ability of each of the modified DsiRNA in Table 2 to reduce MAPT mRNA was measured using *in vitro* cell-based assays. Briefly, human T98G cells (glioblastoma cell line) expressing endogenous human *MAPT* gene were transfected with each of the DsiRNAs listed in Table 2 at 1 nM in separate wells of a multi-well cell-culture plate. Cells were maintained for 24 hours following transfection with the modified DsiRNA, and then the amount of remaining MAPT mRNA from the transfected cells was determined using TAQMAN®-based qPCR assays. Two qPCR assays, a 3' assay (Forward; GAA GAT TGG GTC CCT GGA (SEQ ID NO: 1683) , Reverse; TGT CTT GGC TTT GGC GTT (SEQ ID NO: 1684), Probe; 5'-6FAM- CGG AAG GTC /ZEN/ AGC TTG TGG GTT TCA (SEQ ID NO: 1685); and a 5' assay (Forward; CAC CAC AGC CAC CTT CTC (SEQ ID NO: 1686), Reverse; CTT CCA TCA CTT CGA ACT CCT (SEQ ID NO: 1687), Probe; 5'-6FAM- CGT CCT CGC /ZEN/ CTC TGT CGA CTA (SEQ ID NO: 1688) were used to determine MAPT mRNA levels as measured using PCR probes conjugated to 6-carboxy-fluorescein (FAM). Primer pairs were assayed for % remaining mRNA as shown in Table 2. DsiRNAs resulting in less than or equal to 10% MAPT mRNA remaining in DsiRNA-transfected cells when compared to mock-transfected cells were considered DsiRNA "hits." The

T98G cell-based assay evaluating the ability of the DsiRNAs listed in Table 2 to inhibit *MAPT* gene expression identified several candidate DsiRNAs.

[00356] Taken together, these results show that DsiRNAs designed to target human MAPT mRNA inhibit *MAPT* gene expression in cells, as determined by a reduced amount of MAPT mRNA in DsiRNA-transfected cells relative to control cells. These results demonstrate that the nucleotide sequences comprising the DsiRNA are useful for generating RNAi oligonucleotides to inhibit *MAPT* gene expression. Further, these results demonstrate that multiple MAPT mRNA target sequences are suitable for the RNAi-mediated inhibition of *MAPT* gene expression.

[00357] Table 2: *In Vitro* Screening Results.

			1 nM; T98G Cells		**HsMAPT-5'/SFRS9-F569**		**HsMAPT-3'/HPRT1-F517**	
Construct	**Sense strand SEQ ID NO**	**Anti-sense strand SEQ ID NO**	**average % remain-ing**	**average SD**	**% remain-ing**	**SEM**	**% remain-ing**	**SEM**
MAPT-2141	1	385	95.01	25.6510056	76.872	12.015	113.148	14.537
MAPT-2142	2	386	45.0915	14.8556064	34.587	3.412	55.596	5.956
MAPT-2303	3	387	49.649	1.54149278	48.559	4.694	50.739	7.759
MAPT-2347	4	388	14.9465	2.79802153	16.925	2.294	12.968	2.03
MAPT-2349	5	389	36.102	6.40497322	40.631	12.81	31.573	8.578
MAPT-2350	6	390	40.698	0.85701342	40.092	7.14	41.304	6.668
MAPT-2351	7	391	34.233	1.88514668	35.566	7.156	32.9	12.834
MAPT-2352	8	392	18.5755	5.96161727	22.791	7.452	14.36	4.732
MAPT-2353	9	393	48.36	11.8822224	39.958	4.633	56.762	6.089
MAPT-2354	10	394	24.094	3.67271262	26.691	5.688	21.497	6.358

MAPT-2355	11	395	18.7485	3.90252233	21.508	3.374	15.989	2.482
MAPT-2459	12	396	14.572	3.86645988	17.306	5.142	11.838	2.977
MAPT-2460	13	397	13.041	4.14647416	15.973	2.64	10.109	1.577
MAPT-2461	14	398	16.537	3.28097546	14.217	6.702	18.857	2.975
MAPT-2462	15	399	21.8695	2.158797	23.396	6.242	20.343	6.622
MAPT-2463	16	400	36.615	1.28127749	35.709	11	37.521	8.285
MAPT-2464	17	401	24.302	4.31335137	21.252	4.336	27.352	3.33
MAPT-2465	18	402	57.3185	24.0494087	40.313	6.657	74.324	8.436
MAPT-2466	19	403	43.9035	1.65109433	42.736	8.925	45.071	6.344
MAPT-2467	20	404	42.107	27.9957717	22.311	4.822	61.903	9.046
MAPT-2495	21	405	38.319	5.58472936	34.37	10.991	42.268	9.76
MAPT-2496	22	406	24.6465	2.92105811	26.712	4.387	22.581	6.794
MAPT-3686	23	407	82.684	13.0956176	73.424	15.054	91.944	13.074
MAPT-3687	24	408	55.0335	15.0691526	65.689	6.468	44.378	10.238
MAPT-3688	25	409	87.266	1.77200959	88.519	15.089	86.013	15.763
MAPT-3691	26	410	44.8115	4.63932759	48.092	12.584	41.531	10.617
MAPT-3692	27	411	42.868	1.70412734	41.663	6.449	44.073	5.791
MAPT-3693	28	412	49.581	11.071878	41.752	5.802	57.41	8.211
MAPT-4534	29	413	47.3565	11.3016877	39.365	3.71	55.348	6.574
MAPT-4535	30	414	56.0275	17.8608102	43.398	5.409	68.657	9.992
MAPT-4536	31	415	62.025	10.3096169	54.735	7.123	69.315	12.404

MAPT-4537	32	416	38.464	6.65811745	43.172	7.528	33.756	11.817
MAPT-4538	33	417	44.9465	13.5743289	35.348	11.081	54.545	9.032
MAPT-4566	34	418	38.0325	1.6058395	36.897	10.035	39.168	10.49
MAPT-4567	35	419	40.872	8.78650886	34.659	6.539	47.085	6.222
MAPT-4568	36	420	39.4745	0.77428193	40.022	6.35	38.927	3.497
MAPT-4569	37	421	44.188	6.29183614	39.739	5.336	48.637	6.198
MAPT-4570	38	422	52.8135	22.3947789	36.978	7.769	68.649	12.743
MAPT-4571	39	423	50.4355	6.61639815	45.757	6.03	55.114	10.233
MAPT-4572	40	424	51.2905	5.50765472	47.396	8.8	55.185	7.514
MAPT-4573	41	425	41.6435	3.91100761	44.409	11.822	38.878	5.955
MAPT-4574	42	426	44.6415	3.87140963	47.379	14.765	41.904	17.629
MAPT-4575	43	427	43.044	4.46184379	39.889	4.461	46.199	6.498
MAPT-4576	44	428	35.613	5.81100353	31.504	2.99	39.722	6.824
MAPT-4577	45	429	32.979	3.62462936	35.542	4.01	30.416	7.004
MAPT-4578	46	430	59.0835	11.5053344	50.948	8.8	67.219	11.491
MAPT-4579	47	431	44.268	11.4565441	36.167	4.845	52.369	5.65
MAPT-4580	48	432	57.2225	22.8713688	41.05	10.952	73.395	8.852
MAPT-4605	49	433	96.059	3.22440692	93.779	15.189	98.339	15.945
MAPT-4606	50	434	57.348	2.49467272	59.112	13.383	55.584	9.058
MAPT-4607	51	435	67.9825	13.5799857	58.38	10.161	77.585	9.466
MAPT-4608	52	436	35.004	14.4589195	45.228	5.369	24.78	7.968

MAPT-4609	53	437	52.854	7.33552575	58.041	9.122	47.667	6.181
MAPT-4610	54	438	56.244	5.2764308	52.513	8.718	59.975	11.85
MAPT-4611	55	439	60.552	13.7489843	70.274	19.308	50.83	9.512
MAPT-4612	56	440	44.801	10.820148	37.15	9.793	52.452	16.948
MAPT-4613	57	441	55.2605	12.1374879	46.678	13.942	63.843	4.47
MAPT-4614	58	442	51.7385	24.0451661	68.741	10.458	34.736	6.591
MAPT-5969	59	443	47.4125	3.24915566	45.115	14.811	49.71	8.998
MAPT-5970	60	444	44.3725	3.58998113	41.834	5.855	46.911	3.033
MAPT-5971	61	445	63.7505	23.6336299	47.039	6.803	80.462	9.959
MAPT-5972	62	446	49.5005	23.8089924	32.665	4.895	66.336	6.085
MAPT-5973	63	447	52.079	7.14884956	57.134	10.719	47.024	8.743
MAPT-5974	64	448	44.9585	12.1686006	36.354	12.432	53.563	8.866
MAPT-5975	65	449	45.1555	0.32456201	45.385	9.699	44.926	10.859
MAPT-5976	66	450	43.056	1.32511811	43.993	18.502	42.119	5.098
MAPT-5977	67	451	47.3185	1.16319066	48.141	6.434	46.496	7.198
MAPT-5978	68	452	58.9385	3.69887557	56.323	8.866	61.554	8.153
MAPT-5979	69	453	90.251	49.5568717	55.209	23.067	125.293	41.072
MAPT-5980	70	454	93.5025	1.75433192	92.262	15.249	94.743	12.851
MAPT-5981	71	455	73.614	15.0401612	62.979	9.331	84.249	10.224
MAPT-5982	72	456	52.7605	4.23627673	55.756	7.219	49.765	6.897
MAPT-5983	73	457	52.0305	13.3805816	61.492	16.873	42.569	15.962

MAPT-5984	74	458	39.226	13.1267303	29.944	8.671	48.508	18.496
MAPT-5985	75	459	47.514	0.09475231	47.581	10.955	47.447	15.502
MAPT-6662	76	460	56.8945	5.52321107	52.989	23.098	60.8	21.716
MAPT-6663	77	461	50.6	16.8984379	38.651	7.897	62.549	14.03
MAPT-6664	78	462	59.894	1.37461558	60.866	17.793	58.922	20.062
MAPT-6665	79	463	45.514	6.31022092	49.976	19.816	41.052	16.434
MAPT-6800	80	464	49.963	1.58391919	51.083	13.407	48.843	10.693
MAPT-6801	81	465	78.6545	21.2761359	63.61	10.347	93.699	12.651
MAPT-6802	82	466	36.959	2.8468119	34.946	11.719	38.972	6.592
MAPT-6803	83	467	60.1565	7.48896792	54.861	6.209	65.452	7.341
MAPT-6804	84	468	58.1295	25.573931	40.046	7.718	76.213	14.881
MAPT-6805	85	469	40.6695	7.0180348	35.707	8.81	45.632	6.173
MAPT-6806	86	470	49.47	9.29421153	42.898	13.633	56.042	8.573
MAPT-6807	87	471	44.6315	14.4172002	34.437	12.547	54.826	14.094
MAPT-6808	88	472	47.8265	1.73311872	46.601	15.127	49.052	9.845
MAPT-6809	89	473	100.4455	12.3199214	91.734	32.653	109.157	62.617
MAPT-6810	90	474	38.2355	5.25168206	34.522	8.787	41.949	19.197
MAPT-6811	91	475	64.862	2.72801796	66.791	6.959	62.933	10.212
MAPT-6812	92	476	78.776	32.6782328	55.669	16.433	101.883	16.548
MAPT-6813	93	477	67.15	7.39068008	61.924	11.954	72.376	13.616
MAPT-6814	94	478	44.55	0.562857	44.152	9.142	44.948	5.743

MAPT-6815	95	479	72.563	12.5695301	63.675	13.171	81.451	15.732
MAPT-6816	96	480	42.662	7.06258253	37.668	7.799	47.656	9.971
MAPT-363	97	481	10.801	0.99843478	11.507	5.145	10.095	2.3
MAPT-364	98	482	17.493	1.23319423	18.365	8.672	16.621	3.855
MAPT-365	99	483	49.6115	18.8917719	36.253	12.86	62.97	12.877
MAPT-367	100	484	60.2915	5.79898271	64.392	9.598	56.191	8.387
MAPT-369	101	485	18.496	5.14349473	14.859	2.908	22.133	5.121
MAPT-374	102	486	54.2605	7.24855161	49.135	6.979	59.386	8.929
MAPT-395	103	487	29.862	11.7125167	38.144	8.293	21.58	5.252
MAPT-400	104	488	34.402	16.4246763	22.788	7.436	46.016	11.445
MAPT-443	105	489	17.7005	6.73802052	12.936	4.852	22.465	4.318
MAPT-688	106	490	62.8045	3.40047651	65.209	13.424	60.4	5.794
MAPT-689	107	491	26.4395	3.02853834	28.581	4.295	24.298	6.236
MAPT-690	108	492	14.6445	4.81327586	11.241	2.659	18.048	2.561
MAPT-693	109	493	63.3205	15.4368481	52.405	6.513	74.236	8.881
MAPT-695	110	494	116.4165	9.93838581	123.444	17.981	109.389	37.256
MAPT-696	111	495	31.593	2.7322606	33.525	9.92	29.661	8.245
MAPT-1475	112	496	26.2465	9.29491864	19.674	5.59	32.819	7.787
MAPT-1476	113	497	30.5425	1.07975205	29.779	5.507	31.306	6.256
MAPT-1479	114	498	13.127	0.9588368	13.805	1.935	12.449	2.983
MAPT-1480	115	499	47.5765	5.71554411	43.535	9.405	51.618	7.164

MAPT-1481	116	500	37.489	3.0349023	39.635	3.962	35.343	5.214
MAPT-1484	117	501	24.0215	8.67690731	17.886	3.238	30.157	3.712
MAPT-1485	118	502	55.319	27.0807755	36.17	8.411	74.468	21.392
MAPT-1492	119	503	77.784	20.2685088	63.452	9.291	92.116	8.346
MAPT-1494	120	504	15.4475	3.58432427	12.913	5.176	17.982	3.997
MAPT-1495	121	505	18.204	1.04793225	18.945	3.15	17.463	3.766
MAPT-1498	122	506	20.014	2.4607316	18.274	6.805	21.754	5.32
MAPT-1499	123	507	65.7465	24.832883	48.187	11.539	83.306	19.091
MAPT-1500	124	508	18.62	5.80393246	14.516	4.376	22.724	5.504
MAPT-1502	125	509	34.775	5.02187236	38.326	10.536	31.224	4.366
MAPT-1503	126	510	31.277	11.1058191	39.13	11.069	23.424	3.92
MAPT-1504	127	511	24.627	3.87211673	27.365	4.52	21.889	2.089
MAPT-1505	128	512	10.3425	2.81074946	12.33	1.998	8.355	2.686
MAPT-1506	129	513	57.631	0.21354625	57.48	23.99	57.782	17.417
MAPT-1507	130	514	32.112	3.45068109	34.552	9.62	29.672	4.255
MAPT-1508	131	515	27.841	5.67099639	31.851	8.28	23.831	6.196
MAPT-1509	132	516	38.7	4.51699812	41.894	7.785	35.506	5.674
MAPT-1733	133	517	15.758	4.39961839	18.869	4.717	12.647	3.372
MAPT-1796	134	518	78.742	9.03116781	85.128	12.726	72.356	9.03
MAPT-1835	135	519	77.3505	24.4199327	94.618	20.422	60.083	13.368
MAPT-1912	136	520	24.699	5.16329372	28.35	13.873	21.048	4.701

MAPT-2094	137	521	18.8405	9.74463855	25.731	6.678	11.95	1.689
MAPT-2096	138	522	13.6925	1.29471252	14.608	3.403	12.777	2.067
MAPT-2097	139	523	21.9025	4.07081374	19.024	4.924	24.781	3.696
MAPT-2098	140	524	17.656	9.87828173	10.671	3.205	24.641	2.915
MAPT-2105	141	525	22.912	10.0098036	29.99	6.919	15.834	5.794
MAPT-2106	142	526	16.6545	1.53937146	17.743	3.658	15.566	3.854
MAPT-2107	143	527	33.657	2.05343809	35.109	4.469	32.205	5.491
MAPT-2108	144	528	27.0645	15.2940126	37.879	8.018	16.25	2.844
MAPT-2109	145	529	18.066	0.36769553	18.326	6.375	17.806	4.395
MAPT-2117	146	530	70.417	5.66958217	66.408	16.607	74.426	11.191
MAPT-2136	147	531	30.333	0.4794184	30.672	6.394	29.994	3.926
MAPT-2137	148	532	30.2155	0.61023315	29.784	5.066	30.647	4.74
MAPT-2269	149	533	22.638	2.83974083	20.63	4.29	24.646	6.881
MAPT-2270	150	534	12.216	1.87241876	10.892	3.111	13.54	3.021
MAPT-2271	151	535	31.5845	14.4270997	21.383	9.46	41.786	5.402
MAPT-2272	152	536	27.5985	12.4514433	36.403	7.932	18.794	4.51
MAPT-2273	153	537	14.2115	3.25764094	11.908	3.525	16.515	2.483
MAPT-2274	154	538	13.829	4.75317178	10.468	4.009	17.19	2.488
MAPT-2275	155	539	19.6215	0.85772053	19.015	6.27	20.228	3.6
MAPT-2276	156	540	13.741	6.74155605	8.974	4.323	18.508	4.472
MAPT-2277	157	541	35.06	2.40133463	33.362	8.636	36.758	4.222

MAPT-2278	158	542	62.9755	7.38007348	57.757	15.426	68.194	14.479
MAPT-2279	159	543	12.3635	0.0629325	12.408	6.106	12.319	4.131
MAPT-2280	160	544	22.4485	4.5672027	19.219	6.284	25.678	6.587
MAPT-2281	161	545	11.262	3.82544769	13.967	4.235	8.557	4.509
MAPT-2282	162	546	22.766	10.3704281	30.099	11.793	15.433	2.563
MAPT-2283	163	547	22.093	2.21748687	23.661	9.459	20.525	5.485
MAPT-2284	164	548	9.3375	0.48578236	9.681	3.741	8.994	2.065
MAPT-2286	165	549	43.909	5.46452121	40.045	5.708	47.773	11.236
MAPT-2288	166	550	44.999	0.15839192	45.111	3.984	44.887	11.572
MAPT-2289	167	551	16.7085	2.74710984	18.651	6.81	14.766	5.374
MAPT-2291	168	552	20.7095	1.76423142	19.462	4.227	21.957	4.191
MAPT-2294	169	553	36.6055	15.5033162	47.568	9.742	25.643	7.144
MAPT-2299	170	554	12.62	3.60624458	15.17	3.604	10.07	3.636
MAPT-2300	171	555	17.296	0.32385491	17.525	5.091	17.067	4.382
MAPT-2301	172	556	14.4115	2.7838794	12.443	3.439	16.38	5.47
MAPT-2308	173	557	39.5035	12.6225632	48.429	8.232	30.578	4.345
MAPT-2316	174	558	36.121	1.50755166	35.055	9.878	37.187	6.948
MAPT-2317	175	559	23.2925	4.71145248	19.961	7.977	26.624	5.453
MAPT-2319	176	560	46.479	18.4795286	33.412	7.15	59.546	16.236
MAPT-2320	177	561	34.5325	16.1340554	45.941	18.317	23.124	5.385
MAPT-2322	178	562	49.3475	9.8747462	56.33	10.684	42.365	6.267

MAPT-2323	179	563	37.4055	9.99071171	44.47	7.337	30.341	7.651
MAPT-2324	180	564	29.453	6.20981175	25.062	3.998	33.844	9.822
MAPT-2326	181	565	40.7595	0.49709607	41.111	8.995	40.408	14.253
MAPT-2330	182	566	53.6645	1.63129534	54.818	11.735	52.511	11.097
MAPT-2356	183	567	41.555	10.4071976	34.196	6.582	48.914	10.912
MAPT-2357	184	568	16.16	7.5702852	21.513	1.827	10.807	3.58
MAPT-2358	185	569	15.9115	0.34718943	16.157	5.317	15.666	2.953
MAPT-2359	186	570	38.779	13.5198817	48.339	12.534	29.219	3.728
MAPT-2360	187	571	56.6595	2.41759808	58.369	9.583	54.95	7.626
MAPT-2361	188	572	19.9675	15.8893965	31.203	7.037	8.732	1.814
MAPT-2362	189	573	25.7945	4.27021785	28.814	11.436	22.775	6.312
MAPT-2363	190	574	29.327	6.8094383	34.142	13.111	24.512	10.071
MAPT-2364	191	575	13.174	2.66154992	11.292	3.193	15.056	3.026
MAPT-2365	192	576	22.5375	0.18314066	22.408	4.494	22.667	3.198
MAPT-2372	193	577	10.775	5.70918015	14.812	6.29	6.738	2.466
MAPT-2373	194	578	14.297	0.80468752	13.728	3.586	14.866	3.452
MAPT-2374	195	579	11.664	0.88529769	11.038	4.433	12.29	2.181
MAPT-2375	196	580	19.954	1.3449171	20.905	3.625	19.003	5.119
MAPT-2376	197	581	11.6305	7.16228459	6.566	2.913	16.695	5.49
MAPT-2377	198	582	17.774	4.86630887	14.333	4.695	21.215	5.419
MAPT-2378	199	583	15.912	6.94096016	11.004	7.297	20.82	6.571

MAPT-2379	200	584	10.8575	3.47825826	8.398	3.267	13.317	2.091
MAPT-2380	201	585	54.1995	16.1213275	42.8	16.849	65.599	12.511
MAPT-2381	202	586	23.8745	5.39027499	20.063	5.735	27.686	4.702
MAPT-2382	203	587	6.365	0.30547013	6.581	2.357	6.149	2.123
MAPT-2390	204	588	6.377	0.34931075	6.13	2.062	6.624	1.482
MAPT-2391	205	589	12.498	2.13121984	10.991	5.358	14.005	4.476
MAPT-2414	206	590	66.506	38.9842111	38.94	9.142	94.072	16.71
MAPT-2448	207	591	101.6285	16.4791235	89.976	32.779	113.281	40.057
MAPT-2449	208	592	6.118	1.94171522	7.491	2.885	4.745	2.142
MAPT-2450	209	593	5.428	0.44264885	5.741	1.379	5.115	0.708
MAPT-2451	210	594	9.3195	2.04141728	7.876	3.092	10.763	3.026
MAPT-2452	211	595	12.4495	0.23688077	12.282	3.89	12.617	3.728
MAPT-2453	212	596	6.363	2.26981277	4.758	1.495	7.968	1.487
MAPT-2454	213	597	7.1635	0.37264527	7.427	3.314	6.9	1.49
MAPT-2456	214	598	5.641	0.69437886	6.132	1.582	5.15	2.739
MAPT-2457	215	599	16.472	7.58584155	11.108	2.63	21.836	5.922
MAPT-2567	216	600	12.6805	3.12329065	14.889	6.56	10.472	3.719
MAPT-2598	217	601	64.8695	33.2927086	41.328	16.719	88.411	33.918
MAPT-2657	218	602	68.409	37.9249651	41.592	8.109	95.226	13.823
MAPT-2723	219	603	11.61	0.04384062	11.579	8.192	11.641	11.451
MAPT-2724	220	604	233.808		233.808	161.639		

MAPT-2726	221	605	1302.476		1302.476	848.106		
MAPT-2784	222	606	10.97	5.81100353	6.861	1.876	15.079	4.091
MAPT-2963	223	607	40.636	1.52876486	39.555	13.364	41.717	9.834
MAPT-3110	224	608	67.4985	25.5979726	49.398	18.559	85.599	30.988
MAPT-3114	225	609	34.0185	10.2622407	26.762	7.333	41.275	9.007
MAPT-3116	226	610	23.677	5.0883404	20.079	5.942	27.275	7.786
MAPT-3118	227	611	17.6195	5.74948524	21.685	7.03	13.554	4.395
MAPT-3158	228	612	33.388	17.8502036	20.766	7.711	46.01	13.684
MAPT-3503	229	613	108.324	38.5344911	135.572	60.571	81.076	13.918
MAPT-3589	230	614	39.759	3.12258355	41.967	10.832	37.551	6.071
MAPT-3591	231	615	204.4415	111.869243	125.338	69.843	283.545	162.626
MAPT-3592	232	616	136.1045	32.3423571	113.235	30.524	158.974	46.677
MAPT-3593	233	617	63.914	14.1619346	53.9	10.02	73.928	12.246
MAPT-3594	234	618	80.7265	46.8465314	47.601	28.291	113.852	56.081
MAPT-3595	235	619	33.518	3.51997756	31.029	3.774	36.007	4.987
MAPT-3596	236	620	50.5415	9.44623949	57.221	22.189	43.862	7.353
MAPT-3597	237	621	207.694	70.014885	158.186	64.728	257.202	178.898
MAPT-3598	238	622	52.1005	3.0865211	49.918	5.249	54.283	7.413
MAPT-3599	239	623	364.1355	362.407075	620.396	189.266	107.875	48.489
MAPT-3600	240	624	100.4525	30.5364063	122.045	56.065	78.86	42.186
MAPT-3601	241	625	47.233	12.1297097	38.656	5.821	55.81	7.764

MAPT-3602	242	626	43.078	9.10894956	36.637	5.569	49.519	8.21
MAPT-3603	243	627	46.1485	9.83797665	39.192	6.61	53.105	14.334
MAPT-3605	244	628	38.537	6.97490129	43.469	6.803	33.605	12.721
MAPT-3607	245	629	52.929	12.1099107	44.366	6.167	61.492	10.195
MAPT-3609	246	630	61.4085	31.4839294	39.146	5.412	83.671	11.371
MAPT-3610	247	631	53.294	26.6211561	34.47	5.122	72.118	6.918
MAPT-3677	248	632	72.7675	16.9755125	60.764	8.013	84.771	12.398
MAPT-3678	249	633	44.9005	19.9778879	30.774	5.138	59.027	10.698
MAPT-3679	250	634	72.05	31.5638325	49.731	5.218	94.369	10.439
MAPT-3680	251	635	58.9445	1.90565278	60.292	9.168	57.597	15.808
MAPT-3958	252	636	60.937	9.03682466	54.547	8.505	67.327	20.084
MAPT-3959	253	637	76.6655	34.4580206	52.3	5.769	101.031	26.056
MAPT-3960	254	638	75.305	39.354735	47.477	5.803	103.133	19.335
MAPT-3961	255	639	45.3385	7.61483293	39.954	10.197	50.723	5.643
MAPT-3965	256	640	72.0995	2.20688026	70.539	7.456	73.66	8.937
MAPT-3970	257	641	74.1615	12.9549033	65.001	14.647	83.322	16.913
MAPT-4146	258	642	77.359	47.5543452	43.733	6.924	110.985	17.09
MAPT-4474	259	643	42.89	0.51194531	43.252	6.788	42.528	13.112
MAPT-4475	260	644	66.3895	44.1764962	35.152	5.684	97.627	19.713
MAPT-4477	261	645	68.927	35.8870834	43.551	6.949	94.303	12.932
MAPT-4478	262	646	50.6895	22.0624387	35.089	7.887	66.29	21.359

MAPT-4479	263	647	40.2915	16.0223326	51.621	8.132	28.962	6.75
MAPT-4480	264	648	62.963	18.7227734	76.202	15.622	49.724	17.779
MAPT-4481	265	649	62.488	35.7329341	37.221	8.557	87.755	19.687
MAPT-4482	266	650	96.4665	98.6859437	26.685	10.537	166.248	71.368
MAPT-4485	267	651	67.466	56.8216867	27.287	9.898	107.645	19.981
MAPT-4486	268	652	64.4675	54.6770319	25.805	8.223	103.13	13.135
MAPT-4532	269	653	50.712	44.6028815	19.173	5.038	82.251	13.252
MAPT-4533	270	654	56.2795	28.997742	35.775	6.797	76.784	17.19
MAPT-4539	271	655	84.0985	66.4744014	37.094	8.676	131.103	23.594
MAPT-4540	272	656	56.93	25.0980481	39.183	14.927	74.677	14.251
MAPT-4541	273	657	42.061	23.7969716	25.234	4.689	58.888	6.414
MAPT-4543	274	658	37.3465	16.4183124	25.737	2.55	48.956	6.301
MAPT-4544	275	659	49.8975	30.8022785	28.117	6.319	71.678	14.003
MAPT-4545	276	660	52.179	17.3524004	39.909	9.44	64.449	17.044
MAPT-4546	277	661	34.6085	5.14420183	30.971	6.568	38.246	10.405
MAPT-4547	278	662	38.51	12.7293363	29.509	9.311	47.511	5.308
MAPT-4548	279	663	46.233	8.19678181	52.029	9.095	40.437	10.11
MAPT-4549	280	664	46.195	5.19440641	49.868	9.773	42.522	9.731
MAPT-4550	281	665	64.53	30.5625693	42.919	7.626	86.141	16.456
MAPT-4551	282	666	48.566	4.18890057	45.604	10.327	51.528	13.065
MAPT-4552	283	667	38.5625	36.1041651	13.033	5.295	64.092	10.666

MAPT-4554	284	668	58.8795	40.1375022	30.498	5.099	87.261	14.948
MAPT-4556	285	669	60.179	22.017891	44.61	13.332	75.748	6.493
MAPT-4557	286	670	44.634	7.32704047	39.453	7.608	49.815	7.645
MAPT-4558	287	671	44.4695	15.0436968	55.107	13.83	33.832	4.355
MAPT-4559	288	672	62.3795	19.7912117	76.374	17.486	48.385	7.434
MAPT-4560	289	673	48.0585	20.8518719	33.314	11.514	62.803	7.869
MAPT-4561	290	674	45.0945	0.04030509	45.123	15.353	45.066	13.72
MAPT-4562	291	675	31.412	1.63341666	32.567	5.823	30.257	5.108
MAPT-4563	292	676	40.812	16.5957962	29.077	4.004	52.547	13.653
MAPT-4564	293	677	51.221	23.9878904	34.259	9.457	68.183	17.349
MAPT-4615	294	678	50.634	4.53396868	47.428	11.37	53.84	9.461
MAPT-4616	295	679	50.985	5.68372431	55.004	11.45	46.966	8.038
MAPT-4617	296	680	55.1025	21.5702924	70.355	20.557	39.85	5.507
MAPT-4618	297	681	48.908	3.70665375	46.287	11.781	51.529	19.126
MAPT-4619	298	682	38.3115	20.5859997	23.755	5.348	52.868	12.438
MAPT-4620	299	683	34.8815	12.0597062	26.354	7.457	43.409	13.598
MAPT-4621	300	684	50.155	18.3437641	37.184	8.204	63.126	8.376
MAPT-4622	301	685	32.6225	1.30178358	33.543	5.593	31.702	6.676
MAPT-4623	302	686	45.0005	13.5983705	35.385	8.943	54.616	7.648
MAPT-4625	303	687	48.5845	6.76347636	43.802	5.103	53.367	7.374
MAPT-4627	304	688	54.916	15.3710872	65.785	13.194	44.047	13.218

MAPT-4628	305	689	35.7	2.4508321	33.967	6.77	37.433	7.946
MAPT-4629	306	690	31.7615	4.28718841	28.73	7.064	34.793	10.844
MAPT-4630	307	691	26.347	10.6235723	18.835	4.239	33.859	12.366
MAPT-4632	308	692	39.4495	7.60917607	34.069	5.742	44.83	10.263
MAPT-4633	309	693	61.3835	14.1074874	51.408	15.912	71.359	22.804
MAPT-4825	310	694	52.238	12.4252804	43.452	10.809	61.024	10.061
MAPT-4828	311	695	48.2045	2.66508546	46.32	8.016	50.089	16.64
MAPT-5682	312	696	89.127	35.3779665	114.143	29.128	64.111	16.557
MAPT-5958	313	697	46.249	12.6359982	37.314	6.879	55.184	14.344
MAPT-5959	314	698	43.587	19.7523208	29.62	8.048	57.554	13.293
MAPT-5961	315	699	40.428	6.24658131	36.011	10.381	44.845	4.108
MAPT-5963	316	700	38.295	2.01808275	36.868	5.593	39.722	10.772
MAPT-5964	317	701	52.7395	16.4678098	41.095	8.774	64.384	7.757
MAPT-5965	318	702	45.2395	21.7541401	29.857	7.021	60.622	8.921
MAPT-5966	319	703	51.0255	9.61877354	44.224	6.395	57.827	9.074
MAPT-5967	320	704	56.756	19.2488608	43.145	10.168	70.367	13.456
MAPT-5968	321	705	49.755	14.8365145	60.246	12.788	39.264	9.459
MAPT-6006	322	706	30.953	2.88358145	32.992	7.492	28.914	6.891
MAPT-6007	323	707	46.1245	14.5968053	35.803	7.552	56.446	6.025
MAPT-6008	324	708	52.218	3.03065966	54.361	9.738	50.075	7.532
MAPT-6009	325	709	76.4995	42.195183	106.336	19.189	46.663	11.419

MAPT-6010	326	710	58.729	23.2892689	42.261	7.547	75.197	5.272
MAPT-6011	327	711	52.692	4.01212388	49.855	12.113	55.529	14.5
MAPT-6012	328	712	63.9645	0.68377226	64.448	15.339	63.481	10.773
MAPT-6013	329	713	53.8995	17.2314852	66.084	23.254	41.715	10.372
MAPT-6014	330	714	33.9865	1.58886894	32.863	4.884	35.11	8.916
MAPT-6015	331	715	47.801	25.4077609	29.835	8.764	65.767	6.147
MAPT-6017	332	716	46.9375	0.02192031	46.953	10.206	46.922	11.089
MAPT-6119	333	717	54.6625	9.43492578	61.334	13.818	47.991	12.587
MAPT-6628	334	718	64.7155	0.73468395	65.235	6.382	64.196	10.199
MAPT-6629	335	719	50.0975	11.687768	58.362	10.929	41.833	14.095
MAPT-6631	336	720	81.9435	12.0568777	73.418	19.87	90.469	17.638
MAPT-6672	337	721	33.822	12.4677068	25.006	8.472	42.638	12.985
MAPT-6731	338	722	24.959	10.8512607	17.286	2.982	32.632	9.031
MAPT-6732	339	723	38.0145	13.7228213	28.311	11.443	47.718	15.906
MAPT-6738	340	724	34.031	28.3691241	13.971	3.303	54.091	13.69
MAPT-6739	341	725	38.316	29.593833	17.39	2.841	59.242	14.056
MAPT-6740	342	726	34.866	13.8847488	25.048	11.345	44.684	6.187
MAPT-6741	343	727	34.507	11.2825958	26.529	7.507	42.485	10.487
MAPT-6742	344	728	62.1435	29.7882874	41.08	12.738	83.207	17.359
MAPT-6743	345	729	29.6205	23.3790715	13.089	2.767	46.152	5.76
MAPT-6745	346	730	26.926	10.1229407	19.768	4.146	34.084	5.015

MAPT-6748	347	731	60.0265	3.40471915	57.619	11.694	62.434	11.211
MAPT-6749	348	732	50.6395	36.3502383	24.936	4.104	76.343	16.107
MAPT-6750	349	733	44.856	3.86080303	47.586	12.024	42.126	13.817
MAPT-6751	350	734	78.4055	17.0730932	66.333	7.978	90.478	12.547
MAPT-6752	351	735	50.173	15.0231907	60.796	7.566	39.55	9.59
MAPT-6753	352	736	71.371	11.5413969	63.21	16.035	79.532	21.212
MAPT-6754	353	737	36.8455	3.50654253	34.366	6.737	39.325	9.505
MAPT-6755	354	738	49.7045	24.223357	66.833	10.306	32.576	5.734
MAPT-6756	355	739	44.4755	32.1599235	21.735	7.721	67.216	9.314
MAPT-6757	356	740	33.5075	4.63225652	30.232	9.588	36.783	6.407
MAPT-6758	357	741	31.353	12.2753737	22.673	6.04	40.033	9.561
MAPT-6759	358	742	41.85	0.46669048	41.52	10.866	42.18	7.164
MAPT-6760	359	743	32.4735	18.9158135	45.849	11.71	19.098	3.864
MAPT-6761	360	744	45.049	19.3718974	31.351	10.31	58.747	11.659
MAPT-6762	361	745	38.174	8.13031377	43.923	15.429	32.425	4.765
MAPT-6763	362	746	53.7735	2.06828733	52.311	15.07	55.236	8.063
MAPT-6764	363	747	53.1035	33.2686669	29.579	9.81	76.628	17.226
MAPT-6765	364	748	52.8995	16.5795327	41.176	10.853	64.623	15.24
MAPT-6766	365	749	49.2605	4.00293149	52.091	10.614	46.43	16.518
MAPT-6767	366	750	71.423	0.85701342	72.029	26.702	70.817	16.417
MAPT-6768	367	751	55.4255	9.05308812	61.827	22.465	49.024	12.369

MAPT-6769	368	752	72.08	0.29839906	71.869	16.441	72.291	37.177
MAPT-6772	369	753	49.619	14.4377063	59.828	20.675	39.41	13.235
MAPT-6773	370	754	48.624	11.5583674	56.797	12.783	40.451	6.391
MAPT-6774	371	755	52.4405	31.8855661	29.894	6.706	74.987	5.573
MAPT-6775	372	756	28.415	6.30456406	32.873	8.748	23.957	5.955
MAPT-6777	373	757	39.772	4.84509566	43.198	3.707	36.346	9.384
MAPT-6778	374	758	50.719	5.85342993	54.858	14.257	46.58	14.17
MAPT-6779	375	759	35.5865	10.7459018	43.185	6.174	27.988	3.65
MAPT-6780	376	760	71.501	11.9614183	79.959	23.953	63.043	14.252
MAPT-6781	377	761	43.875	9.50210093	37.156	6.446	50.594	8.933
MAPT-6789	378	762	43.4265	3.49381461	40.956	13.993	45.897	6.518
MAPT-6792	379	763	46.25	28.0028427	26.449	10.778	66.051	11.602
MAPT-6793	380	764	33.324	13.8762635	43.136	13.663	23.512	6.983
MAPT-6795	381	765	33.747	11.8765655	42.145	13.155	25.349	9.4
MAPT-6796	382	766	65.7615	8.10556503	71.493	9.454	60.03	12.964
MAPT-6797	383	767	55.439	15.7302975	66.562	17.934	44.316	16.313
MAPT-6798	384	768	50.3055	4.55023214	47.088	13.033	53.523	13.441

[00358] Example 3: GalNAc-Conjugated *MAPT* RNAi Oligonucleotides Inhibit Human MAPT mRNA Expression *In Vivo*

[00359] The *in vitro* screening assays in Example 2 validated the ability of *MAPT*-targeting oligonucleotides to knockdown target mRNA. To further evaluate the ability of *MAPT* RNAi oligonucleotides to inhibit MAPT mRNA expression, GalNAc-conjugated *MAPT*-targeting

oligonucleotides were generated to confirm knockdown *in vivo*.

[00360] Specifically, a subset of the DsiRNAs identified in Example 2 were used to generate corresponding ds RNAi oligonucleotides comprising a nicked tetraloop GalNAc-conjugated structure (referred to herein as "GalNAc-conjugated *MAPT* oligonucleotides" or "GalNAc-*MAPT* oligonucleotides") having a 36-mer sense strand and a 22-mer antisense strand (Tables 4 and 5). Further, the nucleotide sequences comprising the sense strand and antisense strand have a distinct pattern of modified nucleotides and phosphorothioate linkages. Three of the nucleotides comprising the tetraL were each conjugated to a GalNAc moiety (CAS#14131-60-3). The benchmark control (MAPT-2460) has a different modification pattern than the remaining oligonucleotides. The modification patterns are illustrated below:

Sense Strand: 5'-X-*S*-mX-fX-mX-fX-mX-mX-fX-mX-fX-mX-fX-fX-mX-fX-mX-fX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-[ademX-GalNAc]-[ademX-GalNAc]-[ademX-GalNAc]-mX-mX-mX-mX-mX-mX-3' hybridized to:

Antisense Strand: 5'-[MePhosphonate-4O-mX]-*S*-fX-*S*-fX-fX-fX-mX-fX-mX-mX-fX-mX-mX-mX-fX-mX-fX-mX-mX-fX-mX-*S*-mX-*S*-mX-3'.

(Modification key: Table 3).

[00361] Or, represented as:

Sense Strand: [mXs][mX][fX][mX][fX][mX][mX][fX][mX][fX][mX][fX][fX][mX][fX][mX][fX][mX][mX][mX][mX][mX][mX][mX][mX][mX][mX][ademX-GalNAc][ademX-GalNAc][ademX-GalNAc][mX][mX][mX][mX][mX][mX] hybridized to:

Antisense Strand: [MePhosphonate-4O-mXs][fXs][fX][fX][fX][mX][fX][mX][mX][fX][mX][mX][mX][fX][mX][fX][mX][mX][fX][mXs][mXs][mX].

(Modification key: Table 3).

[00362] Benchmark Modification Pattern

Sense Strand: 5'-mX-*S*-mX-mX-mX-mX-mX-mX-fX-fX-fX-fX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-mX-[ademX-GalNAc]-[ademX-GalNAc]-[ademX-GalNAc]-mX-mX-mX-mX-mX-mX-3' hybridized to:

Antisense Strand: 5'-[MePhosphonate-4O-mX]-S-fX-S-fX-S-fX-fX-mX-fX-mX-mX-fX-mX-mX-mX-fX-mX-mX-mX-mX-mX-mX-S-mX-S-mX-3'.

(Modification key: Table 3).

[00363] Or, represented as:

Sense Strand: [mXs][mX][mX][mX][mX][mX][mX][fX][fX][fX][fX][mX][mX][mX][mX][mX][mX][mX][mX][mX][mX][mX][mX][mX][mX][mX][ademX-GalNAc][ademX-GalNAc][ademX-GalNAc][mX][mX][mX][mX][mX][mX] hybridized to:

Antisense Strand: [MePhosphonate-4O-mXs][fXs][fX][fX][fX][mX][fX][mX][mX][fX][mX][mX][mX][fX][mX][mX][mX][mX][mX][mXs][mXs][mX].

(Modification key: Table 3).

[00364] Table 3: Key for Modification Patterns.

Symbol	Modification/linkage
Key 1	
mX	2'-OMe-modified nucleotide
fX	2'-F-modified nucleotide
-*S*-	phosphorothioate linkage
-	phosphodiester linkage
[MePhosphonate-4O-mX]	4'-O-monomethylphosphonate-2'-O-methyl modified nucleotide
ademX-GalNAc	GalNAc attached to a nucleotide
ademX-C16	C_{16} hydrocarbon chain attached to a nucleotide
Key 2	
[mXs]	2'-OMe-modified nucleotide with a phosphorothioate linkage to the neighboring nucleotide
[fXs]	2'-F-modified nucleotide with a phosphorothioate linkage to the neighboring nucleotide
[mX]	2'-OMe-modified nucleotide with phosphodiester linkages to neighboring nucleotides
[fX]	2'-F-modified nucleotide with phosphodiester linkages to neighboring nucleotides
[ademXs-C16]	C_{16} hydrocarbon chain attached to a nucleotide with phosphodiester linkages to neighboring nucleotides

[00365] The GalNAc-conjugated *MAPT*-targeting oligonucleotides were used in an HDI model to confirm the ability of the RNAi oligonucleotides to knockdown *MAPT* gene expression *in vivo*. The GalNAc-conjugated *MAPT*-targeting oligonucleotides listed in Tables 4 and 5 were evaluated in mice engineered to transiently express human MAPT mRNA in hepatocytes of the mouse liver. Briefly, 6-8-week-old female CD-1 mice (n = 4-5) were subcutaneously administered the indicated GalNAc-conjugated *MAPT*-targeting oligonucleotides at a dose of 3 mg/kg formulated in PBS. A

control group of mice (n = 5) were administered only PBS. Four days later (96 hours), the mice were HDI with a DNA plasmid encoding the full human *MAPT* gene (SEQ ID NO: 909) (10 μg) under control of a ubiquitous cytomegalovirus (CMV) promoter sequence. One day after introduction of the DNA plasmid, liver samples from HDI mice were collected. Total RNA derived from these HDI mice were subjected to qRT-PCR analysis to determine human MAPT mRNA levels as described in Example 2. The values were normalized for transfection efficiency using the NeoR gene included on the DNA plasmid. Benchmark controls (MAPT-2460) were used to confirm successful knock-down.

[00366] Table 4: GalNAc-Conjugated Human *MAPT*-Targeting RNAi Oligonucleotides for HDI Screen (Set I).

RNAi Oligonucleotide	**SEQ ID NO (Sense)**	**SEQ ID NO (Antisense)**	**SEQ ID NO (Sense)**	**SEQ ID NO (Antisense)**
	Unmodified		**Modified**	
MAPT-1479	787	822	857	892
MAPT-1505	788	823	858	893
MAPT-2096	789	824	859	894
MAPT-2270	790	825	860	895
MAPT-2279	791	826	861	896
MAPT-2281	792	827	862	897
MAPT-2284	793	828	863	898
MAPT-2299	794	829	864	899
MAPT-2376	795	830	865	900
MAPT-2379	796	831	866	901
MAPT-2382	797	832	867	902
MAPT-2449	798	833	868	903
MAPT-2450	799	834	869	904
MAPT-2451	800	835	870	905
MAPT-2452	801	836	871	906
MAPT-2453	802	837	872	907
MAPT-2454	803	838	873	908
MAPT-2460	786	821	856	891

[00367] Table 5: GalNAc-Conjugated Human *MAPT*-Targeting RNAi Oligonucleotides for HDI Screen (Set II).

RNAi Oligonucleotide	**SEQ ID NO (Sense)**	**SEQ ID NO (Antisense)**	**SEQ ID NO (Sense)**	**SEQ ID NO (Antisense)**

	Unmodified		Modified	
MAPT-2456	769	804	839	874
MAPT-2567	770	805	840	875
MAPT-2723	771	806	841	876
MAPT-0690	772	807	842	877
MAPT-1494	773	808	843	878
MAPT-1733	774	809	844	879
MAPT-2273	775	810	845	880
MAPT-2274	776	811	846	881
MAPT-2276	777	812	847	882
MAPT-2301	778	813	848	883
MAPT-2347	779	814	849	884
MAPT-2357	780	815	850	885
MAPT-2358	781	816	851	886
MAPT-2364	782	817	852	887
MAPT-2378	783	818	853	888
MAPT-2459	784	819	854	889
MAPT-2461	785	820	855	890
MAPT-2460	786	821	856	891

[00368] The results in FIGs. 1A and 1B demonstrate that GalNAc-conjugated *MAPT*-targeting oligonucleotides (as shown in Tables 4 and 5, respectively) designed to target human MAPT mRNA successfully inhibited human MAPT mRNA expression in HDI mice, as determined by a reduction in the amount of human MAPT mRNA expression in liver samples from HDI mice treated with GalNAc-conjugated *MAPT*-targeting oligonucleotides relative to control HDI mice treated with only PBS.

[00369] Example 4: GalNAc-Conjugated *MAPT*-Targeting RNAi Oligonucleotides Inhibit Human *MAPT* Gene Expression in A Dose-Dependent Manner

[00370] To further evaluate the ability of GalNAc-conjugated *MAPT*-targeting RNAi oligonucleotides to inhibit *MAPT* gene expression, a dose response study was carried out. Specifically, in separate treatment groups, selected GalNAc-conjugated *MAPT*-targeting RNAi oligonucleotides (Tables 6 and 7) were formulated in PBS and were administered to CD-1 mice at doses of 0.3 mg/kg, 1 mg/kg, or 3 mg/kg subcutaneously. As described in Example 3, a human *MAPT* DNA expression plasmid was administered to the mice 4 days post-oligonucleotide dosing,

and livers were collected 20 hours later for qRT-PCR analysis. As shown in FIGs. 2A and 2B, all of the GalNAc-conjugated *MAPT*-targeting RNAi oligonucleotides tested inhibited human *MAPT* gene expression in a dose-dependent manner. Potent GalNAc-conjugated *MAPT*-targeting oligonucleotides (*i.e.*, MAPT-2449, MAPT-2357, MAPT-2450, MAPT-2358, MAPT-2454, and MAPT-2723) reduced MAPT mRNA by around 50% or more at 1 mg/kg and even further at 3 mg/kg. These constructs were selected for further studies in NHPs.

[00371] Table 6: GalNAc-Conjugated Human *MAPT*-Targeting RNAi Oligonucleotides for Dose Screen (Set I).

RNAi Oligonucleotide	**SEQ ID NO (Sense)**	**SEQ ID NO (Antisense)**	**SEQ ID NO (Sense)**	**SEQ ID NO (Antisense)**
	Unmodified		**Modified**	
MAPT-2270	790	825	860	895
MAPT-2376	795	830	865	900
MAPT-2449	798	833	868	903
MAPT-2450	799	834	869	904
MAPT-2454	803	838	873	908

[00372] Table 7: GalNAc-Conjugated Human *MAPT*-Targeting RNAi Oligonucleotides for Dose Screen (Set II).

RNAi Oligonucleotide	**SEQ ID NO (Sense)**	**SEQ ID NO (Antisense)**	**SEQ ID NO (Sense)**	**SEQ ID NO (Antisense)**
	Unmodified		**Modified**	
MAPT-2723	771	806	841	876
MAPT-2274	776	811	846	881
MAPT-2357	780	815	850	885
MAPT-2358	781	816	851	886
MAPT-2364	782	817	852	887

[00373] Example 5: RNAi Oligonucleotide Inhibition of *MAPT* Gene Expression in NHP CNS

[00374] Effective GalNAc-conjugated *MAPT*-targeting oligonucleotides identified in the HDI mouse studies were assayed for inhibition in NHP. Specifically, GalNAc-conjugated *MAPT*-targeting oligonucleotides listed in Table 8 were evaluated in non-naïve cynomolgus monkeys (*Macaca fascicularis*; *Mf*). Each cohort contained 4 female subjects weighing 2.6-4.3 kg. The

GalNAc-conjugated *MAPT*-targeting oligonucleotides were administered at a dose of 50 mg in 1.6 mL of artificial cerebrospinal fluid (aCSF) on study days 0 and 7 via intra cisterna magna (i.c.m.) injection.

[00375] Table 8: GalNAc-Conjugated *MAPT*-Targeting RNAi Oligonucleotides for NHP Study.

RNAi Oligonucleotide	**Alternate name**	**SEQ ID NO (Sense)**	**SEQ ID NO (Antisense)**	**SEQ ID NO (Sense)**	**SEQ ID NO (Antisense)**
		Unmodified		**Modified**	
MAPT-2723	DCR 214	771	806	841	876
MAPT-2357	DCR 211	780	815	850	885
MAPT-2358	DCR 212	781	816	851	886
MAPT-2449	DCR 207	798	833	868	903
MAPT-2450	DCR 208	799	834	869	904
MAPT-2454	DCR 209	803	838	873	908

[00376] On study day 14, CNS tissue was collected and subjected to qRT-PCR analysis to measure MAPT mRNA in oligonucleotide-treated monkeys relative to those treated with a comparable volume of aCSF. To normalize the data, the measurements were made relative to the reference gene, RPL23. The following SYBR assays purchased from Integrated DNA Technologies were used to evaluate gene expressions:

Forward: AGGACAGAGTGCAGTCGAAGATC;

Reverse: AGGTCAGCTTGTGGGTTTCAA; and

Probe: CACCCATGTCCCTGGCGGAGG.

[00377] As shown in FIGs. 3A-3M (Day 14), treating NHPs with the GalNAc-conjugated *MAPT*-targeting oligonucleotides inhibited *MAPT* gene expression in several regions of the CNS, as determined by a reduced amount of MAPT mRNA in brain samples from oligonucleotide-treated NHPs relative to NHPs treated with aCSF. Several GalNAc-conjugated *MAPT*-targeting oligonucleotides reduced *MAPT* gene expression throughout the CNS. MAPT-2357 (DCR 211) was particularly potent in the cervical spinal cord, thoracic spinal cord, lumbar spinal cord, frontal cortex, temporal cortex, occipital cortex, and brain stem. These results demonstrate that treating NHPs with the GalNAc-conjugated *MAPT*-targeting oligonucleotides reduces the amount of MAPT mRNA in the CNS.

[00378] Example 6: Lipid Conjugation of *MAPT*-Targeting Oligonucleotides Reduces Expression in NHP CNS

[00379] To further investigate the efficacy of oligonucleotides targeting *MAPT*, a lipid-conjugated oligonucleotide was assessed in NHP compared to a GalNAc-conjugated oligonucleotide. Specifically, the GalNAc-conjugated MAPT-2357 (DCR 211) described in Example 3, having a 36-mer sense strand and 22-mer antisense strand (SEQ ID NOs: 850 and 885, respectively) was compared to a lipid-conjugated MAPT-2357 (DCR 211), having a 20-mer sense strand and 22-mer antisense strand (SEQ ID NOs: 1682 and 885, respectively). FIGs. 4A-4B show the chemical modification patterns of each oligonucleotide, and the chemical modification pattern of the lipid-conjugated oligonucleotide is provided below:

Sense Strand: 5'-[ademX-C16]-*S*-mX-fX-mX-fX-mX-mX-fX-mX-fX-mX-fX-fX-mX-fX-mX-fX-mX- *S*-mX-*S*-mX-3' hybridized to:

Antisense Strand: 5'-[MePhosphonate-4O-mX]-*S*-fX-*S*-fX-fX-fX-mX-fX-mX-mX-fX-mX-mX-mX-fX-mX-fX-mX-mX-fX-mX-*S*-mX-*S*-mX-3'.

(Modification key: Table 3).

[00380] Or, represented as:

Sense Strand: [ademXs-C16][mX][fX][mX][fX][mX][mX][fX][mX][fX][mX][fX] [fX][mX][fX][mX][fX][mXs][mXs][mX] hybridized to:

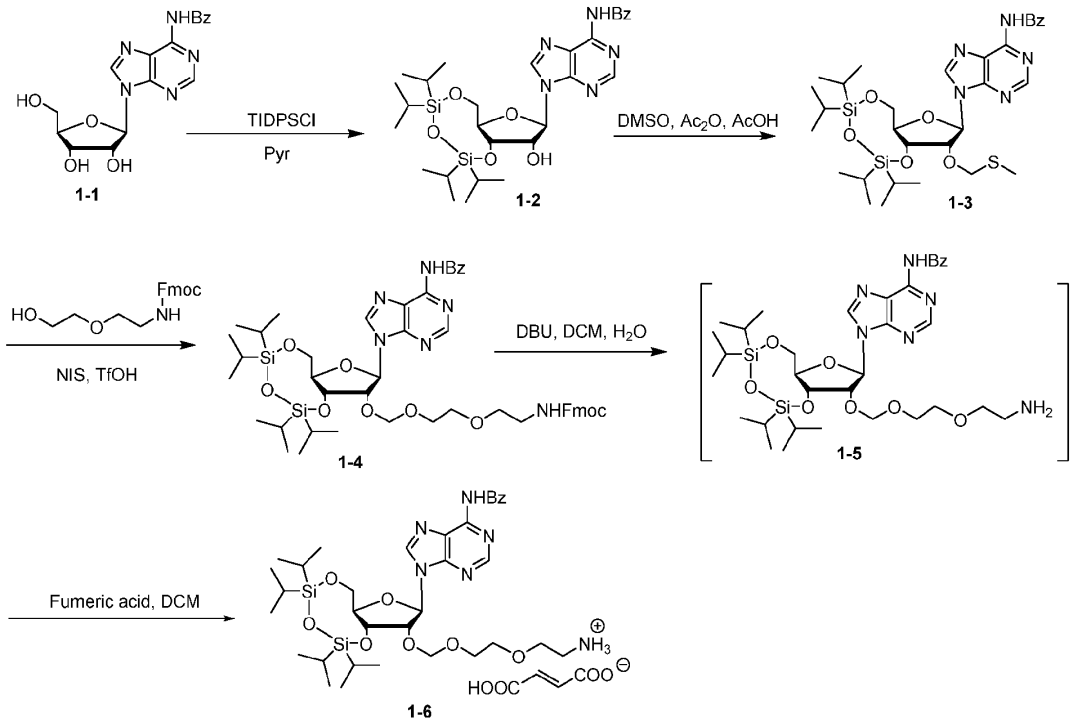
Antisense Strand: [MePhosphonate-4O-mXs][fXs][fX][fX][fX][mX][fX][mX][mX] [fX][mX][mX][mX][fX][mX][fX][mX][mX][fX][mXs][mXs][mX]

(Modification key: Table 3).

[00381] *Lipid Conjugation*

[00382] Conjugation of a lipid moiety to the *MAPT*-targeting oligonucleotide was carried out using phosphoramidite synthesis as shown below.

[00383] *Synthesis of 2-(2-((((6aR,8R,9R,9aR)-8-(6-benzamido-9H-purin-9-yl)-2,2,4,4-tetraisopropyltetrahydro-6H-furo[3,2-f][1,3,5,2,4]trioxadisilocin-9-yl)oxy)methoxy)ethoxy) ethan-1-ammonium formate (1-6)*



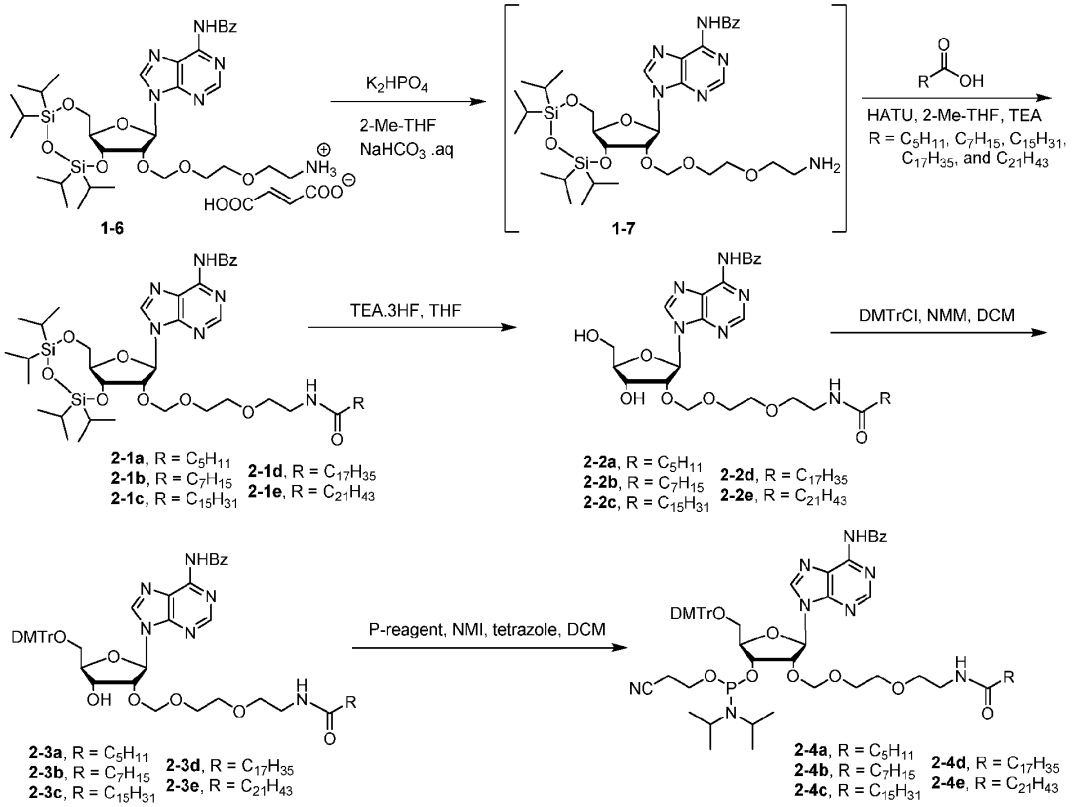
[00384] A solution of compound 1-1 (25.00 g, 67.38 mmol) in 20 mL of dimethylformamide (DMF) was treated with pyridine (11 mL, 134.67 mmol) and tetraisopropyldisiloxane dichloride (22.63 mL, 70.75 mmol) at 10 °C. The resulting mixture was stirred at 25 °C for 3 hours and quenched with 20% citric acid (50 mL). The aqueous layer was extracted with ethyl acetate (EtOAc; 3X50 mL) and the combined organic layers were concentrated *in vacuo*. The crude residue was recrystallized from a mixture of methyl tert-butyl ether (MTBE) and n-heptane (1:15, 320 mL) to afford compound 1-2 (37.20 g, 90%) as a white oily solid.

[00385] A solution of compound 1-2 (37.00 g, 60.33 mmol) in 20 mL of DMSO was treated with acetic acid (AcOH; 20 mL, 317.20 mmol) and Ac_2O (15 mL, 156.68 mmol). The mixture was stirred at 25 °C for 15 h. The reaction was diluted with EtOAc (100 mL) and quenched with sat. potassium carbonate (K_2CO_3; 50 mL). The aqueous layer was extracted with EtOAc (3X50 mL). The combined organic layers were concentrated and recrystallized with acetonitrile (can; 30 mL) to afford compound 1-3 (15.65 g, 38.4%) as a white solid.

[00386] A solution of compound 1-3 (20.00 g, 29.72 mmol) in 120 mL of dichloromethane (DCM) was treated with Fmoc-amino-ethoxy ethanol (11.67 g, 35.66 mmol) at 25 °C. The mixture was stirred to afford a clear solution and then treated with 4Å molecular sieves (20.0 g), *N*-iodosuccinimide (8.02 g, 35.66 mmol), and trifluoromethanesulfonic acid (TfOH; 5.25 mL, 59.44 mmol). The mixture was stirred at 30 °C until the HPLC analysis indicated >95% consumption of compound 1-3. The reaction was quenched with TEA (6 mL) and filtered. The filtrate was diluted with EtOAc, washed with sat. Sodium bicarbonate ($NaHCO_3$; 2X100 mL), sat. sodium sulfite (Na_2SO_3; 2X100 mL), and water (2X100 mL) and concentrated *in vacuo* to afford crude compound 1-4 (26.34 g, 93.9%) as a yellow solid, which was used directly for the next step without further purification.

[00387] A solution of compound 1-4 (26.34 g, 27.62 mmol) in a mixture of DCM/water (10:7, 170 mL) was treated with 1,8-diazabicyclo[5.4.0] undec-7-ene (DBU; 7.00 mL, 45.08 mmol) at 5 °C. The mixture was stirred at 5-25 °C for 1 hour. The organic layer was then separated, washed with water (100 mL), and diluted with DCM (130 mL). The solution was treated with fumaric acid (7.05 g, 60.76 mmol) and 4Å molecular sieves (26.34 g) in four portions. The mixture was stirred for 1 hour, concentrated, and recrystallized from a mixture of MTBE and DCM (5:1) to afford compound 1-6 (14.74 g, 62.9%) as a white solid: ^{1}H NMR (400 MHz, d_6-DMSO) 8.73 (s, 1H), 8.58 (s, 1H), 8.15-8.02 (m, 2H), 7.65-7.60 (m, 1H), 7.59-7.51 (m, 2H), 6.52 (s, 2H), 6.15(s, 1H), 5.08-4.90 (m, 3H), 4.83-4.78 (m, 1H), 4.15-3.90 (m, 3H), 3.79-3.65 (m, 2H), 2.98-2.85 (m, 6H), 1.20-0.95 (m, 28H).

[00388] *Synthesis of (2R,3R,4R,5R)-5-(6-benzamido-9H-purin-9-yl)-2-((bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-4-((2-(2-[lipid]-amidoethoxy)ethoxy)methoxy) tetrahydrofuran-3-yl (2-cyanoethyl) diisopropylphosphoramidite (2-4a to 2-4e)*



[00389] A solution of compound 1-6 (50.00 g, 59.01 mmol) in 150 mL of 2-methyltetrahydrofuran was washed with ice cold aqueous dipotassium hydrogen phosphate (K_2HPO_4; 6%, 100 mL) and brine (20%, 2X100 mL). The organic layer was separated and treated with hexanoic acid (10.33 mL, 82.61 mmol), 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU; 33.66 g, 88.52 mmol), and 4-dimethylaminopyridine (DMAP; 10.81 g, 147.52 mmol) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 1 hour. The solution was washed with water (2X100 mL), brine (100 mL), and concentrated *in vacuo* to afford a crude residue. Flash chromatography on silica gel (1:1 hexanes/acetone) gave compound 2-1a (34.95 g, 71.5%) as a white solid.

[00390] A mixture of compound 2-1a (34.95 g, 42.19 mmol) and TEA (9.28 mL, 126.58 mmol) in 80 mL of tetrahydrofuran (THF) was treated with triethylamine trihydrofluoride (20.61 mL, 126.58 mmol) dropwise at 10 °C. The mixture was warmed to 25 °C and stirred for 2 hours. The

reaction was concentrated, dissolved in DCM (100 mL), and washed with sat. $NaHCO_3$ (5X20 mL) and brine (50 mL). The organic layer was concentrated *in vacuo* to afford crude compound 2-2a (24.72 g, 99%), which was used directly for the next step without further purification.

[00391] A solution of compound 2-2a (24.72 g, 42.18 mmol) in 50 mL of DCM was treated with *N*-methylmorpholine (18.54 mL, 168.67 mmol) and DMTr-Cl (15.69 g, 46.38 mmol). The mixture was stirred at 25 °C for 2 hours and quenched with sat. $NaHCO_3$ (50 mL). The organic layer was separated, washed with water, and concentrated to afford a slurry crude. Flash chromatography on silica gel (1:1 hexanes/acetone) gave compound 2-3a (30.05 g, 33.8 mmol, 79.9%) as a white solid.

[00392] A solution of compound 2-3a (25.00 g, 28.17 mmol) in 50 mL of DCM was treated with *N*-methylmorpholine (3.10 mL, 28.17 mmol) and tetrazole (0.67 mL, 14.09 mmol) under nitrogen atmosphere. Bis(diisopropylamino) chlorophosphine (9.02 g, 33.80 mmol) was added to the solution dropwise, and the resulting mixture was stirred at 25 °C for 4 hours. The reaction was quenched with water (15 mL), and the aqueous layer was extracted with DCM (3X50 mL). The combined organic layers were washed with sat. $NaHCO_3$ (50 mL), concentrated to afford a crude solid that was recrystallized from a mixture of DCM/MTBE/n-hexane (1:4:40) to afford compound **2**-4a (25.52 g, 83.4%) as a white solid: ^{1}H NMR (400 MHz, d_6-DMSO) 11.25 (s, 1H), 8.65-8.60 (m, 2 H), 8.09-8.02 (m, 2H), 7.71 (s, 1H), 7.67-7.60 (m, 1H), 7.59-7.51 (m, 2H), 7.38-7.34 (m, 2H), 7.30-7.25 (m, 7H), 6.85-6.79 (m, 4H), 6.23-6.20 (m, 1H), 5.23-5.14 (m, 1H), 4. 80-4.69 (m, 3H), 4.33-4.23 (m, 2H), 3.90-3.78 (m, 1H), 3.75 (s, 6H), 3.74-3.52 (m, 3H), 3.50-3.20 (m, 6H), 3.14-3.09 (m, 2H), 3.09 (s, 1H), 2.82-2.80 (m, 1H), 2.65-2.60 (m, 1H), 2.05-1.96 (m, 2H), 1.50-1.39 (m, 2H), 1.31-1.10 (m, 14H), 1.08-1.05 (m, 2 H), 0.85-0.79 (m, 3H); ^{31}P NMR (162 MHz, d_6-DMSO) 149.43, 149.18.

[00393] Compound 2-4b, 2-4c, 2-4d, and 2-4e were prepared using similar procedures described above for compound 2-4a. Compound 2-4b was obtained (25.50 g, 85.4%) as a white solid: ^{1}H NMR (400 MHz, d_6-DMSO) 11.23 (s, 1H), 8.65-8.60 (m, 2 H), 8.05-8.02 (m, 2H), 7.73-7.70 (m, 1H), 7.67-7.60 (m, 1H), 7.59-7.51 (m, 2H), 7.38-7.34 (m, 2H), 7.30-7.25 (m, 7H), 6.89-6.80 (m, 4H), 6.21-6.15 (m, 1H), 5.23-5.17 (m, 1H), 4. 80-4.69 (m, 3H), 4.40-4.21 (m, 2H), 3.91-3.80 (m, 1H), 3.74 (s, 6H), 3.74-3.52 (m, 3H), 3.50-3.20 (m, 6H), 3.14-3.09 (m, 2H), 3.09 (s, 1H), 2.83-

2.79 (m, 1H), 2.68-2.62 (m, 1H), 2.05-1.97 (m, 2H), 1.50-1.38 (m, 2H), 1.31-1.10 (m, 18H), 1.08-1.05 (m, 2H), 0.85-0.78 (m, 3H); ^{31}P NMR (162 MHz, d_6-DMSO) 149.43, 149.19.

[00394] Compound 2-4c was obtained (36.60 g, 66.3%) as an off-white solid: ^{1}H NMR (400 MHz, d_6-DMSO) 11.22 (s, 1H), 8.64-8.59 (m, 2H), 8.05-8.00 (m, 2H), 7.73-7.70 (m, 1H), 7.67-7.60 (m, 1H), 7.59-7.51 (m, 2H), 7.38-7.34 (m, 2H), 7.30-7.25 (m, 7H), 6.89-6.80 (m, 4H), 6.21-6.15 (m, 1H), 5.25-5.17 (m, 1H), 4.80-4.69 (m, 3H), 4.40-4.21 (m, 2H), 3.91-3.80 (m, 1H), 3.74 (s, 6H), 3.74-3.50 (m, 3H), 3.50-3.20 (m, 6H), 3.14-3.09 (m, 2H), 3.09 (s, 1H), 2.83-2.79 (m, 1H), 2.68-2.62 (m, 1H), 2.05-1.99 (m, 2H), 1.50-1.38 (m, 2H), 1.33-1.12 (m, 38H), 1.08-1.05 (m, 2 H), 0.86-0.80 (m, 3H); ^{31}P NMR (162 MHz, d_6-DMSO) 149.42, 149.17.

[00395] Compound 2-4d was obtained (26.60 g, 72.9%) as an off-white solid: ^{1}H NMR (400 MHz, d_6-DMSO) 11.22 (s, 1H), 8.64-8.59 (m, 2H), 8.05-8.00 (m, 2H), 7.73-7.70 (m, 1H), 7.67-7.60 (m, 1H), 7.59-7.51 (m, 2H), 7.38-7.33 (m, 2H), 7.30-7.25 (m, 7H), 6.89-6.80 (m, 4H), 6.21-6.15 (m, 1H), 5.22-5.17 (m, 1H), 4.80-4.69 (m, 3H), 4.40-4.21 (m, 2H), 3.91-3.80 (m, 1H), 3.74 (s, 6H), 3.74-3.52 (m, 3H), 3.50-3.20 (m, 6H), 3.14-3.09 (m, 2H), 3.09 (s, 1H), 2.83-2.79 (m, 1H), 2.68-2.62 (m, 1H), 2.05-1.99 (m, 2H), 1.50-1.38 (m, 2H), 1.35-1.08 (m, 38H), 1.08-1.05 (m, 2 H), 0.85-0.79 (m, 3H); ^{31}P NMR (162 MHz, d_6-DMSO) 149.47, 149.22.

[00396] Compound 2-4e was obtained (38.10 g, 54.0%) as a white solid: ^{1}H NMR (400 MHz, d_6-DMSO) 11.21 (s, 1H), 8.64-8.59 (m, 2H), 8.05-8.00 (m, 2H), 7.73-7.70 (m, 1H), 7.67-7.60 (m, 1H), 7.59-7.51 (m, 2H), 7.38-7.34 (m, 2H), 7.30-7.25 (m, 7H), 6.89-6.80 (m, 4H), 6.21-6.15 (m, 1H), 5.23-5.17 (m, 1H), 4.80-4.69 (m, 3H), 4.40-4.21 (m, 2H), 3.91-3.80 (m, 1H), 3.73 (s, 6H), 3.74-3.52 (m, 3H), 3.47-3.22 (m, 6H), 3.14-3.09 (m, 2H), 3.09 (s, 1H), 2.83-2.79 (m, 1H), 2.68-2.62 (m, 1H), 2.05-1.99 (m, 2H), 1.50-1.38 (m, 2H), 1.35-1.06 (m, 46H), 1.08-1.06 (m, 2 H), 0.85-0.77 (m, 3H); ^{31}P NMR (162 MHz, d_6-DMSO) 149.41, 149.15.

[00397] Lipid-conjugated blunt-ended oligonucleotides described herein were synthesized using a standard procedure known in the literature for oligo synthesis on a synthesizer using amidite chemistry.

[00398] *NHP Study*

[00399] NHPs (n=4) were intrathecally administered 37.5 mg lipid-conjugated or 45mg GalNAc-

conjugated MAPT-2357 (DCR 211) via lumbar infusion at L1 (*see* Table 9). Artificial cerebral spinal fluid (aCSF) was used as a control.

[00400] Table 9: Conjugated *MAPT* RNAi Oligonucleotides for NHP Study.

RNAi Oligo	Alternate Name	Conjugate	SEQ ID NO (Sense)	SEQ ID NO (Antisense)	SEQ ID NO (Sense)	SEQ ID NO (Antisense)
			Unmodified		Modified	
MAPT-2357	DCR 211	C_{16}	1681	815	1682	885
MAPT-2357	DCR 211	GalNAc	780	815	850	885

[00401] 28 days after administration, CNS tissue was collected to determine the concentration of the oligonucleotide and the level of *MAPT* gene expression. AD is a chronic neurodegenerative disease characterized by a progressive decline in cognitive abilities such as memory, thinking, language, and learning; whereas, PSP is a less common brain disorder characterized by deterioration in brain regions responsible for movement, coordination, and eventually cognition. Accordingly, CNS tissues associated with AD or PSP were analyzed separately.

[00402] As shown in FIG. 5A, *MAPT* gene expression was reduced in tissues associated with AD, including the prefrontal cortex, motor cortex, temporal cortex, parietal cortex, and hippocampus, with both lipid-conjugated and GalNAc-conjugated MAPT-2357. Lipid conjugation resulted in a higher reduction of *MAPT* gene expression compared to GalNAc conjugation. *MAPT* gene expression was determined as described in the above Examples. FIG. 5B shows a higher concentration of lipid-conjugated MAPT-2357 in the same tissues compared to GalNAc-conjugated MAPT-2357. These results indicate lipid-conjugated *MAPT*-targeting oligonucleotides have enhanced potency even at a reduced dose compared to GalNAc-conjugated *MAPT*-targeting oligonucleotides across tissues associated with AD.

[00403] As shown in FIG. 6A, *MAPT* gene expression was reduced in tissues associated with PSP, including the caudate nucleus, thalamus, midbrain tegmentum, substantia nigra, pons, cerebellar white matter, cerebellar dentate nucleus, medulla, cervical spinal cord, thoracic spinal cord, and lumbar spinal cord with both lipid-conjugated and GalNAc-conjugated MAPT-2357. Lipid-conjugation resulted in a higher reduction of *MAPT* gene expression compared to GalNAc-conjugation. *MAPT* gene expression was determined as described in the above Examples. FIG. 6B

shows a higher concentration of lipid-conjugated MAPT-2357 in the same tissues compared to GalNAc-conjugated MAPT-2357. These results indicate lipid-conjugated *MAPT*-targeting oligonucleotides have enhanced potency even at a reduced dose compared to GalNAc-conjugated *MAPT*-targeting oligonucleotides across tissues associated with PSP.

SEQUENCE LISTING

[00404] The following nucleic and/or amino acid sequences are referred to in the disclosure and are provided below for reference.

Construct		Species and location	Sequence	SEQ ID NO
MAPT-2141	25mer sense strand	2141-2218-966 (Hs-Mf-Mm)	GAGAACCUGAAGCACCAGCAGGGAG	1
MAPT-2142	25mer sense strand	2142-2219-967 (Hs-Mf-Mm)	AGAACCUGAAGCACCAGCCAGGAGG	2
MAPT-2303	25mer sense strand	2303-2380-1128 (Hs-Mf-Mm)	GUGACCUCCAAGUGUGGCUAAUUAG	3
MAPT-2347	25mer sense strand	2347-2424-1172 (Hs-Mf-Mm)	AGGAGGUGGCCAGGUGGAAAUAAAA	4
MAPT-2349	25mer sense strand	2349-2426-1174 (Hs-Mf-Mm)	GAGGUGGCCAGGUGGAAGUAAAATC	5
MAPT-2350	25mer sense strand	2350-2427-1175 (Hs-Mf-Mm)	AGGUGGCCAGGUGGAAGUAAAAUCT	6
MAPT-2351	25mer sense strand	2351-2428-1176 (Hs-Mf-Mm)	GGUGGCCAGGUGGAAGUAAAAUCTG	7
MAPT-2352	25mer sense strand	2352-2429-1177 (Hs-Mf-Mm)	GUGGCCAGGUGGAAGUAAAAUCUGA	8
MAPT-2353	25mer sense strand	2353-2430-1178 (Hs-Mf-Mm)	UGGCCAGGUGGAAGUAAAAACUGAG	9
MAPT-2354	25mer sense strand	2354-2431-1179 (Hs-Mf-Mm)	GGCCAGGUGGAAGUAAAAUAUGAGA	10
MAPT-2355	25mer sense strand	2355-2432-1180 (Hs-Mf-Mm)	GCCAGGUGGAAGUAAAAUCAGAGAA	11
MAPT-2459	25mer sense strand	2459-2536-1284 (Hs-Mf-Mm)	AAGAUUGAAACCCACAAGCAGACCT	12

MAPT-2460	25mer sense strand	2460-2537-1285 (Hs-Mf-Mm)	AGAUUGAAACCCACAAGCUAACCTT	13
MAPT-2461	25mer sense strand	2461-2538-1286 (Hs-Mf-Mm)	GAUUGAAACCCACAAGCUGACCUTC	14
MAPT-2462	25mer sense strand	2462-2539-1287 (Hs-Mf-Mm)	AUUGAAACCCACAAGCUGAACUUCC	15
MAPT-2463	25mer sense strand	2463-2540-1288 (Hs-Mf-Mm)	UUGAAACCCACAAGCUGACAUUCCG	16
MAPT-2464	25mer sense strand	2464-2541-1289 (Hs-Mf-Mm)	UGAAACCCACAAGCUGACCAUCCGC	17
MAPT-2465	25mer sense strand	2465-2542-1290 (Hs-Mf-Mm)	GAAACCCACAAGCUGACCUACCGCG	18
MAPT-2466	25mer sense strand	2466-2543-1291 (Hs-Mf-Mm)	AAACCCACAAGCUGACCUUACGCGA	19
MAPT-2467	25mer sense strand	2467-2544-1292 (Hs-Mf-Mm)	AACCCACAAGCUGACCUUCAGCGAG	20
MAPT-2495	25mer sense strand	2495-2572-1320 (Hs-Mf-Mm)	GCCAAAGCCAAGACAGACCACGGGG	21
MAPT-2496	25mer sense strand	2496-2573-1321 (Hs-Mf-Mm)	CCAAAGCCAAGACAGACCAAGGGGC	22
MAPT-3686	25mer sense strand	3686-3758-2505 (Hs-Mf-Mm)	UCUUUGUAAGGACUUGUGCAUCUTG	23
MAPT-3687	25mer sense strand	3687-3759-2506 (Hs-Mf-Mm)	CUUUGUAAGGACUUGUGCCACUUGG	24
MAPT-3688	25mer sense strand	3688-3760-2507 (Hs-Mf-Mm)	UUUGUAAGGACUUGUGCCUAUUGGG	25
MAPT-3691	25mer sense strand	3691-3763-2510 (Hs-Mf-Mm)	GUAAGGACUUGUGCCUCUUAGGAGA	26

MAPT-3692	25mer sense strand	3692-3764-2511 (Hs-Mf-Mm)	UAAGGACUUGUGCCUCUUGAGAGAC	27
MAPT-3693	25mer sense strand	3693-3765-2512 (Hs-Mf-Mm)	AAGGACUUGUGCCUCUUGGAAGACG	28
MAPT-4534	25mer sense strand	4534-4605-3332 (Hs-Mf-Mm)	GUUGUAGUUGGAUUUGUCUAUUUAT	29
MAPT-4535	25mer sense strand	4535-4606-3333 (Hs-Mf-Mm)	UUGUAGUUGGAUUUGUCUGAUUATG	30
MAPT-4536	25mer sense strand	4536-4607-3334 (Hs-Mf-Mm)	UGUAGUUGGAUUUGUCUGUAUAUGC	31
MAPT-4537	25mer sense strand	4537-4608-3335 (Hs-Mf-Mm)	GUAGUUGGAUUUGUCUGUUAAUGCT	32
MAPT-4538	25mer sense strand	4538-4609-3336 (Hs-Mf-Mm)	UAGUUGGAUUUGUCUGUUUAUGCTT	33
MAPT-4566	25mer sense strand	4566-4637-3362 (Hs-Mf-Mm)	UUCACCAGAGUGACUAUGAAAGUGA	34
MAPT-4567	25mer sense strand	4567-4638-3363 (Hs-Mf-Mm)	UCACCAGAGUGACUAUGAUAGUGAA	35
MAPT-4568	25mer sense strand	4568-4639-3364 (Hs-Mf-Mm)	CACCAGAGUGACUAUGAUAAUGAAA	36
MAPT-4569	25mer sense strand	4569-4640-3365 (Hs-Mf-Mm)	ACCAGAGUGACUAUGAUAGAGAAAA	37
MAPT-4570	25mer sense strand	4570-4641-3366 (Hs-Mf-Mm)	CCAGAGUGACUAUGAUAGUAAAAAG	38
MAPT-4571	25mer sense strand	4571-4642-3367 (Hs-Mf-Mm)	CAGAGUGACUAUGAUAGUGAAAAGA	39
MAPT-4572	25mer sense strand	4572-4643-3368 (Hs-Mf-Mm)	AGAGUGACUAUGAUAGUGAAAAGAA	40

MAPT-4573	25mer sense strand	4573-4644-3369 (Hs-Mf-Mm)	GAGUGACUAUGAUAGUGAAAAGAAA	41
MAPT-4574	25mer sense strand	4574-4645-3370 (Hs-Mf-Mm)	AGUGACUAUGAUAGUGAAAAGAAAA	42
MAPT-4575	25mer sense strand	4575-4646-3371 (Hs-Mf-Mm)	GUGACUAUGAUAGUGAAAAAAAAAA	43
MAPT-4576	25mer sense strand	4576-4647-3372 (Hs-Mf-Mm)	UGACUAUGAUAGUGAAAAGAAAAAA	44
MAPT-4577	25mer sense strand	4577-4648-3373 (Hs-Mf-Mm)	GACUAUGAUAGUGAAAAGAAAAAAA	45
MAPT-4578	25mer sense strand	4578-4649-3374 (Hs-Mf-Mm)	ACUAUGAUAGUGAAAAGAAAAAAAA	46
MAPT-4579	25mer sense strand	4579-4650-3375 (Hs-Mf-Mm)	CUAUGAUAGUGAAAAGAAAAAAAAA	47
MAPT-4580	25mer sense strand	4580-4651-3376 (Hs-Mf-Mm)	UAUGAUAGUGAAAAGAAAAAAAAAA	48
MAPT-4605	25mer sense strand	4605-4677-3439 (Hs-Mf-Mm)	AAAAAAAAGGACGCAUGUAACUUGA	49
MAPT-4606	25mer sense strand	4606-4678-3440 (Hs-Mf-Mm)	AAAAAAAGGACGCAUGUAUAUUGAA	50
MAPT-4607	25mer sense strand	4607-4679-3441 (Hs-Mf-Mm)	AAAAAAGGACGCAUGUAUCAUGAAA	51
MAPT-4608	25mer sense strand	4608-4680-3442 (Hs-Mf-Mm)	AAAAAGGACGCAUGUAUCUAGAAAT	52
MAPT-4609	25mer sense strand	4609-4681-3443 (Hs-Mf-Mm)	AAAAGGACGCAUGUAUCUUAAAATG	53
MAPT-4610	25mer sense strand	4610-4682-3444 (Hs-Mf-Mm)	AAAGGACGCAUGUAUCUUGAAAUGC	54

MAPT-4611	25mer sense strand	4611-4683-3445 (Hs-Mf-Mm)	AAGGACGCAUGUAUCUUGAAAUGCT	55
MAPT-4612	25mer sense strand	4612-4684-3446 (Hs-Mf-Mm)	AGGACGCAUGUAUCUUGAAAUGCTT	56
MAPT-4613	25mer sense strand	4613-4685-3447 (Hs-Mf-Mm)	GGACGCAUGUAUCUUGAAAAGCUTG	57
MAPT-4614	25mer sense strand	4614-4686-3448 (Hs-Mf-Mm)	GACGCAUGUAUCUUGAAAUACUUGT	58
MAPT-5969	25mer sense strand	5969-6024-4540 (Hs-Mf-Mm)	UCACUUUAUCAAUAGUUCCAUUUAA	59
MAPT-5970	25mer sense strand	5970-6025-4541 (Hs-Mf-Mm)	CACUUUAUCAAUAGUUCCAAUUAAA	60
MAPT-5971	25mer sense strand	5971-6026-4542 (Hs-Mf-Mm)	ACUUUAUCAAUAGUUCCAUAUAAAT	61
MAPT-5972	25mer sense strand	5972-6027-4543 (Hs-Mf-Mm)	CUUUAUCAAUAGUUCCAUUAAAATT	62
MAPT-5973	25mer sense strand	5973-6028-4544 (Hs-Mf-Mm)	UUUAUCAAUAGUUCCAUUUAAAUTG	63
MAPT-5974	25mer sense strand	5974-6029-4545 (Hs-Mf-Mm)	UUAUCAAUAGUUCCAUUUAAAUUGA	64
MAPT-5975	25mer sense strand	5975-6030-4546 (Hs-Mf-Mm)	UAUCAAUAGUUCCAUUUAAAUUGAC	65
MAPT-5976	25mer sense strand	5976-6031-4547 (Hs-Mf-Mm)	AUCAAUAGUUCCAUUUAAAAUGACT	66
MAPT-5977	25mer sense strand	5977-6032-4548 (Hs-Mf-Mm)	UCAAUAGUUCCAUUUAAAUAGACTT	67
MAPT-5978	25mer sense strand	5978-6033-4549 (Hs-Mf-Mm)	CAAUAGUUCCAUUUAAAUUAACUTC	68

MAPT-5979	25mer sense strand	5979-6034-4550 (Hs-Mf-Mm)	AAUAGUUCCAUUUAAAUUGACUUCA	69
MAPT-5980	25mer sense strand	5980-6035-4551 (Hs-Mf-Mm)	AUAGUUCCAUUUAAAUUGAAUUCAG	70
MAPT-5981	25mer sense strand	5981-6036-4552 (Hs-Mf-Mm)	UAGUUCCAUUUAAAUUGACAUCAGT	71
MAPT-5982	25mer sense strand	5982-6037-4553 (Hs-Mf-Mm)	AGUUCCAUUUAAAUUGACUACAGTG	72
MAPT-5983	25mer sense strand	5983-6038-4554 (Hs-Mf-Mm)	GUUCCAUUUAAAUUGACUUAAGUGG	73
MAPT-5984	25mer sense strand	5984-6039-4555 (Hs-Mf-Mm)	UUCCAUUUAAAUUGACUUCAGUGGT	74
MAPT-5985	25mer sense strand	5985-6040-4556 (Hs-Mf-Mm)	UCCAUUUAAAUUGACUUCAAUGGTG	75
MAPT-6662	25mer sense strand	6662-6723-5230 (Hs-Mf-Mm)	CUUGCAAGUCCCAUGAUUUAUUCGG	76
MAPT-6663	25mer sense strand	6663-6724-5231 (Hs-Mf-Mm)	UUGCAAGUCCCAUGAUUUCAUCGGT	77
MAPT-6664	25mer sense strand	6664-6725-5232 (Hs-Mf-Mm)	UGCAAGUCCCAUGAUUUCUACGGTA	78
MAPT-6665	25mer sense strand	6665-6726-5233 (Hs-Mf-Mm)	GCAAGUCCCAUGAUUUCUUAGGUAA	79
MAPT-6800	25mer sense strand	6800-6861-5365 (Hs-Mf-Mm)	GUAAAAGUGAAUUUGGAAAAAAAGT	80
MAPT-6801	25mer sense strand	6801-6862-5366 (Hs-Mf-Mm)	UAAAAGUGAAUUUGGAAAUAAAGTT	81
MAPT-6802	25mer sense strand	6802-6863-5367 (Hs-Mf-Mm)	AAAAGUGAAUUUGGAAAUAAAGUTA	82

MAPT-6803	25mer sense strand	6803-6864-5368 (Hs-Mf-Mm)	AAAGUGAAUUUGGAAAUAAAGUUAT	83
MAPT-6804	25mer sense strand	6804-6865-5369 (Hs-Mf-Mm)	AAGUGAAUUUGGAAAUAAAAUUATT	84
MAPT-6805	25mer sense strand	6805-6866-5370 (Hs-Mf-Mm)	AGUGAAUUUGGAAAUAAAGAUAUTA	85
MAPT-6806	25mer sense strand	6806-6867-5371 (Hs-Mf-Mm)	GUGAAUUUGGAAAUAAAGUAAUUAC	86
MAPT-6807	25mer sense strand	6807-6868-5372 (Hs-Mf-Mm)	UGAAUUUGGAAAUAAAGUUAUUACT	87
MAPT-6808	25mer sense strand	6808-6869-5373 (Hs-Mf-Mm)	GAAUUUGGAAAUAAAGUUAAUACTC	88
MAPT-6809	25mer sense strand	6809-6870-5374 (Hs-Mf-Mm)	AAUUUGGAAAUAAAGUUAUAACUCT	89
MAPT-6810	25mer sense strand	6810-6871-5375 (Hs-Mf-Mm)	AUUUGGAAAUAAAGUUAUUACUCTG	90
MAPT-6811	25mer sense strand	6811-6872-5376 (Hs-Mf-Mm)	UUUGGAAAUAAAGUUAUUAAUCUGA	91
MAPT-6812	25mer sense strand	6812-6873-5377 (Hs-Mf-Mm)	UUGGAAAUAAAGUUAUUACACUGAT	92
MAPT-6813	25mer sense strand	6813-6874-5378 (Hs-Mf-Mm)	UGGAAAUAAAGUUAUUACUAUGATT	93
MAPT-6814	25mer sense strand	6814-6875-5379 (Hs-Mf-Mm)	GGAAAUAAAGUUAUUACUCAGAUTA	94
MAPT-6815	25mer sense strand	6815-6876-5380 (Hs-Mf-Mm)	GAAAUAAAGUUAUUACUCUAAUUAA	95
MAPT-6816	25mer sense strand	6816-6877-5381 (Hs-Mf-Mm)	AAAUAAAGUUAUUACUCUGAUUAAA	96

MAPT-363	25mer sense strand	363 (Hs)	AGGAGUUCGAAGUGAUGGAAGAUCA	97
MAPT-364	25mer sense strand	364 (Hs)	GGAGUUCGAAGUGAUGGAAAAUCAC	98
MAPT-365	25mer sense strand	365 (Hs)	GAGUUCGAAGUGAUGGAAGAUCACG	99
MAPT-367	25mer sense strand	367 (Hs)	GUUCGAAGUGAUGGAAGAUAACGCT	100
MAPT-369	25mer sense strand	369 (Hs)	UCGAAGUGAUGGAAGAUCAAGCUGG	101
MAPT-374	25mer sense strand	374-226 (Hs-Mf)	GUGAUGGAAGAUCACGCUGAGACGT	102
MAPT-395	25mer sense strand	395-247 (Hs-Mf)	ACGUACGGGUUGGGGGACAAGAAAG	103
MAPT-400	25mer sense strand	400-252 (Hs-Mf)	CGGGUUGGGGGACAGGAAAAAUCAG	104
MAPT-443	25mer sense strand	443-295 (Hs-Mf)	CAAGACCAAGAGGGUGACAAGGACG	105
MAPT-688	25mer sense strand	688-453 (Hs-Mf)	GGAAGACGAAGCUGCUGGUAACGTG	106
MAPT-689	25mer sense strand	689-454 (Hs-Mf)	GAAGACGAAGCUGCUGGUCACGUGA	107
MAPT-690	25mer sense strand	690-455 (Hs-Mf)	AAGACGAAGCUGCUGGUCAAGUGAC	108
MAPT-693	25mer sense strand	693-458 (Hs-Mf)	ACGAAGCUGCUGGUCACGUAACCCA	109
MAPT-695	25mer sense strand	695-460 (Hs-Mf)	GAAGCUGCUGGUCACGUGAACCAAG	110

MAPT-696	25mer sense strand	696-461 (Hs-Mf)	AAGCUGCUGGUCACGUGACACAAGA	111
MAPT-1475	25mer sense strand	1475-1552 (Hs-Mf)	CGCAUGGUCAGUAAAAGCAAAGACG	112
MAPT-1476	25mer sense strand	1476-1553 (Hs-Mf)	GCAUGGUCAGUAAAAGCAAAGACGG	113
MAPT-1479	25mer sense strand	1479-1556 (Hs-Mf)	UGGUCAGUAAAAGCAAAGAAGGGAC	114
MAPT-1480	25mer sense strand	1480-1557 (Hs-Mf)	GGUCAGUAAAAGCAAAGACAGGACT	115
MAPT-1481	25mer sense strand	1481-1558 (Hs-Mf)	GUCAGUAAAAGCAAAGACGAGACTG	116
MAPT-1484	25mer sense strand	1484-1561 (Hs-Mf)	AGUAAAAGCAAAGACGGGAAUGGAA	117
MAPT-1485	25mer sense strand	1485-1562 (Hs-Mf)	GUAAAAGCAAAGACGGGACAGGAAG	118
MAPT-1492	25mer sense strand	1492-1569 (Hs-Mf)	CAAAGACGGGACUGGAAGCAAUGAC	119
MAPT-1494	25mer sense strand	1494-1571 (Hs-Mf)	AAGACGGGACUGGAAGCGAAGACAA	120
MAPT-1495	25mer sense strand	1495-1572 (Hs-Mf)	AGACGGGACUGGAAGCGAUAACAAA	121
MAPT-1498	25mer sense strand	1498-1575 (Hs-Mf)	CGGGACUGGAAGCGAUGACAAAAAA	122
MAPT-1499	25mer sense strand	1499-1576 (Hs-Mf)	GGGACUGGAAGCGAUGACAAAAAAG	123
MAPT-1500	25mer sense strand	1500-1577 (Hs-Mf)	GGACUGGAAGCGAUGACAAAAAAGC	124

MAPT-1502	25mer sense strand	1502-1579 (Hs-Mf)	ACUGGAAGCGAUGACAAAAAAGCCA	125
MAPT-1503	25mer sense strand	1503-1580 (Hs-Mf)	CUGGAAGCGAUGACAAAAAAGCCAA	126
MAPT-1504	25mer sense strand	1504-1581 (Hs-Mf)	UGGAAGCGAUGACAAAAAAACCAAG	127
MAPT-1505	25mer sense strand	1505-1582 (Hs-Mf)	GGAAGCGAUGACAAAAAAGACAAGA	128
MAPT-1506	25mer sense strand	1506-1583 (Hs-Mf)	GAAGCGAUGACAAAAAAGCAAAGAC	129
MAPT-1507	25mer sense strand	1507-1584 (Hs-Mf)	AAGCGAUGACAAAAAAGCCAAGACA	130
MAPT-1508	25mer sense strand	1508-1585 (Hs-Mf)	AGCGAUGACAAAAAAGCCAAGACAT	131
MAPT-1509	25mer sense strand	1509-1586 (Hs-Mf)	GCGAUGACAAAAAAGCCAAAACATC	132
MAPT-1733	25mer sense strand	1733 (Hs)	GAUGGUAAAACGAAGAUCGACACAC	133
MAPT-1796	25mer sense strand	1796-1873 (Hs-Mf)	AACGCCACCAGGAUUCCAGAAAAAA	134
MAPT-1835	25mer sense strand	1835-1912 (Hs-Mf)	AAGACACCACCCAGCUCUGAGACTA	135
MAPT-1912	25mer sense strand	1912-1989 (Hs-Mf)	ACCUCCAAAAUCAGGGGAUAGCAGC	136
MAPT-2094	25mer sense strand	2094-2171 (Hs-Mf)	UGCCCAUGCCAGACCUGAAAAAUGT	137
MAPT-2096	25mer sense strand	2096-2173 (Hs-Mf)	CCCAUGCCAGACCUGAAGAAUGUCA	138

MAPT-2097	25mer sense strand	2097-2174 (Hs-Mf)	CCAUGCCAGACCUGAAGAAAGUCAA	139
MAPT-2098	25mer sense strand	2098 (Hs)	CAUGCCAGACCUGAAGAAUAUCAAG	140
MAPT-2105	25mer sense strand	2105 (Hs)	GACCUGAAGAAUGUCAAGUACAAGA	141
MAPT-2106	25mer sense strand	2106 (Hs)	ACCUGAAGAAUGUCAAGUCAAAGAT	142
MAPT-2107	25mer sense strand	2107 (Hs)	CCUGAAGAAUGUCAAGUCCAAGATC	143
MAPT-2108	25mer sense strand	2108 (Hs)	CUGAAGAAUGUCAAGUCCAAGAUCG	144
MAPT-2109	25mer sense strand	2109 (Hs)	UGAAGAAUGUCAAGUCCAAAAUCGG	145
MAPT-2117	25mer sense strand	2117-2194 (Hs-Mf)	GUCAAGUCCAAGAUCGGCUACACTG	146
MAPT-2136	25mer sense strand	2136 (Hs)	CCACUGAGAACCUGAAGCAACAGCC	147
MAPT-2137	25mer sense strand	2137 (Hs)	CACUGAGAACCUGAAGCACAAGCCG	148
MAPT-2269	25mer sense strand	2269-2346 (Hs-Mf)	GCAAAUAGUCUACAAACCAAUUGAC	149
MAPT-2270	25mer sense strand	2270-2347 (Hs-Mf)	CAAAUAGUCUACAAACCAGAUGACC	150
MAPT-2271	25mer sense strand	2271-2348 (Hs-Mf)	AAAUAGUCUACAAACCAGUAGACCT	151
MAPT-2272	25mer sense strand	2272-2349 (Hs-Mf)	AAUAGUCUACAAACCAGUUAACCTG	152

MAPT-2273	25mer sense strand	2273-2350 (Hs-Mf)	AUAGUCUACAAACCAGUUGACCUGA	153
MAPT-2274	25mer sense strand	2274-2351 (Hs-Mf)	UAGUCUACAAACCAGUUGAACUGAG	154
MAPT-2275	25mer sense strand	2275-2352 (Hs-Mf)	AGUCUACAAACCAGUUGACAUGAGC	155
MAPT-2276	25mer sense strand	2276-2353 (Hs-Mf)	GUCUACAAACCAGUUGACCAGAGCA	156
MAPT-2277	25mer sense strand	2277-2354 (Hs-Mf)	UCUACAAACCAGUUGACCUAAGCAA	157
MAPT-2278	25mer sense strand	2278-2355 (Hs-Mf)	CUACAAACCAGUUGACCUGAGCAAG	158
MAPT-2279	25mer sense strand	2279-2356 (Hs-Mf)	UACAAACCAGUUGACCUGAACAAGG	159
MAPT-2280	25mer sense strand	2280-2357 (Hs-Mf)	ACAAACCAGUUGACCUGAGAAAGGT	160
MAPT-2281	25mer sense strand	2281-2358 (Hs-Mf)	CAAACCAGUUGACCUGAGCAAGGTG	161
MAPT-2282	25mer sense strand	2282-2359 (Hs-Mf)	AAACCAGUUGACCUGAGCAAGGUGA	162
MAPT-2283	25mer sense strand	2283-2360 (Hs-Mf)	AACCAGUUGACCUGAGCAAAGUGAC	163
MAPT-2284	25mer sense strand	2284-2361 (Hs-Mf)	ACCAGUUGACCUGAGCAAGAUGACC	164
MAPT-2286	25mer sense strand	2286-2363 (Hs-Mf)	CAGUUGACCUGAGCAAGGUAACCTC	165
MAPT-2288	25mer sense strand	2288-2365 (Hs-Mf)	GUUGACCUGAGCAAGGUGAACUCCA	166

MAPT-2289	25mer sense strand	2289-2366 (Hs-Mf)	UUGACCUGAGCAAGGUGACAUCCAA	167
MAPT-2291	25mer sense strand	2291-2368 (Hs-Mf)	GACCUGAGCAAGGUGACCUACAAGT	168
MAPT-2294	25mer sense strand	2294-2371 (Hs-Mf)	CUGAGCAAGGUGACCUCCAAGUGTG	169
MAPT-2299	25mer sense strand	2299-2376 (Hs-Mf)	CAAGGUGACCUCCAAGUGUAGCUCA	170
MAPT-2300	25mer sense strand	2300-2377 (Hs-Mf)	AAGGUGACCUCCAAGUGUGACUCAT	171
MAPT-2301	25mer sense strand	2301-2378 (Hs-Mf)	AGGUGACCUCCAAGUGUGGAUCATT	172
MAPT-2308	25mer sense strand	2308-2385 (Hs-Mf)	CUCCAAGUGUGGCUCAUUAAGCAAC	173
MAPT-2316	25mer sense strand	2316-2393 (Hs-Mf)	GUGGCUCAUUAGGCAACAUACAUCA	174
MAPT-2317	25mer sense strand	2317-2394 (Hs-Mf)	UGGCUCAUUAGGCAACAUCAAUCAT	175
MAPT-2319	25mer sense strand	2319-2396 (Hs-Mf)	GCUCAUUAGGCAACAUCCAACAUAA	176
MAPT-2320	25mer sense strand	2320-2397 (Hs-Mf)	CUCAUUAGGCAACAUCCAUAAUAAA	177
MAPT-2322	25mer sense strand	2322-2399 (Hs-Mf)	CAUUAGGCAACAUCCAUCAAAAACC	178
MAPT-2323	25mer sense strand	2323-2400 (Hs-Mf)	AUUAGGCAACAUCCAUCAUAAACCA	179
MAPT-2324	25mer sense strand	2324-2401 (Hs-Mf)	UUAGGCAACAUCCAUCAUAAACCAG	180

MAPT-2326	25mer sense strand	2326-2403 (Hs-Mf)	AGGCAACAUCCAUCAUAAAACAGGA	181
MAPT-2330	25mer sense strand	2330-2407 (Hs-Mf)	AACAUCCAUCAUAAACCAGAAGGTG	182
MAPT-2356	25mer sense strand	2356-2433 (Hs-Mf)	CCAGGUGGAAGUAAAAUCUAAGAAG	183
MAPT-2357	25mer sense strand	2357-2434 (Hs-Mf)	CAGGUGGAAGUAAAAUCUGAGAAGC	184
MAPT-2358	25mer sense strand	2358-2435 (Hs-Mf)	AGGUGGAAGUAAAAUCUGAAAAGCT	185
MAPT-2359	25mer sense strand	2359-2436 (Hs-Mf)	GGUGGAAGUAAAAUCUGAGAAGCTT	186
MAPT-2360	25mer sense strand	2360-2437 (Hs-Mf)	GUGGAAGUAAAAUCUGAGAAGCUTG	187
MAPT-2361	25mer sense strand	2361-2438 (Hs-Mf)	UGGAAGUAAAAUCUGAGAAACUUGA	188
MAPT-2362	25mer sense strand	2362-2439 (Hs-Mf)	GGAAGUAAAAUCUGAGAAGAUUGAC	189
MAPT-2363	25mer sense strand	2363-2440 (Hs-Mf)	GAAGUAAAAUCUGAGAAGCAUGACT	190
MAPT-2364	25mer sense strand	2364-2441 (Hs-Mf)	AAGUAAAAUCUGAGAAGCUAGACTT	191
MAPT-2365	25mer sense strand	2365 (Hs)	AGUAAAAUCUGAGAAGCUUAACUTC	192
MAPT-2372	25mer sense strand	2372 (Hs)	UCUGAGAAGCUUGACUUCAAGGACA	193
MAPT-2373	25mer sense strand	2373 (Hs)	CUGAGAAGCUUGACUUCAAAGACAG	194

MAPT-2374	25mer sense strand	2374 (Hs)	UGAGAAGCUUGACUUCAAGAACAGA	195
MAPT-2375	25mer sense strand	2375 (Hs)	GAGAAGCUUGACUUCAAGGACAGAG	196
MAPT-2376	25mer sense strand	2376 (Hs)	AGAAGCUUGACUUCAAGGAAAGAGT	197
MAPT-2377	25mer sense strand	2377 (Hs)	GAAGCUUGACUUCAAGGACAGAGTC	198
MAPT-2378	25mer sense strand	2378 (Hs)	AAGCUUGACUUCAAGGACAAAGUCC	199
MAPT-2379	25mer sense strand	2379 (Hs)	AGCUUGACUUCAAGGACAGAGUCCA	200
MAPT-2380	25mer sense strand	2380 (Hs)	GCUUGACUUCAAGGACAGAAUCCAG	201
MAPT-2381	25mer sense strand	2381 (Hs)	CUUGACUUCAAGGACAGAGACCAGT	202
MAPT-2382	25mer sense strand	2382 (Hs)	UUGACUUCAAGGACAGAGUACAGTC	203
MAPT-2390	25mer sense strand	2390 (Hs)	AAGGACAGAGUCCAGUCGAAGAUTG	204
MAPT-2391	25mer sense strand	2391 (Hs)	AGGACAGAGUCCAGUCGAAAAUUGG	205
MAPT-2414	25mer sense strand	2414-2491 (Hs-Mf)	GGGUCCCUGGACAAUAUCAACCACG	206
MAPT-2448	25mer sense strand	2448-2525 (Hs-Mf)	GAGGAAAUAAAAAGAUUGAAACCCA	207
MAPT-2449	25mer sense strand	2449-2526 (Hs-Mf)	AGGAAAUAAAAAGAUUGAAACCCAC	208

MAPT-2450	25mer sense strand	2450-2527 (Hs-Mf)	GGAAAUAAAAAGAUUGAAAACCACA	209
MAPT-2451	25mer sense strand	2451-2528 (Hs-Mf)	GAAAUAAAAAGAUUGAAACACACAA	210
MAPT-2452	25mer sense strand	2452-2529 (Hs-Mf)	AAAUAAAAAGAUUGAAACCAACAAG	211
MAPT-2453	25mer sense strand	2453-2530 (Hs-Mf)	AAUAAAAAGAUUGAAACCCACAAGC	212
MAPT-2454	25mer sense strand	2454-2531 (Hs-Mf)	AUAAAAAGAUUGAAACCCAAAAGCT	213
MAPT-2456	25mer sense strand	2456-2533 (Hs-Mf)	AAAAAGAUUGAAACCCACAAGCUGA	214
MAPT-2457	25mer sense strand	2457-2534 (Hs-Mf)	AAAAGAUUGAAACCCACAAACUGAC	215
MAPT-2567	25mer sense strand	2567 (Hs)	CGGCAUCUCAGCAAUGUCUACUCCA	216
MAPT-2598	25mer sense strand	2598-2675 (Hs-Mf)	GCAUCGACAUGGUAGACUCACCCCA	217
MAPT-2657	25mer sense strand	2657-2734 (Hs-Mf)	CUGGCCAAGCAGGGUUUGUAAUCAG	218
MAPT-2723	25mer sense strand	2723-2800 (Hs-Mf)	AGAGUGUGGAAAAAAAAAGAAUAAT	219
MAPT-2724	25mer sense strand	2724-2801 (Hs-Mf)	GAGUGUGGAAAAAAAAAGAAUAATG	220
MAPT-2726	25mer sense strand	2726-2803 (Hs-Mf)	GUGUGGAAAAAAAAAGAAUAAUGAC	221
MAPT-2784	25mer sense strand	2784-2860-1 mismatch (Hs-Mf)	GCAGUUCGGUUAAUUGGUUAAUCAC	222

MAPT-2963	25mer sense strand	2963-3039 (Hs-Mf)	GGCAAUUCCUUUUGAUUCUAUUUTC	223
MAPT-3110	25mer sense strand	3110-3186 (Hs-Mf)	AGCAACAAAGGAUUUGAAAAUUGGT	224
MAPT-3114	25mer sense strand	3114-3190 (Hs-Mf)	ACAAAGGAUUUGAAACUUGAUGUGT	225
MAPT-3116	25mer sense strand	3116-3192 (Hs-Mf)	AAAGGAUUUGAAACUUGGUAUGUTC	226
MAPT-3118	25mer sense strand	3118-3194 (Hs-Mf)	AGGAUUUGAAACUUGGUGUAUUCGT	227
MAPT-3158	25mer sense strand	3158-3234 (Hs-Mf)	CGAUGUCAACCUUGUGUGAAUGUGA	228
MAPT-3503	25mer sense strand	3503-3576 (Hs-Mf)	AAAGACUGACCUUGAUGUCAUGAGA	229
MAPT-3589	25mer sense strand	3589-3661 (Hs-Mf)	CUCCACAGAAACCCUGUUUAAUUGA	230
MAPT-3591	25mer sense strand	3591-3663 (Hs-Mf)	CCACAGAAACCCUGUUUUAAUGAGT	231
MAPT-3592	25mer sense strand	3592-3664 (Hs-Mf)	CACAGAAACCCUGUUUUAUAGAGTT	232
MAPT-3593	25mer sense strand	3593-3665 (Hs-Mf)	ACAGAAACCCUGUUUUAUUAAGUTC	233
MAPT-3594	25mer sense strand	3594-3666 (Hs-Mf)	CAGAAACCCUGUUUUAUUGAGUUCT	234
MAPT-3595	25mer sense strand	3595-3667 (Hs-Mf)	AGAAACCCUGUUUUAUUGAAUUCTG	235
MAPT-3596	25mer sense strand	3596-3668 (Hs-Mf)	GAAACCCUGUUUUAUUGAGAUCUGA	236

MAPT-3597	25mer sense strand	3597-3669 (Hs-Mf)	AAACCCUGUUUUAUUGAGUACUGAA	237
MAPT-3598	25mer sense strand	3598-3670 (Hs-Mf)	AACCCUGUUUUAUUGAGUUAUGAAG	238
MAPT-3599	25mer sense strand	3599-3671 (Hs-Mf)	ACCCUGUUUUAUUGAGUUCAGAAGG	239
MAPT-3600	25mer sense strand	3600-3672 (Hs-Mf)	CCCUGUUUUAUUGAGUUCUAAAGGT	240
MAPT-3601	25mer sense strand	3601-3673 (Hs-Mf)	CCUGUUUUAUUGAGUUCUGAAGGTT	241
MAPT-3602	25mer sense strand	3602-3674 (Hs-Mf)	CUGUUUUAUUGAGUUCUGAAGGUTG	242
MAPT-3603	25mer sense strand	3603-3675 (Hs-Mf)	UGUUUUAUUGAGUUCUGAAAGUUGG	243
MAPT-3605	25mer sense strand	3605-3677 (Hs-Mf)	UUUUAUUGAGUUCUGAAGGAUGGAA	244
MAPT-3607	25mer sense strand	3607-3679 (Hs-Mf)	UUAUUGAGUUCUGAAGGUUAGAACT	245
MAPT-3609	25mer sense strand	3609-3681 (Hs-Mf)	AUUGAGUUCUGAAGGUUGGAACUGC	246
MAPT-3610	25mer sense strand	3610-3682 (Hs-Mf)	UUGAGUUCUGAAGGUUGGAACUGCT	247
MAPT-3677	25mer sense strand	3677-3749 (Hs-Mf)	AACCAGUUCUCUUUGUAAGAACUTG	248
MAPT-3678	25mer sense strand	3678-3750 (Hs-Mf)	ACCAGUUCUCUUUGUAAGGACUUGT	249
MAPT-3679	25mer sense strand	3679-3751 (Hs-Mf)	CCAGUUCUCUUUGUAAGGAAUUGTG	250

MAPT-3680	25mer sense strand	3680-3752 (Hs-Mf)	CAGUUCUCUUUGUAAGGACAUGUGC	251
MAPT-3958	25mer sense strand	3958-4030 (Hs-Mf)	CUACUCCAUACUGAGGGUGAAAUTA	252
MAPT-3959	25mer sense strand	3959-4031 (Hs-Mf)	UACUCCAUACUGAGGGUGAAAUUAA	253
MAPT-3960	25mer sense strand	3960-4032 (Hs-Mf)	ACUCCAUACUGAGGGUGAAAUUAAG	254
MAPT-3961	25mer sense strand	3961-4033 (Hs-Mf)	CUCCAUACUGAGGGUGAAAAUAAGG	255
MAPT-3965	25mer sense strand	3965-4037 (Hs-Mf)	AUACUGAGGGUGAAAUUAAAGGAAG	256
MAPT-3970	25mer sense strand	3970-4042 (Hs-Mf)	GAGGGUGAAAUUAAGGGAAAGCAAA	257
MAPT-4146	25mer sense strand	4146-4218 (Hs-Mf)	GGUGUUUCUGCCUUGUUGAAAUGGA	258
MAPT-4474	25mer sense strand	4474-4545 (Hs-Mf)	CUGGAGCAGCUGAACAUAUACAUAG	259
MAPT-4475	25mer sense strand	4475-4546 (Hs-Mf)	UGGAGCAGCUGAACAUAUAAAUAGA	260
MAPT-4477	25mer sense strand	4477-4548 (Hs-Mf)	GAGCAGCUGAACAUAUACAAAGATG	261
MAPT-4478	25mer sense strand	4478-4549 (Hs-Mf)	AGCAGCUGAACAUAUACAUAGAUGT	262
MAPT-4479	25mer sense strand	4479-4550 (Hs-Mf)	GCAGCUGAACAUAUACAUAAAUGTT	263
MAPT-4480	25mer sense strand	4480-4551 (Hs-Mf)	CAGCUGAACAUAUACAUAGAUGUTG	264

MAPT-4481	25mer sense strand	4481-4552 (Hs-Mf)	AGCUGAACAUAUACAUAGAAGUUGC	265
MAPT-4482	25mer sense strand	4482-4553 (Hs-Mf)	GCUGAACAUAUACAUAGAUAUUGCC	266
MAPT-4485	25mer sense strand	4485-4556 (Hs-Mf)	GAACAUAUACAUAGAUGUUACCCTG	267
MAPT-4486	25mer sense strand	4486-4557 (Hs-Mf)	AACAUAUACAUAGAUGUUGACCUGC	268
MAPT-4532	25mer sense strand	4532 (Hs)	GAGUUGUAGUUGGAUUUGUAUGUTT	269
MAPT-4533	25mer sense strand	4533 (Hs)	AGUUGUAGUUGGAUUUGUCAGUUTA	270
MAPT-4539	25mer sense strand	4539-4610 (Hs-Mf)	AGUUGGAUUUGUCUGUUUAAGCUTG	271
MAPT-4540	25mer sense strand	4540-4611 (Hs-Mf)	GUUGGAUUUGUCUGUUUAUACUUGG	272
MAPT-4541	25mer sense strand	4541-4612 (Hs-Mf)	UUGGAUUUGUCUGUUUAUGAUUGGA	273
MAPT-4543	25mer sense strand	4543-4614 (Hs-Mf)	GGAUUUGUCUGUUUAUGCUAGGATT	274
MAPT-4544	25mer sense strand	4544-4615 (Hs-Mf)	GAUUUGUCUGUUUAUGCUUAGAUTC	275
MAPT-4545	25mer sense strand	4545-4616 (Hs-Mf)	AUUUGUCUGUUUAUGCUUGAAUUCA	276
MAPT-4546	25mer sense strand	4546-4617 (Hs-Mf)	UUUGUCUGUUUAUGCUUGGAUUCAC	277
MAPT-4547	25mer sense strand	4547-4618 (Hs-Mf)	UUGUCUGUUUAUGCUUGGAAUCACC	278

MAPT-4548	25mer sense strand	4548-4619 (Hs-Mf)	UGUCUGUUUAUGCUUGGAUACACCA	279
MAPT-4549	25mer sense strand	4549-4620 (Hs-Mf)	GUCUGUUUAUGCUUGGAUUAACCAG	280
MAPT-4550	25mer sense strand	4550-4621 (Hs-Mf)	UCUGUUUAUGCUUGGAUUCACCAGA	281
MAPT-4551	25mer sense strand	4551-4622 (Hs-Mf)	CUGUUUAUGCUUGGAUUCAACAGAG	282
MAPT-4552	25mer sense strand	4552-4623 (Hs-Mf)	UGUUUAUGCUUGGAUUCACAAGAGT	283
MAPT-4554	25mer sense strand	4554-4625 (Hs-Mf)	UUUAUGCUUGGAUUCACCAAAGUGA	284
MAPT-4556	25mer sense strand	4556-4627 (Hs-Mf)	UAUGCUUGGAUUCACCAGAAUGACT	285
MAPT-4557	25mer sense strand	4557-4628 (Hs-Mf)	AUGCUUGGAUUCACCAGAGAGACTA	286
MAPT-4558	25mer sense strand	4558-4629 (Hs-Mf)	UGCUUGGAUUCACCAGAGUAACUAT	287
MAPT-4559	25mer sense strand	4559-4630 (Hs-Mf)	GCUUGGAUUCACCAGAGUGACUATG	288
MAPT-4560	25mer sense strand	4560-4631 (Hs-Mf)	CUUGGAUUCACCAGAGUGAAUAUGA	289
MAPT-4561	25mer sense strand	4561-4632 (Hs-Mf)	UUGGAUUCACCAGAGUGACAAUGAT	290
MAPT-4562	25mer sense strand	4562-4633 (Hs-Mf)	UGGAUUCACCAGAGUGACUAUGATA	291
MAPT-4563	25mer sense strand	4563-4634 (Hs-Mf)	GGAUUCACCAGAGUGACUAAGAUAG	292

MAPT-4564	25mer sense strand	4564-4635 (Hs-Mf)	GAUUCACCAGAGUGACUAUAAUAGT	293
MAPT-4615	25mer sense strand	4615-4687 (Hs-Mf)	ACGCAUGUAUCUUGAAAUGAUUGTA	294
MAPT-4616	25mer sense strand	4616-4688 (Hs-Mf)	CGCAUGUAUCUUGAAAUGCAUGUAA	295
MAPT-4617	25mer sense strand	4617-4689 (Hs-Mf)	GCAUGUAUCUUGAAAUGCUAGUAAA	296
MAPT-4618	25mer sense strand	4618-4690 (Hs-Mf)	CAUGUAUCUUGAAAUGCUUAUAAAG	297
MAPT-4619	25mer sense strand	4619-4691 (Hs-Mf)	AUGUAUCUUGAAAUGCUUGAAAAGA	298
MAPT-4620	25mer sense strand	4620-4692 (Hs-Mf)	UGUAUCUUGAAAUGCUUGUAAAGAG	299
MAPT-4621	25mer sense strand	4621-4693 (Hs-Mf)	GUAUCUUGAAAUGCUUGUAAAGAGG	300
MAPT-4622	25mer sense strand	4622-4694 (Hs-Mf)	UAUCUUGAAAUGCUUGUAAAGAGGT	301
MAPT-4623	25mer sense strand	4623-4695 (Hs-Mf)	AUCUUGAAAUGCUUGUAAAAAGGTT	302
MAPT-4625	25mer sense strand	4625-4697 (Hs-Mf)	CUUGAAAUGCUUGUAAAGAAGUUTC	303
MAPT-4627	25mer sense strand	4627-4699 (Hs-Mf)	UGAAAUGCUUGUAAAGAGGAUUCTA	304
MAPT-4628	25mer sense strand	4628-4700 (Hs-Mf)	GAAAUGCUUGUAAAGAGGUAUCUAA	305
MAPT-4629	25mer sense strand	4629-4701 (Hs-Mf)	AAAUGCUUGUAAAGAGGUUACUAAC	306

MAPT-4630	25mer sense strand	4630-4702 (Hs-Mf)	AAUGCUUGUAAAGAGGUUUAUAACC	307
MAPT-4632	25mer sense strand	4632-4704 (Hs-Mf)	UGCUUGUAAAGAGGUUUCUAACCCA	308
MAPT-4633	25mer sense strand	4633-4705 (Hs-Mf)	GCUUGUAAAGAGGUUUCUAACCCAC	309
MAPT-4825	25mer sense strand	4825-4897 (Hs-Mf)	ACAGGAUUAGGACUGAAGCAAUGAT	310
MAPT-4828	25mer sense strand	4828-4900 (Hs-Mf)	GGAUUAGGACUGAAGCGAUAAUGTC	311
MAPT-5682	25mer sense strand	5682-5743 (Hs-Mf)	GAAGUUCUUGUGCCCUGCUAUUCAG	312
MAPT-5958	25mer sense strand	5958 (Hs)	AAGCUGCUGACUCACUUUAACAATA	313
MAPT-5959	25mer sense strand	5959 (Hs)	AGCUGCUGACUCACUUUAUAAAUAG	314
MAPT-5961	25mer sense strand	5961 (Hs)	CUGCUGACUCACUUUAUCAAUAGTT	315
MAPT-5963	25mer sense strand	5963 (Hs)	GCUGACUCACUUUAUCAAUAGUUCC	316
MAPT-5964	25mer sense strand	5964 (Hs)	CUGACUCACUUUAUCAAUAAUUCCA	317
MAPT-5965	25mer sense strand	5965 (Hs)	UGACUCACUUUAUCAAUAGUUCCAU	318
MAPT-5966	25mer sense strand	5966-6021 (Hs-Mf)	GACUCACUUUAUCAAUAGUACCATT	319
MAPT-5967	25mer sense strand	5967-6022 (Hs-Mf)	ACUCACUUUAUCAAUAGUUACAUTT	320

MAPT-5968	25mer sense strand	5968-6023 (Hs-Mf)	CUCACUUUAUCAAUAGUUCAAUUTA	321
MAPT-6006	25mer sense strand	6006-6061 (Hs-Mf)	GGUGAGACUGUAUCCUGUUAGCUAT	322
MAPT-6007	25mer sense strand	6007-6062 (Hs-Mf)	GUGAGACUGUAUCCUGUUUACUATT	323
MAPT-6008	25mer sense strand	6008-6063 (Hs-Mf)	UGAGACUGUAUCCUGUUUGAUAUTG	324
MAPT-6009	25mer sense strand	6009-6064 (Hs-Mf)	GAGACUGUAUCCUGUUUGCAAUUGC	325
MAPT-6010	25mer sense strand	6010-6065 (Hs-Mf)	AGACUGUAUCCUGUUUGCUAUUGCT	326
MAPT-6011	25mer sense strand	6011-6066 (Hs-Mf)	GACUGUAUCCUGUUUGCUAAUGCTT	327
MAPT-6012	25mer sense strand	6012-6067 (Hs-Mf)	ACUGUAUCCUGUUUGCUAUAGCUTG	328
MAPT-6013	25mer sense strand	6013-6068 (Hs-Mf)	CUGUAUCCUGUUUGCUAUUACUUGT	329
MAPT-6014	25mer sense strand	6014-6069 (Hs-Mf)	UGUAUCCUGUUUGCUAUUGAUUGTT	330
MAPT-6015	25mer sense strand	6015-6070 (Hs-Mf)	GUAUCCUGUUUGCUAUUGCAUGUTG	331
MAPT-6017	25mer sense strand	6017-6072 (Hs-Mf)	AUCCUGUUUGCUAUUGCUUAUUGTG	332
MAPT-6119	25mer sense strand	6119-6174 (Hs-Mf)	GCCUCGUAACCCUUUUCAUAAUUTC	333
MAPT-6628	25mer sense strand	6628-6689 (Hs-Mf)	GAGUUUGCCAUGUUGAGCAAGACTA	334

MAPT-6629	25mer sense strand	6629-6690 (Hs-Mf)	AGUUUGCCAUGUUGAGCAGAACUAT	335
MAPT-6631	25mer sense strand	6631-6692 (Hs-Mf)	UUUGCCAUGUUGAGCAGGAAUAUTT	336
MAPT-6672	25mer sense strand	6672-6733 (Hs-Mf)	CCAUGAUUUCUUCGGUAAUACUGAG	337
MAPT-6731	25mer sense strand	6731 (Hs)	GCUUUCUGUCUGUGAAUGUAUAUAT	338
MAPT-6732	25mer sense strand	6732 (Hs)	CUUUCUGUCUGUGAAUGUCAAUATA	339
MAPT-6738	25mer sense strand	6738-6799 (Hs-Mf)	GUCUGUGAAUGUCUAUAUAAUGUAT	340
MAPT-6739	25mer sense strand	6739-6800 (Hs-Mf)	UCUGUGAAUGUCUAUAUAGAGUATT	341
MAPT-6740	25mer sense strand	6740-6801 (Hs-Mf)	CUGUGAAUGUCUAUAUAGUAUAUTG	342
MAPT-6741	25mer sense strand	6741-6802 (Hs-Mf)	UGUGAAUGUCUAUAUAGUGAAUUGT	343
MAPT-6742	25mer sense strand	6742-6803 (Hs-Mf)	GUGAAUGUCUAUAUAGUGUAUUGTG	344
MAPT-6743	25mer sense strand	6743-6804 (Hs-Mf)	UGAAUGUCUAUAUAGUGUAAUGUGT	345
MAPT-6745	25mer sense strand	6745-6806 (Hs-Mf)	AAUGUCUAUAUAGUGUAUUAUGUGT	346
MAPT-6748	25mer sense strand	6748-6809 (Hs-Mf)	GUCUAUAUAGUGUAUUGUGAGUUTT	347
MAPT-6749	25mer sense strand	6749-6810 (Hs-Mf)	UCUAUAUAGUGUAUUGUGUAUUUTA	348

MAPT-6750	25mer sense strand	6750-6811 (Hs-Mf)	CUAUAUAGUGUAUUGUGUGAUUUAA	349
MAPT-6751	25mer sense strand	6751-6812 (Hs-Mf)	UAUAUAGUGUAUUGUGUGUAUUAAC	350
MAPT-6752	25mer sense strand	6752-6813 (Hs-Mf)	AUAUAGUGUAUUGUGUGUUAUAACA	351
MAPT-6753	25mer sense strand	6753-6814 (Hs-Mf)	UAUAGUGUAUUGUGUGUUUAAACAA	352
MAPT-6754	25mer sense strand	6754-6815 (Hs-Mf)	AUAGUGUAUUGUGUGUUUUAACAAA	353
MAPT-6755	25mer sense strand	6755-6816 (Hs-Mf)	UAGUGUAUUGUGUGUUUUAACAAAT	354
MAPT-6756	25mer sense strand	6756-6817 (Hs-Mf)	AGUGUAUUGUGUGUUUUAAAAAATG	355
MAPT-6757	25mer sense strand	6757-6818 (Hs-Mf)	GUGUAUUGUGUGUUUUAACAAAUGA	356
MAPT-6758	25mer sense strand	6758-6819 (Hs-Mf)	UGUAUUGUGUGUUUUAACAAAUGAT	357
MAPT-6759	25mer sense strand	6759-6820 (Hs-Mf)	GUAUUGUGUGUUUUAACAAAUGATT	358
MAPT-6760	25mer sense strand	6760-6821 (Hs-Mf)	UAUUGUGUGUUUUAACAAAAGAUTT	359
MAPT-6761	25mer sense strand	6761-6822 (Hs-Mf)	AUUGUGUGUUUUAACAAAUAAUUTA	360
MAPT-6762	25mer sense strand	6762-6823 (Hs-Mf)	UUGUGUGUUUUAACAAAUGAUUUAC	361
MAPT-6763	25mer sense strand	6763-6824 (Hs-Mf)	UGUGUGUUUUAACAAAUGAAUUACA	362

MAPT-6764	25mer sense strand	6764-6825 (Hs-Mf)	GUGUGUUUUAACAAAUGAUAUACAC	363
MAPT-6765	25mer sense strand	6765-6826 (Hs-Mf)	UGUGUUUUAACAAAUGAUUAACACT	364
MAPT-6766	25mer sense strand	6766-6827 (Hs-Mf)	GUGUUUUAACAAAUGAUUUACACTG	365
MAPT-6767	25mer sense strand	6767-6828 (Hs-Mf)	UGUUUUAACAAAUGAUUUAAACUGA	366
MAPT-6768	25mer sense strand	6768-6829 (Hs-Mf)	GUUUUAACAAAUGAUUUACACUGAC	367
MAPT-6769	25mer sense strand	6769-6830 (Hs-Mf)	UUUUAACAAAUGAUUUACAAUGACT	368
MAPT-6772	25mer sense strand	6772-6833 (Hs-Mf)	UAACAAAUGAUUUACACUGACUGTT	369
MAPT-6773	25mer sense strand	6773-6834 (Hs-Mf)	AACAAAUGAUUUACACUGAAUGUTG	370
MAPT-6774	25mer sense strand	6774-6835 (Hs-Mf)	ACAAAUGAUUUACACUGACAGUUGC	371
MAPT-6775	25mer sense strand	6775-6836 (Hs-Mf)	CAAAUGAUUUACACUGACUAUUGCT	372
MAPT-6777	25mer sense strand	6777-6838 (Hs-Mf)	AAUGAUUUACACUGACUGUAGCUGT	373
MAPT-6778	25mer sense strand	6778-6839 (Hs-Mf)	AUGAUUUACACUGACUGUUACUGTA	374
MAPT-6779	25mer sense strand	6779-6840 (Hs-Mf)	UGAUUUACACUGACUGUUGAUGUAA	375
MAPT-6780	25mer sense strand	6780-6841 (Hs-Mf)	GAUUUACACUGACUGUUGCAGUAAA	376

MAPT-6781	25mer sense strand	6781 (Hs)	AUUUACACUGACUGUUGCUAUAAAA	377
MAPT-6789	25mer sense strand	6789 (Hs)	UGACUGUUGCUGUAAAAGUAAAUTT	378
MAPT-6792	25mer sense strand	6792 (Hs)	CUGUUGCUGUAAAAGUGAAAUUGGA	379
MAPT-6793	25mer sense strand	6793 (Hs)	UGUUGCUGUAAAAGUGAAUAUGGAA	380
MAPT-6795	25mer sense strand	6795 (Hs)	UUGCUGUAAAAGUGAAUUUAGAAAT	381
MAPT-6796	25mer sense strand	6796 (Hs)	UGCUGUAAAAGUGAAUUUGAAAATA	382
MAPT-6797	25mer sense strand	6797 (Hs)	GCUGUAAAAGUGAAUUUGGAAAUAA	383
MAPT-6798	25mer sense strand	6798 (Hs)	CUGUAAAAGUGAAUUUGGAAAUAAA	384
MAPT-2141	27 mer antisense strand	2141-2218-966 (Hs-Mf-Mm)	CUCCCUGCUGGUGCUUCAGGUUCUCAG	385
MAPT-2142	27 mer antisense strand	2142-2219-967 (Hs-Mf-Mm)	CCUCCUGGCUGGUGCUUCAGGUUCUCA	386
MAPT-2303	27 mer antisense strand	2303-2380-1128 (Hs-Mf-Mm)	CUAAUUAGCCACACUUGGAGGUCACCU	387
MAPT-2347	27 mer antisense strand	2347-2424-1172 (Hs-Mf-Mm)	UUUUAUUUCCACCUGGCCACCUCCUGG	388
MAPT-2349	27 mer antisense strand	2349-2426-1174 (Hs-Mf-Mm)	GAUUUUACUUCCACCUGGCCACCUCCU	389
MAPT-2350	27 mer antisense strand	2350-2427-1175 (Hs-Mf-Mm)	AGAUUUUACUUCCACCUGGCCACCUCC	390

MAPT-2351	27 mer antisense strand	2351-2428-1176 (Hs-Mf-Mm)	CAGAUUUUACUUCCACCUGGCCACCUC	391
MAPT-2352	27 mer antisense strand	2352-2429-1177 (Hs-Mf-Mm)	UCAGAUUUUACUUCCACCUGGCCACCU	392
MAPT-2353	27 mer antisense strand	2353-2430-1178 (Hs-Mf-Mm)	CUCAGUUUUUACUUCCACCUGGCCACC	393
MAPT-2354	27 mer antisense strand	2354-2431-1179 (Hs-Mf-Mm)	UCUCAUAUUUUACUUCCACCUGGCCAC	394
MAPT-2355	27 mer antisense strand	2355-2432-1180 (Hs-Mf-Mm)	UUCUCUGAUUUUACUUCCACCUGGCCA	395
MAPT-2459	27 mer antisense strand	2459-2536-1284 (Hs-Mf-Mm)	AGGUCUGCUUGUGGGUUUCAAUCUUUU	396
MAPT-2460	27 mer antisense strand	2460-2537-1285 (Hs-Mf-Mm)	AAGGUUAGCUUGUGGGUUUCAAUCUUU	397
MAPT-2461	27 mer antisense strand	2461-2538-1286 (Hs-Mf-Mm)	GAAGGUCAGCUUGUGGGUUUCAAUCUU	398
MAPT-2462	27 mer antisense strand	2462-2539-1287 (Hs-Mf-Mm)	GGAAGUUCAGCUUGUGGGUUUCAAUCU	399
MAPT-2463	27 mer antisense strand	2463-2540-1288 (Hs-Mf-Mm)	CGGAAUGUCAGCUUGUGGGUUUCAAUC	400
MAPT-2464	27 mer antisense strand	2464-2541-1289 (Hs-Mf-Mm)	GCGGAUGGUCAGCUUGUGGGUUUCAAU	401
MAPT-2465	27 mer antisense strand	2465-2542-1290 (Hs-Mf-Mm)	CGCGGUAGGUCAGCUUGUGGGUUUCAA	402
MAPT-2466	27 mer antisense strand	2466-2543-1291 (Hs-Mf-Mm)	UCGCGUAAGGUCAGCUUGUGGGUUUCA	403
MAPT-2467	27 mer antisense strand	2467-2544-1292 (Hs-Mf-Mm)	CUCGCUGAAGGUCAGCUUGUGGGUUUC	404

MAPT-2495	27 mer antisense strand	2495-2572-1320 (Hs-Mf-Mm)	CCCCGUGGUCUGUCUUGGCUUUGGCGU	405
MAPT-2496	27 mer antisense strand	2496-2573-1321 (Hs-Mf-Mm)	GCCCCUUGGUCUGUCUUGGCUUUGGCG	406
MAPT-3686	27 mer antisense strand	3686-3758-2505 (Hs-Mf-Mm)	CAAGAUGCACAAGUCCUUACAAAGAGA	407
MAPT-3687	27 mer antisense strand	3687-3759-2506 (Hs-Mf-Mm)	CCAAGUGGCACAAGUCCUUACAAAGAG	408
MAPT-3688	27 mer antisense strand	3688-3760-2507 (Hs-Mf-Mm)	CCCAAUAGGCACAAGUCCUUACAAAGA	409
MAPT-3691	27 mer antisense strand	3691-3763-2510 (Hs-Mf-Mm)	UCUCCUAAGAGGCACAAGUCCUUACAA	410
MAPT-3692	27 mer antisense strand	3692-3764-2511 (Hs-Mf-Mm)	GUCUCUCAAGAGGCACAAGUCCUUACA	411
MAPT-3693	27 mer antisense strand	3693-3765-2512 (Hs-Mf-Mm)	CGUCUUCCAAGAGGCACAAGUCCUUAC	412
MAPT-4534	27 mer antisense strand	4534-4605-3332 (Hs-Mf-Mm)	AUAAAUAGACAAAUCCAACUACAACUC	413
MAPT-4535	27 mer antisense strand	4535-4606-3333 (Hs-Mf-Mm)	CAUAAUCAGACAAAUCCAACUACAACU	414
MAPT-4536	27 mer antisense strand	4536-4607-3334 (Hs-Mf-Mm)	GCAUAUACAGACAAAUCCAACUACAAC	415
MAPT-4537	27 mer antisense strand	4537-4608-3335 (Hs-Mf-Mm)	AGCAUUAACAGACAAAUCCAACUACAA	416
MAPT-4538	27 mer antisense strand	4538-4609-3336 (Hs-Mf-Mm)	AAGCAUAAACAGACAAAUCCAACUACA	417
MAPT-4566	27 mer antisense strand	4566-4637-3362 (Hs-Mf-Mm)	UCACUUUCAUAGUCACUCUGGUGAAUC	418

MAPT-4567	27 mer antisense strand	4567-4638-3363 (Hs-Mf-Mm)	UUCACUAUCAUAGUCACUCUGGUGAAU	419
MAPT-4568	27 mer antisense strand	4568-4639-3364 (Hs-Mf-Mm)	UUUCAUUAUCAUAGUCACUCUGGUGAA	420
MAPT-4569	27 mer antisense strand	4569-4640-3365 (Hs-Mf-Mm)	UUUUCUCUAUCAUAGUCACUCUGGUGA	421
MAPT-4570	27 mer antisense strand	4570-4641-3366 (Hs-Mf-Mm)	CUUUUUACUAUCAUAGUCACUCUGGUG	422
MAPT-4571	27 mer antisense strand	4571-4642-3367 (Hs-Mf-Mm)	UCUUUUCACUAUCAUAGUCACUCUGGU	423
MAPT-4572	27 mer antisense strand	4572-4643-3368 (Hs-Mf-Mm)	UUCUUUUCACUAUCAUAGUCACUCUGG	424
MAPT-4573	27 mer antisense strand	4573-4644-3369 (Hs-Mf-Mm)	UUUCUUUUCACUAUCAUAGUCACUCUG	425
MAPT-4574	27 mer antisense strand	4574-4645-3370 (Hs-Mf-Mm)	UUUUCUUUUCACUAUCAUAGUCACUCU	426
MAPT-4575	27 mer antisense strand	4575-4646-3371 (Hs-Mf-Mm)	UUUUUUUUUUCACUAUCAUAGUCACUC	427
MAPT-4576	27 mer antisense strand	4576-4647-3372 (Hs-Mf-Mm)	UUUUUUCUUUUCACUAUCAUAGUCACU	428
MAPT-4577	27 mer antisense strand	4577-4648-3373 (Hs-Mf-Mm)	UUUUUUUCUUUUCACUAUCAUAGUCAC	429
MAPT-4578	27 mer antisense strand	4578-4649-3374 (Hs-Mf-Mm)	UUUUUUUUCUUUUCACUAUCAUAGUCA	430
MAPT-4579	27 mer antisense strand	4579-4650-3375 (Hs-Mf-Mm)	UUUUUUUUUCUUUUCACUAUCAUAGUC	431
MAPT-4580	27 mer antisense strand	4580-4651-3376 (Hs-Mf-Mm)	UUUUUUUUUUCUUUUCACUAUCAUAGU	432

MAPT-4605	27 mer antisense strand	4605-4677-3439 (Hs-Mf-Mm)	UCAAGUUACAUGCGUCCUUUUUUUUU	433
MAPT-4606	27 mer antisense strand	4606-4678-3440 (Hs-Mf-Mm)	UUCAAUAUACAUGCGUCCUUUUUUUUU	434
MAPT-4607	27 mer antisense strand	4607-4679-3441 (Hs-Mf-Mm)	UUUCAUGAUACAUGCGUCCUUUUUUUU	435
MAPT-4608	27 mer antisense strand	4608-4680-3442 (Hs-Mf-Mm)	AUUUCUAGAUACAUGCGUCCUUUUUUU	436
MAPT-4609	27 mer antisense strand	4609-4681-3443 (Hs-Mf-Mm)	CAUUUUAAGAUACAUGCGUCCUUUUUU	437
MAPT-4610	27 mer antisense strand	4610-4682-3444 (Hs-Mf-Mm)	GCAUUUCAAGAUACAUGCGUCCUUUUU	438
MAPT-4611	27 mer antisense strand	4611-4683-3445 (Hs-Mf-Mm)	AGCAUUUCAAGAUACAUGCGUCCUUUU	439
MAPT-4612	27 mer antisense strand	4612-4684-3446 (Hs-Mf-Mm)	AAGCAUUUCAAGAUACAUGCGUCCUUU	440
MAPT-4613	27 mer antisense strand	4613-4685-3447 (Hs-Mf-Mm)	CAAGCUUUUCAAGAUACAUGCGUCCUU	441
MAPT-4614	27 mer antisense strand	4614-4686-3448 (Hs-Mf-Mm)	ACAAGUAUUUCAAGAUACAUGCGUCCU	442
MAPT-5969	27 mer antisense strand	5969-6024-4540 (Hs-Mf-Mm)	UUAAAUGGAACUAUUGAUAAAGUGAGU	443
MAPT-5970	27 mer antisense strand	5970-6025-4541 (Hs-Mf-Mm)	UUUAAUUGGAACUAUUGAUAAAGUGAG	444
MAPT-5971	27 mer antisense strand	5971-6026-4542 (Hs-Mf-Mm)	AUUUAUAUGGAACUAUUGAUAAAGUGA	445
MAPT-5972	27 mer antisense strand	5972-6027-4543 (Hs-Mf-Mm)	AAUUUUAAUGGAACUAUUGAUAAAGUG	446

MAPT-5973	27 mer antisense strand	5973-6028-4544 (Hs-Mf-Mm)	CAAUUUAAAUGGAACUAUUGAUAAAGU	447
MAPT-5974	27 mer antisense strand	5974-6029-4545 (Hs-Mf-Mm)	UCAAUUUAAAUGGAACUAUUGAUAAAG	448
MAPT-5975	27 mer antisense strand	5975-6030-4546 (Hs-Mf-Mm)	GUCAAUUUAAAUGGAACUAUUGAUAAA	449
MAPT-5976	27 mer antisense strand	5976-6031-4547 (Hs-Mf-Mm)	AGUCAUUUUAAAUGGAACUAUUGAUAA	450
MAPT-5977	27 mer antisense strand	5977-6032-4548 (Hs-Mf-Mm)	AAGUCUAUUUAAAUGGAACUAUUGAUA	451
MAPT-5978	27 mer antisense strand	5978-6033-4549 (Hs-Mf-Mm)	GAAGUUAAUUUAAAUGGAACUAUUGAU	452
MAPT-5979	27 mer antisense strand	5979-6034-4550 (Hs-Mf-Mm)	UGAAGUCAAUUUAAAUGGAACUAUUGA	453
MAPT-5980	27 mer antisense strand	5980-6035-4551 (Hs-Mf-Mm)	CUGAAUUCAAUUUAAAUGGAACUAUUG	454
MAPT-5981	27 mer antisense strand	5981-6036-4552 (Hs-Mf-Mm)	ACUGAUGUCAAUUUAAAUGGAACUAUU	455
MAPT-5982	27 mer antisense strand	5982-6037-4553 (Hs-Mf-Mm)	CACUGUAGUCAAUUUAAAUGGAACUAU	456
MAPT-5983	27 mer antisense strand	5983-6038-4554 (Hs-Mf-Mm)	CCACUUAAGUCAAUUUAAAUGGAACUA	457
MAPT-5984	27 mer antisense strand	5984-6039-4555 (Hs-Mf-Mm)	ACCACUGAAGUCAAUUUAAAUGGAACU	458
MAPT-5985	27 mer antisense strand	5985-6040-4556 (Hs-Mf-Mm)	CACCAUUGAAGUCAAUUUAAAUGGAAC	459
MAPT-6662	27 mer antisense strand	6662-6723-5230 (Hs-Mf-Mm)	CCGAAUAAAUCAUGGGACUUGCAAGUG	460

MAPT-6663	27 mer antisense strand	6663-6724-5231 (Hs-Mf-Mm)	ACCGAUGAAAUCAUGGGACUUGCAAGU	461
MAPT-6664	27 mer antisense strand	6664-6725-5232 (Hs-Mf-Mm)	UACCGUAGAAAUCAUGGGACUUGCAAG	462
MAPT-6665	27 mer antisense strand	6665-6726-5233 (Hs-Mf-Mm)	UUACCUAAGAAAUCAUGGGACUUGCAA	463
MAPT-6800	27 mer antisense strand	6800-6861-5365 (Hs-Mf-Mm)	ACUUUUUUUCCAAAUUCACUUUUACAG	464
MAPT-6801	27 mer antisense strand	6801-6862-5366 (Hs-Mf-Mm)	AACUUUAUUUCCAAAUUCACUUUUACA	465
MAPT-6802	27 mer antisense strand	6802-6863-5367 (Hs-Mf-Mm)	UAACUUUAUUUCCAAAUUCACUUUUAC	466
MAPT-6803	27 mer antisense strand	6803-6864-5368 (Hs-Mf-Mm)	AUAACUUUAUUUCCAAAUUCACUUUUA	467
MAPT-6804	27 mer antisense strand	6804-6865-5369 (Hs-Mf-Mm)	AAUAAUUUUAUUUCCAAAUUCACUUUU	468
MAPT-6805	27 mer antisense strand	6805-6866-5370 (Hs-Mf-Mm)	UAAUAUCUUUAUUUCCAAAUUCACUUU	469
MAPT-6806	27 mer antisense strand	6806-6867-5371 (Hs-Mf-Mm)	GUAAUUACUUUAUUUCCAAAUUCACUU	470
MAPT-6807	27 mer antisense strand	6807-6868-5372 (Hs-Mf-Mm)	AGUAAUAACUUUAUUUCCAAAUUCACU	471
MAPT-6808	27 mer antisense strand	6808-6869-5373 (Hs-Mf-Mm)	GAGUAUUAACUUUAUUUCCAAAUUCAC	472
MAPT-6809	27 mer antisense strand	6809-6870-5374 (Hs-Mf-Mm)	AGAGUUAUAACUUUAUUUCCAAAUUCA	473
MAPT-6810	27 mer antisense strand	6810-6871-5375 (Hs-Mf-Mm)	CAGAGUAAUAACUUUAUUUCCAAAUUC	474

MAPT-6811	27 mer antisense strand	6811-6872-5376 (Hs-Mf-Mm)	UCAGAUUAAUAACUUUAUUUCCAAAUU	475
MAPT-6812	27 mer antisense strand	6812-6873-5377 (Hs-Mf-Mm)	AUCAGUGUAAUAACUUUAUUUCCAAAU	476
MAPT-6813	27 mer antisense strand	6813-6874-5378 (Hs-Mf-Mm)	AAUCAUAGUAAUAACUUUAUUUCCAAA	477
MAPT-6814	27 mer antisense strand	6814-6875-5379 (Hs-Mf-Mm)	UAAUCUGAGUAAUAACUUUAUUUCCAA	478
MAPT-6815	27 mer antisense strand	6815-6876-5380 (Hs-Mf-Mm)	UUAAUUAGAGUAAUAACUUUAUUUCCA	479
MAPT-6816	27 mer antisense strand	6816-6877-5381 (Hs-Mf-Mm)	UUUAAUCAGAGUAAUAACUUUAUUUCC	480
MAPT-363	27 mer antisense strand	363 (Hs)	UGAUCUUCCAUCACUUCGAACUCCUGG	481
MAPT-364	27 mer antisense strand	364 (Hs)	GUGAUUUUCCAUCACUUCGAACUCCUG	482
MAPT-365	27 mer antisense strand	365 (Hs)	CGUGAUCUUCCAUCACUUCGAACUCCU	483
MAPT-367	27 mer antisense strand	367 (Hs)	AGCGUUAUCUUCCAUCACUUCGAACUC	484
MAPT-369	27 mer antisense strand	369 (Hs)	CCAGCUUGAUCUUCCAUCACUUCGAAC	485
MAPT-374	27 mer antisense strand	374-226 (Hs-Mf)	ACGUCUCAGCGUGAUCUUCCAUCACUU	486
MAPT-395	27 mer antisense strand	395-247 (Hs-Mf)	CUUUCUUGUCCCCCAACCCGUACGUCC	487
MAPT-400	27 mer antisense strand	400-252 (Hs-Mf)	CUGAUUUUUCCUGUCCCCCAACCCGUA	488

MAPT-443	27 mer antisense strand	443-295 (Hs-Mf)	CGUCCUUGUCACCCUCUUGGUCUUGGU	489
MAPT-688	27 mer antisense strand	688-453 (Hs-Mf)	CACGUUACCAGCAGCUUCGUCUUCCAG	490
MAPT-689	27 mer antisense strand	689-454 (Hs-Mf)	UCACGUGACCAGCAGCUUCGUCUUCCA	491
MAPT-690	27 mer antisense strand	690-455 (Hs-Mf)	GUCACUUGACCAGCAGCUUCGUCUUCC	492
MAPT-693	27 mer antisense strand	693-458 (Hs-Mf)	UGGGUUACGUGACCAGCAGCUUCGUCU	493
MAPT-695	27 mer antisense strand	695-460 (Hs-Mf)	CUUGGUUCACGUGACCAGCAGCUUCGU	494
MAPT-696	27 mer antisense strand	696-461 (Hs-Mf)	UCUUGUGUCACGUGACCAGCAGCUUCG	495
MAPT-1475	27 mer antisense strand	1475-1552 (Hs-Mf)	CGUCUUUGCUUUUACUGACCAUGCGAG	496
MAPT-1476	27 mer antisense strand	1476-1553 (Hs-Mf)	CCGUCUUUGCUUUUACUGACCAUGCGA	497
MAPT-1479	27 mer antisense strand	1479-1556 (Hs-Mf)	GUCCCUUCUUUGCUUUUACUGACCAUG	498
MAPT-1480	27 mer antisense strand	1480-1557 (Hs-Mf)	AGUCCUGUCUUUGCUUUUACUGACCAU	499
MAPT-1481	27 mer antisense strand	1481-1558 (Hs-Mf)	CAGUCUCGUCUUUGCUUUUACUGACCA	500
MAPT-1484	27 mer antisense strand	1484-1561 (Hs-Mf)	UUCCAUUCCCGUCUUUGCUUUUACUGA	501
MAPT-1485	27 mer antisense strand	1485-1562 (Hs-Mf)	CUUCCUGUCCCGUCUUUGCUUUUACUG	502

MAPT-1492	27 mer antisense strand	1492-1569 (Hs-Mf)	GUCAUUGCUUCCAGUCCCGUCUUUGCU	503
MAPT-1494	27 mer antisense strand	1494-1571 (Hs-Mf)	UUGUCUUCGCUUCCAGUCCCGUCUUUG	504
MAPT-1495	27 mer antisense strand	1495-1572 (Hs-Mf)	UUUGUUAUCGCUUCCAGUCCCGUCUUU	505
MAPT-1498	27 mer antisense strand	1498-1575 (Hs-Mf)	UUUUUUGUCAUCGCUUCCAGUCCCGUC	506
MAPT-1499	27 mer antisense strand	1499-1576 (Hs-Mf)	CUUUUUUGUCAUCGCUUCCAGUCCCGU	507
MAPT-1500	27 mer antisense strand	1500-1577 (Hs-Mf)	GCUUUUUUGUCAUCGCUUCCAGUCCCG	508
MAPT-1502	27 mer antisense strand	1502-1579 (Hs-Mf)	UGGCUUUUUUGUCAUCGCUUCCAGUCC	509
MAPT-1503	27 mer antisense strand	1503-1580 (Hs-Mf)	UUGGCUUUUUUGUCAUCGCUUCCAGUC	510
MAPT-1504	27 mer antisense strand	1504-1581 (Hs-Mf)	CUUGGUUUUUUUGUCAUCGCUUCCAGU	511
MAPT-1505	27 mer antisense strand	1505-1582 (Hs-Mf)	UCUUGUCUUUUUUGUCAUCGCUUCCAG	512
MAPT-1506	27 mer antisense strand	1506-1583 (Hs-Mf)	GUCUUUGCUUUUUUGUCAUCGCUUCCA	513
MAPT-1507	27 mer antisense strand	1507-1584 (Hs-Mf)	UGUCUUGGCUUUUUUGUCAUCGCUUCC	514
MAPT-1508	27 mer antisense strand	1508-1585 (Hs-Mf)	AUGUCUUGGCUUUUUUGUCAUCGCUUC	515
MAPT-1509	27 mer antisense strand	1509-1586 (Hs-Mf)	GAUGUUUUGGCUUUUUUGUCAUCGCUU	516

MAPT-1733	27 mer antisense strand	1733 (Hs)	GUGUGUCGAUCUUCGUUUUACCAUCAG	517
MAPT-1796	27 mer antisense strand	1796-1873 (Hs-Mf)	UUUUUUCUGGAAUCCUGGUGGCGUUGG	518
MAPT-1835	27 mer antisense strand	1835-1912 (Hs-Mf)	UAGUCUCAGAGCUGGGUGGUGUCUUUG	519
MAPT-1912	27 mer antisense strand	1912-1989 (Hs-Mf)	GCUGCUAUCCCCUGAUUUUGGAGGUUC	520
MAPT-2094	27 mer antisense strand	2094-2171 (Hs-Mf)	ACAUUUUUCAGGUCUGGCAUGGGCACG	521
MAPT-2096	27 mer antisense strand	2096-2173 (Hs-Mf)	UGACAUUCUUCAGGUCUGGCAUGGGCA	522
MAPT-2097	27 mer antisense strand	2097-2174 (Hs-Mf)	UUGACUUUCUUCAGGUCUGGCAUGGGC	523
MAPT-2098	27 mer antisense strand	2098 (Hs)	CUUGAUAUUCUUCAGGUCUGGCAUGGG	524
MAPT-2105	27 mer antisense strand	2105 (Hs)	UCUUGUACUUGACAUUCUUCAGGUCUG	525
MAPT-2106	27 mer antisense strand	2106 (Hs)	AUCUUUGACUUGACAUUCUUCAGGUCU	526
MAPT-2107	27 mer antisense strand	2107 (Hs)	GAUCUUGGACUUGACAUUCUUCAGGUC	527
MAPT-2108	27 mer antisense strand	2108 (Hs)	CGAUCUUGGACUUGACAUUCUUCAGGU	528
MAPT-2109	27 mer antisense strand	2109 (Hs)	CCGAUUUUGGACUUGACAUUCUUCAGG	529
MAPT-2117	27 mer antisense strand	2117-2194 (Hs-Mf)	CAGUGUAGCCGAUCUUGGACUUGACAU	530

MAPT-2136	27 mer antisense strand	2136 (Hs)	GGCUGUUGCUUCAGGUUCUCAGUGGAG	531
MAPT-2137	27 mer antisense strand	2137 (Hs)	CGGCUUGUGCUUCAGGUUCUCAGUGGA	532
MAPT-2269	27 mer antisense strand	2269-2346 (Hs-Mf)	GUCAAUUGGUUUGUAGACUAUUUGCAC	533
MAPT-2270	27 mer antisense strand	2270-2347 (Hs-Mf)	GGUCAUCUGGUUUGUAGACUAUUUGCA	534
MAPT-2271	27 mer antisense strand	2271-2348 (Hs-Mf)	AGGUCUACUGGUUUGUAGACUAUUUGC	535
MAPT-2272	27 mer antisense strand	2272-2349 (Hs-Mf)	CAGGUUAACUGGUUUGUAGACUAUUUG	536
MAPT-2273	27 mer antisense strand	2273-2350 (Hs-Mf)	UCAGGUCAACUGGUUUGUAGACUAUUU	537
MAPT-2274	27 mer antisense strand	2274-2351 (Hs-Mf)	CUCAGUUCAACUGGUUUGUAGACUAUU	538
MAPT-2275	27 mer antisense strand	2275-2352 (Hs-Mf)	GCUCAUGUCAACUGGUUUGUAGACUAU	539
MAPT-2276	27 mer antisense strand	2276-2353 (Hs-Mf)	UGCUCUGGUCAACUGGUUUGUAGACUA	540
MAPT-2277	27 mer antisense strand	2277-2354 (Hs-Mf)	UUGCUUAGGUCAACUGGUUUGUAGACU	541
MAPT-2278	27 mer antisense strand	2278-2355 (Hs-Mf)	CUUGCUCAGGUCAACUGGUUUGUAGAC	542
MAPT-2279	27 mer antisense strand	2279-2356 (Hs-Mf)	CCUUGUUCAGGUCAACUGGUUUGUAGA	543
MAPT-2280	27 mer antisense strand	2280-2357 (Hs-Mf)	ACCUUUCUCAGGUCAACUGGUUUGUAG	544

MAPT-2281	27 mer antisense strand	2281-2358 (Hs-Mf)	CACCUUGCUCAGGUCAACUGGUUUGUA	545
MAPT-2282	27 mer antisense strand	2282-2359 (Hs-Mf)	UCACCUUGCUCAGGUCAACUGGUUUGU	546
MAPT-2283	27 mer antisense strand	2283-2360 (Hs-Mf)	GUCACUUUGCUCAGGUCAACUGGUUUG	547
MAPT-2284	27 mer antisense strand	2284-2361 (Hs-Mf)	GGUCAUCUUGCUCAGGUCAACUGGUUU	548
MAPT-2286	27 mer antisense strand	2286-2363 (Hs-Mf)	GAGGUUACCUUGCUCAGGUCAACUGGU	549
MAPT-2288	27 mer antisense strand	2288-2365 (Hs-Mf)	UGGAGUUCACCUUGCUCAGGUCAACUG	550
MAPT-2289	27 mer antisense strand	2289-2366 (Hs-Mf)	UUGGAUGUCACCUUGCUCAGGUCAACU	551
MAPT-2291	27 mer antisense strand	2291-2368 (Hs-Mf)	ACUUGUAGGUCACCUUGCUCAGGUCAA	552
MAPT-2294	27 mer antisense strand	2294-2371 (Hs-Mf)	CACACUUGGAGGUCACCUUGCUCAGGU	553
MAPT-2299	27 mer antisense strand	2299-2376 (Hs-Mf)	UGAGCUACACUUGGAGGUCACCUUGCU	554
MAPT-2300	27 mer antisense strand	2300-2377 (Hs-Mf)	AUGAGUCACACUUGGAGGUCACCUUGC	555
MAPT-2301	27 mer antisense strand	2301-2378 (Hs-Mf)	AAUGAUCCACACUUGGAGGUCACCUUG	556
MAPT-2308	27 mer antisense strand	2308-2385 (Hs-Mf)	GUUGCUUAAUGAGCCACACUUGGAGGU	557
MAPT-2316	27 mer antisense strand	2316-2393 (Hs-Mf)	UGAUGUAUGUUGCCUAAUGAGCCACAC	558

MAPT-2317	27 mer antisense strand	2317-2394 (Hs-Mf)	AUGAUUGAUGUUGCCUAAUGAGCCACA	559
MAPT-2319	27 mer antisense strand	2319-2396 (Hs-Mf)	UUAUGUUGGAUGUUGCCUAAUGAGCCA	560
MAPT-2320	27 mer antisense strand	2320-2397 (Hs-Mf)	UUUAUUAUGGAUGUUGCCUAAUGAGCC	561
MAPT-2322	27 mer antisense strand	2322-2399 (Hs-Mf)	GGUUUUUGAUGGAUGUUGCCUAAUGAG	562
MAPT-2323	27 mer antisense strand	2323-2400 (Hs-Mf)	UGGUUUAUGAUGGAUGUUGCCUAAUGA	563
MAPT-2324	27 mer antisense strand	2324-2401 (Hs-Mf)	CUGGUUUAUGAUGGAUGUUGCCUAAUG	564
MAPT-2326	27 mer antisense strand	2326-2403 (Hs-Mf)	UCCUGUUUUAUGAUGGAUGUUGCCUAA	565
MAPT-2330	27 mer antisense strand	2330-2407 (Hs-Mf)	CACCUUCUGGUUUAUGAUGGAUGUUGC	566
MAPT-2356	27 mer antisense strand	2356-2433 (Hs-Mf)	CUUCUUAGAUUUUACUUCCACCUGGCC	567
MAPT-2357	27 mer antisense strand	2357-2434 (Hs-Mf)	GCUUCUCAGAUUUUACUUCCACCUGGC	568
MAPT-2358	27 mer antisense strand	2358-2435 (Hs-Mf)	AGCUUUUCAGAUUUUACUUCCACCUGG	569
MAPT-2359	27 mer antisense strand	2359-2436 (Hs-Mf)	AAGCUUCUCAGAUUUUACUUCCACCUG	570
MAPT-2360	27 mer antisense strand	2360-2437 (Hs-Mf)	CAAGCUUCUCAGAUUUUACUUCCACCU	571
MAPT-2361	27 mer antisense strand	2361-2438 (Hs-Mf)	UCAAGUUUCUCAGAUUUUACUUCCACC	572

MAPT-2362	27 mer antisense strand	2362-2439 (Hs-Mf)	GUCAAUCUUCUCAGAUUUUACUUCCAC	573
MAPT-2363	27 mer antisense strand	2363-2440 (Hs-Mf)	AGUCAUGCUUCUCAGAUUUUACUUCCA	574
MAPT-2364	27 mer antisense strand	2364-2441 (Hs-Mf)	AAGUCUAGCUUCUCAGAUUUUACUUCC	575
MAPT-2365	27 mer antisense strand	2365 (Hs)	GAAGUUAAGCUUCUCAGAUUUUACUUC	576
MAPT-2372	27 mer antisense strand	2372 (Hs)	UGUCCUUGAAGUCAAGCUUCUCAGAUU	577
MAPT-2373	27 mer antisense strand	2373 (Hs)	CUGUCUUUGAAGUCAAGCUUCUCAGAU	578
MAPT-2374	27 mer antisense strand	2374 (Hs)	UCUGUUCUUGAAGUCAAGCUUCUCAGA	579
MAPT-2375	27 mer antisense strand	2375 (Hs)	CUCUGUCCUUGAAGUCAAGCUUCUCAG	580
MAPT-2376	27 mer antisense strand	2376 (Hs)	ACUCUUUCCUUGAAGUCAAGCUUCUCA	581
MAPT-2377	27 mer antisense strand	2377 (Hs)	GACUCUGUCCUUGAAGUCAAGCUUCUC	582
MAPT-2378	27 mer antisense strand	2378 (Hs)	GGACUUUGUCCUUGAAGUCAAGCUUCU	583
MAPT-2379	27 mer antisense strand	2379 (Hs)	UGGACUCUGUCCUUGAAGUCAAGCUUC	584
MAPT-2380	27 mer antisense strand	2380 (Hs)	CUGGAUUCUGUCCUUGAAGUCAAGCUU	585
MAPT-2381	27 mer antisense strand	2381 (Hs)	ACUGGUCUCUGUCCUUGAAGUCAAGCU	586

MAPT-2382	27 mer antisense strand	2382 (Hs)	GACUGUACUCUGUCCUUGAAGUCAAGC	587
MAPT-2390	27 mer antisense strand	2390 (Hs)	CAAUCUUCGACUGGACUCUGUCCUUGA	588
MAPT-2391	27 mer antisense strand	2391 (Hs)	CCAAUUUUCGACUGGACUCUGUCCUUG	589
MAPT-2414	27 mer antisense strand	2414-2491 (Hs-Mf)	CGUGGUUGAUAUUGUCCAGGGACCCAA	590
MAPT-2448	27 mer antisense strand	2448-2525 (Hs-Mf)	UGGGUUUCAAUCUUUUUAUUUCCUCCG	591
MAPT-2449	27 mer antisense strand	2449-2526 (Hs-Mf)	GUGGGUUUCAAUCUUUUUAUUUCCUCC	592
MAPT-2450	27 mer antisense strand	2450-2527 (Hs-Mf)	UGUGGUUUUCAAUCUUUUUAUUUCCUC	593
MAPT-2451	27 mer antisense strand	2451-2528 (Hs-Mf)	UUGUGUGUUUCAAUCUUUUUAUUUCCU	594
MAPT-2452	27 mer antisense strand	2452-2529 (Hs-Mf)	CUUGUUGGUUUCAAUCUUUUUAUUUCC	595
MAPT-2453	27 mer antisense strand	2453-2530 (Hs-Mf)	GCUUGUGGGUUUCAAUCUUUUUAUUUC	596
MAPT-2454	27 mer antisense strand	2454-2531 (Hs-Mf)	AGCUUUUGGGUUUCAAUCUUUUUAUUU	597
MAPT-2456	27 mer antisense strand	2456-2533 (Hs-Mf)	UCAGCUUGUGGGUUUCAAUCUUUUUAU	598
MAPT-2457	27 mer antisense strand	2457-2534 (Hs-Mf)	GUCAGUUUGUGGGUUUCAAUCUUUUUA	599
MAPT-2567	27 mer antisense strand	2567 (Hs)	UGGAGUAGACAUUGCUGAGAUGCCGUG	600

MAPT-2598	27 mer antisense strand	2598-2675 (Hs-Mf)	UGGGGUGAGUCUACCAUGUCGAUGCUG	601
MAPT-2657	27 mer antisense strand	2657-2734 (Hs-Mf)	CUGAUUACAAACCCUGCUUGGCCAGGG	602
MAPT-2723	27 mer antisense strand	2723-2800 (Hs-Mf)	AUUAUUCUUUUUUUUUCCACACUCUCU	603
MAPT-2724	27 mer antisense strand	2724-2801 (Hs-Mf)	CAUUAUUCUUUUUUUUUCCACACUCUC	604
MAPT-2726	27 mer antisense strand	2726-2803 (Hs-Mf)	GUCAUUAUUCUUUUUUUUUCCACACUC	605
MAPT-2784	27 mer antisense strand	2784-2860-1 mismatch (Hs-Mf)	GUGAUUAACCAAUUAACCGAACUGCGA	606
MAPT-2963	27 mer antisense strand	2963-3039 (Hs-Mf)	GAAAAUAGAAUCAAAAGGAAUUGCCUG	607
MAPT-3110	27 mer antisense strand	3110-3186 (Hs-Mf)	ACCAAUUUUCAAAUCCUUUGUUGCUGC	608
MAPT-3114	27 mer antisense strand	3114-3190 (Hs-Mf)	ACACAUCAAGUUUCAAAUCCUUUGUUG	609
MAPT-3116	27 mer antisense strand	3116-3192 (Hs-Mf)	GAACAUACCAAGUUUCAAAUCCUUUGU	610
MAPT-3118	27 mer antisense strand	3118-3194 (Hs-Mf)	ACGAAUACACCAAGUUUCAAAUCCUUU	611
MAPT-3158	27 mer antisense strand	3158-3234 (Hs-Mf)	UCACAUUCACACAAGGUUGACAUCGUC	612
MAPT-3503	27 mer antisense strand	3503-3576 (Hs-Mf)	UCUCAUGACAUCAAGGUCAGUCUUUUC	613
MAPT-3589	27 mer antisense strand	3589-3661 (Hs-Mf)	UCAAUUAAACAGGGUUUCUGUGGAGCA	614

MAPT-3591	27 mer antisense strand	3591-3663 (Hs-Mf)	ACUCAUUAAAACAGGGUUUCUGUGGAG	615
MAPT-3592	27 mer antisense strand	3592-3664 (Hs-Mf)	AACUCUAUAAAACAGGGUUUCUGUGGA	616
MAPT-3593	27 mer antisense strand	3593-3665 (Hs-Mf)	GAACUUAAUAAAACAGGGUUUCUGUGG	617
MAPT-3594	27 mer antisense strand	3594-3666 (Hs-Mf)	AGAACUCAAUAAAACAGGGUUUCUGUG	618
MAPT-3595	27 mer antisense strand	3595-3667 (Hs-Mf)	CAGAAUUCAAUAAAACAGGGUUUCUGU	619
MAPT-3596	27 mer antisense strand	3596-3668 (Hs-Mf)	UCAGAUCUCAAUAAAACAGGGUUUCUG	620
MAPT-3597	27 mer antisense strand	3597-3669 (Hs-Mf)	UUCAGUACUCAAUAAAACAGGGUUUCU	621
MAPT-3598	27 mer antisense strand	3598-3670 (Hs-Mf)	CUUCAUAACUCAAUAAAACAGGGUUUC	622
MAPT-3599	27 mer antisense strand	3599-3671 (Hs-Mf)	CCUUCUGAACUCAAUAAAACAGGGUUU	623
MAPT-3600	27 mer antisense strand	3600-3672 (Hs-Mf)	ACCUUUAGAACUCAAUAAAACAGGGUU	624
MAPT-3601	27 mer antisense strand	3601-3673 (Hs-Mf)	AACCUUCAGAACUCAAUAAAACAGGGU	625
MAPT-3602	27 mer antisense strand	3602-3674 (Hs-Mf)	CAACCUUCAGAACUCAAUAAAACAGGG	626
MAPT-3603	27 mer antisense strand	3603-3675 (Hs-Mf)	CCAACUUUCAGAACUCAAUAAAACAGG	627
MAPT-3605	27 mer antisense strand	3605-3677 (Hs-Mf)	UUCCAUCCUUCAGAACUCAAUAAAACA	628

MAPT-3607	27 mer antisense strand	3607-3679 (Hs-Mf)	AGUUCUAACCUUCAGAACUCAAUAAAA	629
MAPT-3609	27 mer antisense strand	3609-3681 (Hs-Mf)	GCAGUUCCAACCUUCAGAACUCAAUAA	630
MAPT-3610	27 mer antisense strand	3610-3682 (Hs-Mf)	AGCAGUUCCAACCUUCAGAACUCAAUA	631
MAPT-3677	27 mer antisense strand	3677-3749 (Hs-Mf)	CAAGUUCUUACAAAGAGAACUGGUUAG	632
MAPT-3678	27 mer antisense strand	3678-3750 (Hs-Mf)	ACAAGUCCUUACAAAGAGAACUGGUUA	633
MAPT-3679	27 mer antisense strand	3679-3751 (Hs-Mf)	CACAAUUCCUUACAAAGAGAACUGGUU	634
MAPT-3680	27 mer antisense strand	3680-3752 (Hs-Mf)	GCACAUGUCCUUACAAAGAGAACUGGU	635
MAPT-3958	27 mer antisense strand	3958-4030 (Hs-Mf)	UAAUUUCACCCUCAGUAUGGAGUAGGU	636
MAPT-3959	27 mer antisense strand	3959-4031 (Hs-Mf)	UUAAUUUCACCCUCAGUAUGGAGUAGG	637
MAPT-3960	27 mer antisense strand	3960-4032 (Hs-Mf)	CUUAAUUUCACCCUCAGUAUGGAGUAG	638
MAPT-3961	27 mer antisense strand	3961-4033 (Hs-Mf)	CCUUAUUUUCACCCUCAGUAUGGAGUA	639
MAPT-3965	27 mer antisense strand	3965-4037 (Hs-Mf)	CUUCCUUUAAUUUCACCCUCAGUAUGG	640
MAPT-3970	27 mer antisense strand	3970-4042 (Hs-Mf)	UUUGCUUUCCCUUAAUUUCACCCUCAG	641
MAPT-4146	27 mer antisense strand	4146-4218 (Hs-Mf)	UCCAUUUCAACAAGGCAGAAACACCUA	642

MAPT-4474	27 mer antisense strand	4474-4545 (Hs-Mf)	CUAUGUAUAUGUUCAGCUGCUCCAGCA	643
MAPT-4475	27 mer antisense strand	4475-4546 (Hs-Mf)	UCUAUUUAUAUGUUCAGCUGCUCCAGC	644
MAPT-4477	27 mer antisense strand	4477-4548 (Hs-Mf)	CAUCUUUGUAUAUGUUCAGCUGCUCCA	645
MAPT-4478	27 mer antisense strand	4478-4549 (Hs-Mf)	ACAUCUAUGUAUAUGUUCAGCUGCUCC	646
MAPT-4479	27 mer antisense strand	4479-4550 (Hs-Mf)	AACAUUUAUGUAUAUGUUCAGCUGCUC	647
MAPT-4480	27 mer antisense strand	4480-4551 (Hs-Mf)	CAACAUCUAUGUAUAUGUUCAGCUGCU	648
MAPT-4481	27 mer antisense strand	4481-4552 (Hs-Mf)	GCAACUUCUAUGUAUAUGUUCAGCUGC	649
MAPT-4482	27 mer antisense strand	4482-4553 (Hs-Mf)	GGCAAUAUCUAUGUAUAUGUUCAGCUG	650
MAPT-4485	27 mer antisense strand	4485-4556 (Hs-Mf)	CAGGGUAACAUCUAUGUAUAUGUUCAG	651
MAPT-4486	27 mer antisense strand	4486-4557 (Hs-Mf)	GCAGGUCAACAUCUAUGUAUAUGUUCA	652
MAPT-4532	27 mer antisense strand	4532 (Hs)	AAACAUACAAAUCCAACUACAACUCAA	653
MAPT-4533	27 mer antisense strand	4533 (Hs)	UAAACUGACAAAUCCAACUACAACUCA	654
MAPT-4539	27 mer antisense strand	4539-4610 (Hs-Mf)	CAAGCUUAAACAGACAAAUCCAACUAC	655
MAPT-4540	27 mer antisense strand	4540-4611 (Hs-Mf)	CCAAGUAUAAACAGACAAAUCCAACUA	656

MAPT-4541	27 mer antisense strand	4541-4612 (Hs-Mf)	UCCAAUCAUAAACAGACAAAUCCAACU	657
MAPT-4543	27 mer antisense strand	4543-4614 (Hs-Mf)	AAUCCUAGCAUAAACAGACAAAUCCAA	658
MAPT-4544	27 mer antisense strand	4544-4615 (Hs-Mf)	GAAUCUAAGCAUAAACAGACAAAUCCA	659
MAPT-4545	27 mer antisense strand	4545-4616 (Hs-Mf)	UGAAUUCAAGCAUAAACAGACAAAUCC	660
MAPT-4546	27 mer antisense strand	4546-4617 (Hs-Mf)	GUGAAUCCAAGCAUAAACAGACAAAUC	661
MAPT-4547	27 mer antisense strand	4547-4618 (Hs-Mf)	GGUGAUUCCAAGCAUAAACAGACAAAU	662
MAPT-4548	27 mer antisense strand	4548-4619 (Hs-Mf)	UGGUGUAUCCAAGCAUAAACAGACAAA	663
MAPT-4549	27 mer antisense strand	4549-4620 (Hs-Mf)	CUGGUUAAUCCAAGCAUAAACAGACAA	664
MAPT-4550	27 mer antisense strand	4550-4621 (Hs-Mf)	UCUGGUGAAUCCAAGCAUAAACAGACA	665
MAPT-4551	27 mer antisense strand	4551-4622 (Hs-Mf)	CUCUGUUGAAUCCAAGCAUAAACAGAC	666
MAPT-4552	27 mer antisense strand	4552-4623 (Hs-Mf)	ACUCUUGUGAAUCCAAGCAUAAACAGA	667
MAPT-4554	27 mer antisense strand	4554-4625 (Hs-Mf)	UCACUUUGGUGAAUCCAAGCAUAAACA	668
MAPT-4556	27 mer antisense strand	4556-4627 (Hs-Mf)	AGUCAUUCUGGUGAAUCCAAGCAUAAA	669
MAPT-4557	27 mer antisense strand	4557-4628 (Hs-Mf)	UAGUCUCUCUGGUGAAUCCAAGCAUAA	670

MAPT-4558	27 mer antisense strand	4558-4629 (Hs-Mf)	AUAGUUACUCUGGUGAAUCCAAGCAUA	671
MAPT-4559	27 mer antisense strand	4559-4630 (Hs-Mf)	CAUAGUCACUCUGGUGAAUCCAAGCAU	672
MAPT-4560	27 mer antisense strand	4560-4631 (Hs-Mf)	UCAUAUUCACUCUGGUGAAUCCAAGCA	673
MAPT-4561	27 mer antisense strand	4561-4632 (Hs-Mf)	AUCAUUGUCACUCUGGUGAAUCCAAGC	674
MAPT-4562	27 mer antisense strand	4562-4633 (Hs-Mf)	UAUCAUAGUCACUCUGGUGAAUCCAAG	675
MAPT-4563	27 mer antisense strand	4563-4634 (Hs-Mf)	CUAUCUUAGUCACUCUGGUGAAUCCAA	676
MAPT-4564	27 mer antisense strand	4564-4635 (Hs-Mf)	ACUAUUAUAGUCACUCUGGUGAAUCCA	677
MAPT-4615	27 mer antisense strand	4615-4687 (Hs-Mf)	UACAAUCAUUUCAAGAUACAUGCGUCC	678
MAPT-4616	27 mer antisense strand	4616-4688 (Hs-Mf)	UUACAUGCAUUUCAAGAUACAUGCGUC	679
MAPT-4617	27 mer antisense strand	4617-4689 (Hs-Mf)	UUUACUAGCAUUUCAAGAUACAUGCGU	680
MAPT-4618	27 mer antisense strand	4618-4690 (Hs-Mf)	CUUUAUAAGCAUUUCAAGAUACAUGCG	681
MAPT-4619	27 mer antisense strand	4619-4691 (Hs-Mf)	UCUUUUCAAGCAUUUCAAGAUACAUGC	682
MAPT-4620	27 mer antisense strand	4620-4692 (Hs-Mf)	CUCUUUACAAGCAUUUCAAGAUACAUG	683
MAPT-4621	27 mer antisense strand	4621-4693 (Hs-Mf)	CCUCUUUACAAGCAUUUCAAGAUACAU	684

MAPT-4622	27 mer antisense strand	4622-4694 (Hs-Mf)	ACCUCUUUACAAGCAUUUCAAGAUACA	685
MAPT-4623	27 mer antisense strand	4623-4695 (Hs-Mf)	AACCUUUUUACAAGCAUUUCAAGAUAC	686
MAPT-4625	27 mer antisense strand	4625-4697 (Hs-Mf)	GAAACUUCUUUACAAGCAUUUCAAGAU	687
MAPT-4627	27 mer antisense strand	4627-4699 (Hs-Mf)	UAGAAUCCUCUUUACAAGCAUUUCAAG	688
MAPT-4628	27 mer antisense strand	4628-4700 (Hs-Mf)	UUAGAUACCUCUUUACAAGCAUUUCAA	689
MAPT-4629	27 mer antisense strand	4629-4701 (Hs-Mf)	GUUAGUAACCUCUUUACAAGCAUUUCA	690
MAPT-4630	27 mer antisense strand	4630-4702 (Hs-Mf)	GGUUAUAAACCUCUUUACAAGCAUUUC	691
MAPT-4632	27 mer antisense strand	4632-4704 (Hs-Mf)	UGGGUUAGAAACCUCUUUACAAGCAUU	692
MAPT-4633	27 mer antisense strand	4633-4705 (Hs-Mf)	GUGGGUUAGAAACCUCUUUACAAGCAU	693
MAPT-4825	27 mer antisense strand	4825-4897 (Hs-Mf)	AUCAUUGCUUCAGUCCUAAUCCUGUGC	694
MAPT-4828	27 mer antisense strand	4828-4900 (Hs-Mf)	GACAUUAUCGCUUCAGUCCUAAUCCUG	695
MAPT-5682	27 mer antisense strand	5682-5743 (Hs-Mf)	CUGAAUAGCAGGGCACAAGAACUUCAG	696
MAPT-5958	27 mer antisense strand	5958 (Hs)	UAUUGUUAAAGUGAGUCAGCAGCUUGA	697
MAPT-5959	27 mer antisense strand	5959 (Hs)	CUAUUUAUAAAGUGAGUCAGCAGCUUG	698

MAPT-5961	27 mer antisense strand	5961 (Hs)	AACUAUUGAUAAAGUGAGUCAGCAGCU	699
MAPT-5963	27 mer antisense strand	5963 (Hs)	GGAACUAUUGAUAAAGUGAGUCAGCAG	700
MAPT-5964	27 mer antisense strand	5964 (Hs)	UGGAAUUAUUGAUAAAGUGAGUCAGCA	701
MAPT-5965	27 mer antisense strand	5965 (Hs)	AUGGAACUAUUGAUAAAGUGAGUCAGC	702
MAPT-5966	27 mer antisense strand	5966-6021 (Hs-Mf)	AAUGGUACUAUUGAUAAAGUGAGUCAG	703
MAPT-5967	27 mer antisense strand	5967-6022 (Hs-Mf)	AAAUGUAACUAUUGAUAAAGUGAGUCA	704
MAPT-5968	27 mer antisense strand	5968-6023 (Hs-Mf)	UAAAUUGAACUAUUGAUAAAGUGAGUC	705
MAPT-6006	27 mer antisense strand	6006-6061 (Hs-Mf)	AUAGCUAACAGGAUACAGUCUCACCAC	706
MAPT-6007	27 mer antisense strand	6007-6062 (Hs-Mf)	AAUAGUAAACAGGAUACAGUCUCACCA	707
MAPT-6008	27 mer antisense strand	6008-6063 (Hs-Mf)	CAAUAUCAAACAGGAUACAGUCUCACC	708
MAPT-6009	27 mer antisense strand	6009-6064 (Hs-Mf)	GCAAUUGCAAACAGGAUACAGUCUCAC	709
MAPT-6010	27 mer antisense strand	6010-6065 (Hs-Mf)	AGCAAUAGCAAACAGGAUACAGUCUCA	710
MAPT-6011	27 mer antisense strand	6011-6066 (Hs-Mf)	AAGCAUUAGCAAACAGGAUACAGUCUC	711
MAPT-6012	27 mer antisense strand	6012-6067 (Hs-Mf)	CAAGCUAUAGCAAACAGGAUACAGUCU	712

MAPT-6013	27 mer antisense strand	6013-6068 (Hs-Mf)	ACAAGUAAUAGCAAACAGGAUACAGUC	713
MAPT-6014	27 mer antisense strand	6014-6069 (Hs-Mf)	AACAAUCAAUAGCAAACAGGAUACAGU	714
MAPT-6015	27 mer antisense strand	6015-6070 (Hs-Mf)	CAACAUGCAAUAGCAAACAGGAUACAG	715
MAPT-6017	27 mer antisense strand	6017-6072 (Hs-Mf)	CACAAUAAGCAAUAGCAAACAGGAUAC	716
MAPT-6119	27 mer antisense strand	6119-6174 (Hs-Mf)	GAAAUUAUGAAAAGGGUUACGAGGCAG	717
MAPT-6628	27 mer antisense strand	6628-6689 (Hs-Mf)	UAGUCUUGCUCAACAUGGCAAACUCAU	718
MAPT-6629	27 mer antisense strand	6629-6690 (Hs-Mf)	AUAGUUCUGCUCAACAUGGCAAACUCA	719
MAPT-6631	27 mer antisense strand	6631-6692 (Hs-Mf)	AAAUAUUCCUGCUCAACAUGGCAAACU	720
MAPT-6672	27 mer antisense strand	6672-6733 (Hs-Mf)	CUCAGUAUUACCGAAGAAAUCAUGGGA	721
MAPT-6731	27 mer antisense strand	6731 (Hs)	AUAUAUACAUUCACAGACAGAAAGCUA	722
MAPT-6732	27 mer antisense strand	6732 (Hs)	UAUAUUGACAUUCACAGACAGAAAGCU	723
MAPT-6738	27 mer antisense strand	6738-6799 (Hs-Mf)	AUACAUUAUAUAGACAUUCACAGACAG	724
MAPT-6739	27 mer antisense strand	6739-6800 (Hs-Mf)	AAUACUCUAUAUAGACAUUCACAGACA	725
MAPT-6740	27 mer antisense strand	6740-6801 (Hs-Mf)	CAAUAUACUAUAUAGACAUUCACAGAC	726

MAPT-6741	27 mer antisense strand	6741-6802 (Hs-Mf)	ACAAUUCACUAUAUAGACAUUCACAGA	727
MAPT-6742	27 mer antisense strand	6742-6803 (Hs-Mf)	CACAAUACACUAUAUAGACAUUCACAG	728
MAPT-6743	27 mer antisense strand	6743-6804 (Hs-Mf)	ACACAUUACACUAUAUAGACAUUCACA	729
MAPT-6745	27 mer antisense strand	6745-6806 (Hs-Mf)	ACACAUAAUACACUAUAUAGACAUUCA	730
MAPT-6748	27 mer antisense strand	6748-6809 (Hs-Mf)	AAAACUCACAAUACACUAUAUAGACAU	731
MAPT-6749	27 mer antisense strand	6749-6810 (Hs-Mf)	UAAAAUACACAAUACACUAUAUAGACA	732
MAPT-6750	27 mer antisense strand	6750-6811 (Hs-Mf)	UUAAAUCACACAAUACACUAUAUAGAC	733
MAPT-6751	27 mer antisense strand	6751-6812 (Hs-Mf)	GUUAAUACACACAAUACACUAUAUAGA	734
MAPT-6752	27 mer antisense strand	6752-6813 (Hs-Mf)	UGUUAUAACACACAAUACACUAUAUAG	735
MAPT-6753	27 mer antisense strand	6753-6814 (Hs-Mf)	UUGUUUAAACACACAAUACACUAUAUA	736
MAPT-6754	27 mer antisense strand	6754-6815 (Hs-Mf)	UUUGUUAAAACACACAAUACACUAUAU	737
MAPT-6755	27 mer antisense strand	6755-6816 (Hs-Mf)	AUUUGUUAAAACACACAAUACACUAUA	738
MAPT-6756	27 mer antisense strand	6756-6817 (Hs-Mf)	CAUUUUUUAAAACACACAAUACACUAU	739
MAPT-6757	27 mer antisense strand	6757-6818 (Hs-Mf)	UCAUUUGUUAAAACACACAAUACACUA	740

MAPT-6758	27 mer antisense strand	6758-6819 (Hs-Mf)	AUCAUUUGUUAAAACACACAAUACACU	741
MAPT-6759	27 mer antisense strand	6759-6820 (Hs-Mf)	AAUCAUUUGUUAAAACACACAAUACAC	742
MAPT-6760	27 mer antisense strand	6760-6821 (Hs-Mf)	AAAUCUUUUGUUAAAACACACAAUACA	743
MAPT-6761	27 mer antisense strand	6761-6822 (Hs-Mf)	UAAAUUAUUUGUUAAAACACACAAUAC	744
MAPT-6762	27 mer antisense strand	6762-6823 (Hs-Mf)	GUAAAUCAUUUGUUAAAACACACAAUA	745
MAPT-6763	27 mer antisense strand	6763-6824 (Hs-Mf)	UGUAAUUCAUUUGUUAAAACACACAAU	746
MAPT-6764	27 mer antisense strand	6764-6825 (Hs-Mf)	GUGUAUAUCAUUUGUUAAAACACACAA	747
MAPT-6765	27 mer antisense strand	6765-6826 (Hs-Mf)	AGUGUUAAUCAUUUGUUAAAACACACA	748
MAPT-6766	27 mer antisense strand	6766-6827 (Hs-Mf)	CAGUGUAAAUCAUUUGUUAAAACACAC	749
MAPT-6767	27 mer antisense strand	6767-6828 (Hs-Mf)	UCAGUUUAAAUCAUUUGUUAAAACACA	750
MAPT-6768	27 mer antisense strand	6768-6829 (Hs-Mf)	GUCAGUGUAAAUCAUUUGUUAAAACAC	751
MAPT-6769	27 mer antisense strand	6769-6830 (Hs-Mf)	AGUCAUUGUAAAUCAUUUGUUAAAACA	752
MAPT-6772	27 mer antisense strand	6772-6833 (Hs-Mf)	AACAGUCAGUGUAAAUCAUUUGUUAAA	753
MAPT-6773	27 mer antisense strand	6773-6834 (Hs-Mf)	CAACAUUCAGUGUAAAUCAUUUGUUAA	754

MAPT-6774	27 mer antisense strand	6774-6835 (Hs-Mf)	GCAACUGUCAGUGUAAAUCAUUUGUUA	755
MAPT-6775	27 mer antisense strand	6775-6836 (Hs-Mf)	AGCAAUAGUCAGUGUAAAUCAUUUGUU	756
MAPT-6777	27 mer antisense strand	6777-6838 (Hs-Mf)	ACAGCUACAGUCAGUGUAAAUCAUUUG	757
MAPT-6778	27 mer antisense strand	6778-6839 (Hs-Mf)	UACAGUAACAGUCAGUGUAAAUCAUUU	758
MAPT-6779	27 mer antisense strand	6779-6840 (Hs-Mf)	UUACAUCAACAGUCAGUGUAAAUCAUU	759
MAPT-6780	27 mer antisense strand	6780-6841 (Hs-Mf)	UUUACUGCAACAGUCAGUGUAAAUCAU	760
MAPT-6781	27 mer antisense strand	6781 (Hs)	UUUUAUAGCAACAGUCAGUGUAAAUCA	761
MAPT-6789	27 mer antisense strand	6789 (Hs)	AAAUUUACUUUUACAGCAACAGUCAGU	762
MAPT-6792	27 mer antisense strand	6792 (Hs)	UCCAAUUUCACUUUUACAGCAACAGUC	763
MAPT-6793	27 mer antisense strand	6793 (Hs)	UUCCAUAUUCACUUUUACAGCAACAGU	764
MAPT-6795	27 mer antisense strand	6795 (Hs)	AUUUCUAAAUUCACUUUUACAGCAACA	765
MAPT-6796	27 mer antisense strand	6796 (Hs)	UAUUUUCAAAUUCACUUUUACAGCAAC	766
MAPT-6797	27 mer antisense strand	6797 (Hs)	UUAUUUCCAAAUUCACUUUUACAGCAA	767
MAPT-6798	27 mer antisense strand	6798 (Hs)	UUUAUUUCCAAAUUCACUUUUACAGCA	768

MAPT-2456	Unmodified 36mer sense strand	2456-2533 (Hs-Mf)	AAAAAGAUUGAAACCCACAAGCAGCCGAAAGGCUGC	769
MAPT-2567	Unmodified 36mer sense strand	2567 (Hs)	CGGCAUCUCAGCAAUGUCUAGCAGCCGAAAGGCUGC	770
MAPT-2723	Unmodified 36mer sense strand	2723-2800 (Hs-Mf)	AGAGUGUGGAAAAAAAAAGAGCAGCCGAAAGGCUGC	771
MAPT-0690	Unmodified 36mer sense strand	690-455 (Hs-Mf)	AAGACGAAGCUGCUGGUCAAGCAGCCGAAAGGCUGC	772
MAPT-1494	Unmodified 36mer sense strand	1494-1571 (Hs-Mf)	AAGACGGGACUGGAAGCGAAGCAGCCGAAAGGCUGC	773
MAPT-1733	Unmodified 36mer sense strand	1733 (Hs)	GAUGGUAAAACGAAGAUCGAGCAGCCGAAAGGCUGC	774
MAPT-2273	Unmodified 36mer sense strand	2273-2350 (Hs-Mf)	AUAGUCUACAAACCAGUUGAGCAGCCGAAAGGCUGC	775
MAPT-2274	Unmodified 36mer sense strand	2274-2351 (Hs-Mf)	UAGUCUACAAACCAGUUGAAGCAGCCGAAAGGCUGC	776
MAPT-2276	Unmodified 36mer sense strand	2276-2353 (Hs-Mf)	GUCUACAAACCAGUUGACCAGCAGCCGAAAGGCUGC	777
MAPT-2301	Unmodified 36mer sense strand	2301-2378 (Hs-Mf)	AGGUGACCUCCAAGUGUGGAGCAGCCGAAAGGCUGC	778
MAPT-2347	Unmodified 36mer	2347-2424-1172 (Hs-Mf-Mm)	AGGAGGUGGCCAGGUGGAAAGCAGCCGAAAGGCUGC	779

	sense strand			
MAPT-2357	Unmodified 36mer sense strand	2357-2434 (Hs-Mf)	CAGGUGGAAGUAAAAUCUGAGCAGCCGAAAGGCUGC	780
MAPT-2358	Unmodified 36mer sense strand	2358-2435 (Hs-Mf)	AGGUGGAAGUAAAAUCUGAAGCAGCCGAAAGGCUGC	781
MAPT-2364	Unmodified 36mer sense strand	2364-2441 (Hs-Mf)	AAGUAAAAUCUGAGAAGCUAGCAGCCGAAAGGCUGC	782
MAPT-2378	Unmodified 36mer sense strand	2378 (Hs)	AAGCUUGACUUCAAGGACAAGCAGCCGAAAGGCUGC	783
MAPT-2459	Unmodified 36mer sense strand	2459-2536-1284 (Hs-Mf-Mm)	AAGAUUGAAACCCACAAGCAGCAGCCGAAAGGCUGC	784
MAPT-2461	Unmodified 36mer sense strand	2461-2538-1286 (Hs-Mf-Mm)	GAUUGAAACCCACAAGCUGAGCAGCCGAAAGGCUGC	785
MAPT-2460	Unmodified 36mer sense strand	2460-2537-1285 (Hs-Mf-Mm)	AGAUUGAAACCCACAAGCUAGCAGCCGAAAGGCUGC	786
MAPT-1479	Unmodified 36mer sense strand	1479-1556 (Hs-Mf)	UGGUCAGUAAAAGCAAAGAAGCAGCCGAAAGGCUGC	787
MAPT-1505	Unmodified 36mer sense strand	1505-1582 (Hs-Mf)	GGAAGCGAUGACAAAAAAGAGCAGCCGAAAGGCUGC	788
MAPT-2096	Unmodified 36mer sense strand	2096-2173 (Hs-Mf)	CCCAUGCCAGACCUGAAGAAGCAGCCGAAAGGCUGC	789

MAPT-2270	Unmodified 36mer sense strand	2270-2347 (Hs-Mf)	CAAAUAGUCUACAAACCAGAGCAGCCGAAAGGCUGC	790
MAPT-2279	Unmodified 36mer sense strand	2279-2356 (Hs-Mf)	UACAAACCAGUUGACCUGAAGCAGCCGAAAGGCUGC	791
MAPT-2281	Unmodified 36mer sense strand	2281-2358 (Hs-Mf)	CAAACCAGUUGACCUGAGCAGCAGCCGAAAGGCUGC	792
MAPT-2284	Unmodified 36mer sense strand	2284-2361 (Hs-Mf)	ACCAGUUGACCUGAGCAAGAGCAGCCGAAAGGCUGC	793
MAPT-2299	Unmodified 36mer sense strand	2299-2376 (Hs-Mf)	CAAGGUGACCUCCAAGUGUAGCAGCCGAAAGGCUGC	794
MAPT-2376	Unmodified 36mer sense strand	2376 (Hs)	AGAAGCUUGACUUCAAGGAAGCAGCCGAAAGGCUGC	795
MAPT-2379	Unmodified 36mer sense strand	2379 (Hs)	AGCUUGACUUCAAGGACAGAGCAGCCGAAAGGCUGC	796
MAPT-2382	Unmodified 36mer sense strand	2382 (Hs)	UUGACUUCAAGGACAGAGUAGCAGCCGAAAGGCUGC	797
MAPT-2449	Unmodified 36mer sense strand	2449-2526 (Hs-Mf)	AGGAAAUAAAAAGAUUGAAAGCAGCCGAAAGGCUGC	798
MAPT-2450	Unmodified 36mer sense strand	2450-2527 (Hs-Mf)	GGAAAUAAAAAGAUUGAAAAGCAGCCGAAAGGCUGC	799
MAPT-2451	Unmodified 36mer	2451-2528 (Hs-Mf)	GAAAUAAAAAGAUUGAAACAGCAGCCGAAAGGCUGC	800

	sense strand			
MAPT-2452	Unmodified 36mer sense strand	2452-2529 (Hs-Mf)	AAAUAAAAAGAUUGAAACCAGCAGCCGAAAGGCUGC	801
MAPT-2453	Unmodified 36mer sense strand	2453-2530 (Hs-Mf)	AAUAAAAAGAUUGAAACCCAGCAGCCGAAAGGCUGC	802
MAPT-2454	Unmodified 36mer sense strand	2454-2531 (Hs-Mf)	AUAAAAAGAUUGAAACCCAAGCAGCCGAAAGGCUGC	803
MAPT-2456	unmodified 22mer antisense strand	2456-2533 (Hs-Mf)	UUGUGGGUUUCAAUCUUUUUGG	804
MAPT-2567	unmodified 22mer antisense strand	2567 (Hs)	UAGACAUUGCUGAGAUGCCGGG	805
MAPT-2723	unmodified 22mer antisense strand	2723-2800 (Hs-Mf)	UCUUUUUUUUUCCACACUCUGG	806
MAPT-0690	unmodified 22mer antisense strand	690-455 (Hs-Mf)	UUGACCAGCAGCUUCGUCUUGG	807
MAPT-1494	unmodified 22mer antisense strand	1494-1571 (Hs-Mf)	UUCGCUUCCAGUCCCGUCUUGG	808
MAPT-1733	unmodified 22mer antisense strand	1733 (Hs)	UCGAUCUUCGUUUUACCAUCGG	809
MAPT-2273	unmodified 22mer antisense strand	2273-2350 (Hs-Mf)	UCAACUGGUUUGUAGACUAUGG	810

MAPT-2274	unmodified 22mer antisense strand	2274-2351 (Hs-Mf)	UUCAACUGGUUUGUAGACUAGG	811
MAPT-2276	unmodified 22mer antisense strand	2276-2353 (Hs-Mf)	UGGUCAACUGGUUUGUAGACGG	812
MAPT-2301	unmodified 22mer antisense strand	2301-2378 (Hs-Mf)	UCCACACUUGGAGGUCACCUGG	813
MAPT-2347	unmodified 22mer antisense strand	2347-2424-1172 (Hs-Mf-Mm)	UUUCCACCUGGCCACCUCCUGG	814
MAPT-2357	unmodified 22mer antisense strand	2357-2434 (Hs-Mf)	UCAGAUUUUACUUCCACCUGGG	815
MAPT-2358	unmodified 22mer antisense strand	2358-2435 (Hs-Mf)	UUCAGAUUUUACUUCCACCUGG	816
MAPT-2364	unmodified 22mer antisense strand	2364-2441 (Hs-Mf)	UAGCUUCUCAGAUUUUACUUGG	817
MAPT-2378	unmodified 22mer antisense strand	2378 (Hs)	UUGUCCUUGAAGUCAAGCUUGG	818
MAPT-2459	unmodified 22mer antisense strand	2459-2536-1284 (Hs-Mf-Mm)	UGCUUGUGGGUUUCAAUCUUGG	819
MAPT-2461	unmodified 22mer antisense strand	2461-2538-1286 (Hs-Mf-Mm)	UCAGCUUGUGGGUUUCAAUCGG	820
MAPT-2460	unmodified 22mer	2460-2537-1285 (Hs-Mf-Mm)	UAGCUUGUGGGUUUCAAUCUGG	821

	antisense strand			
MAPT-1479	unmodified 22mer antisense strand	1479-1556 (Hs-Mf)	UUCUUUGCUUUUACUGACCAGG	822
MAPT-1505	unmodified 22mer antisense strand	1505-1582 (Hs-Mf)	UCUUUUUUGUCAUCGCUUCCGG	823
MAPT-2096	unmodified 22mer antisense strand	2096-2173 (Hs-Mf)	UUCUUCAGGUCUGGCAUGGGGG	824
MAPT-2270	unmodified 22mer antisense strand	2270-2347 (Hs-Mf)	UCUGGUUUGUAGACUAUUUGGG	825
MAPT-2279	unmodified 22mer antisense strand	2279-2356 (Hs-Mf)	UUCAGGUCAACUGGUUUGUAGG	826
MAPT-2281	unmodified 22mer antisense strand	2281-2358 (Hs-Mf)	UGCUCAGGUCAACUGGUUUGGG	827
MAPT-2284	unmodified 22mer antisense strand	2284-2361 (Hs-Mf)	UCUUGCUCAGGUCAACUGGUGG	828
MAPT-2299	unmodified 22mer antisense strand	2299-2376 (Hs-Mf)	UACACUUGGAGGUCACCUUGGG	829
MAPT-2376	unmodified 22mer antisense strand	2376 (Hs)	UUCCUUGAAGUCAAGCUUCUGG	830
MAPT-2379	unmodified 22mer antisense strand	2379 (Hs)	UCUGUCCUUGAAGUCAAGCUGG	831

MAPT-2382	unmodified 22mer antisense strand	2382 (Hs)	UACUCUGUCCUUGAAGUCAAGG	832
MAPT-2449	unmodified 22mer antisense strand	2449-2526 (Hs-Mf)	UUUCAAUCUUUUUAUUUCCUGG	833
MAPT-2450	unmodified 22mer antisense strand	2450-2527 (Hs-Mf)	UUUUCAAUCUUUUUAUUUCCGG	834
MAPT-2451	unmodified 22mer antisense strand	2451-2528 (Hs-Mf)	UGUUUCAAUCUUUUUAUUUCGG	835
MAPT-2452	unmodified 22mer antisense strand	2452-2529 (Hs-Mf)	UGGUUUCAAUCUUUUUAUUUGG	836
MAPT-2453	unmodified 22mer antisense strand	2453-2530 (Hs-Mf)	UGGGUUUCAAUCUUUUUAUUGG	837
MAPT-2454	unmodified 22mer antisense strand	2454-2531 (Hs-Mf)	UUGGGUUUCAAUCUUUUUAUGG	838
MAPT-2456	Modified 36mer sense strand	2456-2533 (Hs-Mf)	[mAs][mA][fA][mA][fA][mG][mA][fU][mU][fG][mA][fA][fA][mC][fC][mC][fA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	839
MAPT-2567	Modified 36mer sense strand	2567 (Hs)	[mCs][mG][fG][mC][fA][mU][mC][fU][mC][fA][mG][fC][fA][mA][fU][mG][fU][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	840
MAPT-2723	Modified 36mer sense strand	2723-2800 (Hs-Mf)	[mAs][mG][fA][mG][fU][mG][mU][fG][mG][fA][mA][fA][fA][mA][fA][mA][fA][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	841

MAPT-0690	Modified 36mer sense strand	690-455 (Hs-Mf)	[mAs][mA][fG][mA][fC][mG][mA][fA][mG][fC][mU][fG][fC][mU][fG][mG][fU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	842
MAPT-1494	Modified 36mer sense strand	1494-1571 (Hs-Mf)	[mAs][mA][fG][mA][fC][mG][mG][fG][mA][fC][mU][fG][fG][mA][fA][mG][fC][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	843
MAPT-1733	Modified 36mer sense strand	1733 (Hs)	[mGs][mA][fU][mG][fG][mU][mA][fA][mA][fA][mC][fG][fA][mA][fG][mA][fU][mC][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	844
MAPT-2273	Modified 36mer sense strand	2273-2350 (Hs-Mf)	[mAs][mU][fA][mG][fU][mC][mU][fA][mC][fA][mA][fA][fC][mC][fA][mG][fU][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	845
MAPT-2274	Modified 36mer sense strand	2274-2351 (Hs-Mf)	[mUs][mA][fG][mU][fC][mU][mA][fC][mA][fA][mA][fC][fC][mA][fG][mU][fU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	846
MAPT-2276	Modified 36mer sense strand	2276-2353 (Hs-Mf)	[mGs][mU][fC][mU][fA][mC][mA][fA][mA][fC][mC][fA][fG][mU][fU][mG][fA][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	847
MAPT-2301	Modified 36mer sense strand	2301-2378 (Hs-Mf)	[mAs][mG][fG][mU][fG][mA][mC][fC][mU][fC][mC][fA][fA][mG][fU][mG][fU][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	848
MAPT-2347	Modified 36mer sense strand	2347-2424-1172 (Hs-Mf-Mm)	[mAs][mG][fG][mA][fG][mG][mU][fG][mG][fC][mC][fA][fG][mG][fU][mG][fG][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	849
MAPT-2357	Modified 36mer	2357-2434 (Hs-Mf)	[mCs][mA][fG][mG][fU][mG][mG][fA][mA][fG][mU][fA][fA][mA][fA][mU][fC][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][adem	850

	sense strand		A-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	
MAPT-2358	Modified 36mer sense strand	2358-2435 (Hs-Mf)	[mAs][mG][fG][mU][fG][mG][mA][fA][mG][fU][mA][fA][fA][mA][fU][mC][fU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	851
MAPT-2364	Modified 36mer sense strand	2364-2441 (Hs-Mf)	[mAs][mA][fG][mU][fA][mA][mA][fA][mU][fC][mU][fG][fA][mG][fA][mA][fG][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	852
MAPT-2378	Modified 36mer sense strand	2378 (Hs)	[mAs][mA][fG][mC][fU][mU][mG][fA][mC][fU][mU][fC][fA][mA][fG][mG][fA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	853
MAPT-2459	Modified 36mer sense strand	2459-2536-1284 (Hs-Mf-Mm)	[mAs][mA][fG][mA][fU][mU][mG][fA][mA][fA][mC][fC][fC][mA][fC][mA][fA][mG][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	854
MAPT-2461	Modified 36mer sense strand	2461-2538-1286 (Hs-Mf-Mm)	[mGs][mA][fU][mU][fG][mA][mA][fA][mC][fC][mC][fA][fC][mA][fA][mG][fC][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	855
MAPT-2460	Modified 36mer sense strand	2460-2537-1285 (Hs-Mf-Mm)	[mAs][mG][mA][mU][mU][mG][mA][fA][fA][fC][fC][mC][mA][mC][mA][mA][mG][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	856
MAPT-1479	Modified 36mer sense strand	1479-1556 (Hs-Mf)	[mUs][mG][fG][mU][fC][mA][mG][fU][mA][fA][mA][fA][fG][mC][fA][mA][fA][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	857
MAPT-1505	Modified 36mer sense strand	1505-1582 (Hs-Mf)	[mGs][mG][fA][mA][fG][mC][mG][fA][mU][fG][mA][fC][fA][mA][fA][mA][fA][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	858

MAPT-2096	Modified 36mer sense strand	2096-2173 (Hs-Mf)	[mCs][mC][fC][mA][fU][mG][mC][fC][mA][fG][mA][fC][fC][mU][fG][mA][fA][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	859
MAPT-2270	Modified 36mer sense strand	2270-2347 (Hs-Mf)	[mCs][mA][fA][mA][fU][mA][mG][fU][mC][fU][mA][fC][fA][mA][fA][mC][fC][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	860
MAPT-2279	Modified 36mer sense strand	2279-2356 (Hs-Mf)	[mUs][mA][fC][mA][fA][mA][mC][fC][mA][fG][mU][fU][fG][mA][fC][mC][fU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	861
MAPT-2281	Modified 36mer sense strand	2281-2358 (Hs-Mf)	[mCs][mA][fA][mA][fC][mC][mA][fG][mU][fU][mG][fA][fC][mC][fU][mG][fA][mG][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	862
MAPT-2284	Modified 36mer sense strand	2284-2361 (Hs-Mf)	[mAs][mC][fC][mA][fG][mU][mU][fG][mA][fC][mC][fU][fG][mA][fG][mC][fA][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	863
MAPT-2299	Modified 36mer sense strand	2299-2376 (Hs-Mf)	[mCs][mA][fA][mG][fG][mU][mG][fA][mC][fC][mU][fC][fC][mA][fA][mG][fU][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	864
MAPT-2376	Modified 36mer sense strand	2376 (Hs)	[mAs][mG][fA][mA][fG][mC][mU][fU][mG][fA][mC][fU][fU][mC][fA][mA][fG][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	865
MAPT-2379	Modified 36mer sense strand	2379 (Hs)	[mAs][mG][fC][mU][fU][mG][mA][fC][mU][fU][mC][fA][fA][mG][fG][mA][fC][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	866
MAPT-2382	Modified 36mer	2382 (Hs)	[mUs][mU][fG][mA][fC][mU][mU][fC][mA][fA][mG][fG][fA][mC][fA][mG][fA][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][adem	867

	sense strand		A-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	
MAPT-2449	Modified 36mer sense strand	2449-2526 (Hs-Mf)	[mAs][mG][fG][mA][fA][mA][mU][fA][mA][fA][mA][fA][fG][mA][fU][mU][fG][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	868
MAPT-2450	Modified 36mer sense strand	2450-2527 (Hs-Mf)	[mGs][mG][fA][mA][fA][mU][mA][fA][mA][fA][mA][fG][fA][mU][fU][mG][fA][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	869
MAPT-2451	Modified 36mer sense strand	2451-2528 (Hs-Mf)	[mGs][mA][fA][mA][fU][mA][mA][fA][mA][fA][mG][fA][fU][mU][fG][mA][fA][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	870
MAPT-2452	Modified 36mer sense strand	2452-2529 (Hs-Mf)	[mAs][mA][fA][mU][fA][mA][mA][fA][mA][fG][mA][fU][fU][mG][fA][mA][fA][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	871
MAPT-2453	Modified 36mer sense strand	2453-2530 (Hs-Mf)	[mAs][mA][fU][mA][fA][mA][mA][fA][mG][fA][mU][fU][fG][mA][fA][mA][fC][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	872
MAPT-2454	Modified 36mer sense strand	2454-2531 (Hs-Mf)	[mAs][mU][fA][mA][fA][mA][mA][fG][mA][fU][mU][fG][fA][mA][fA][mC][fC][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	873
MAPT-2456	Modified 22mer antisense strand	2456-2533 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fG][fU][fG][mG][fG][mU][mU][fU][mC][mA][mA][fU][mC][fU][mU][mU][fU][mUs][mGs][mG]	874
MAPT-2567	Modified 22mer antisense strand	2567 (Hs)	[MePhosphonate-4O-mUs][fAs][fG][fA][fC][mA][fU][mU][mG][fC][mU][mG][mA][fG][mA][fU][mG][mC][fC][mGs][mGs][mG]	875
MAPT-2723	Modified 22mer	2723-2800 (Hs-Mf)	[MePhosphonate-4O-mUs][fCs][fU][fU][fU][mU][fU][mU][mU][fU][	876

	antisense strand		mU][mC][mC][fA][mC][fA][mC][mU][fC][mUs][mGs][mG]	
MAPT-0690	Modified 22mer antisense strand	690-455 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fG][fA][fC][mC][fA][mG][mC][fA][mG][mC][mU][fU][mC][fG][mU][mC][fU][mUs][mGs][mG]	877
MAPT-1494	Modified 22mer antisense strand	1494-1571 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fC][fG][fC][mU][fU][mC][mC][fA][mG][mU][mC][fC][mC][fG][mU][mC][fU][mUs][mGs][mG]	878
MAPT-1733	Modified 22mer antisense strand	1733 (Hs)	[MePhosphonate-4O-mUs][fCs][fG][fA][fU][mC][fU][mU][mC][fG][mU][mU][mU][fU][mA][fC][mC][mA][fU][mCs][mGs][mG]	879
MAPT-2273	Modified 22mer antisense strand	2273-2350 (Hs-Mf)	[MePhosphonate-4O-mUs][fCs][fA][fA][fC][mU][fG][mG][mU][fU][mU][mG][mU][fA][mG][fA][mC][mU][fA][mUs][mGs][mG]	880
MAPT-2274	Modified 22mer antisense strand	2274-2351 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fC][fA][fA][mC][fU][mG][mG][fU][mU][mU][mG][fU][mA][fG][mA][mC][fU][mAs][mGs][mG]	881
MAPT-2276	Modified 22mer antisense strand	2276-2353 (Hs-Mf)	[MePhosphonate-4O-mUs][fGs][fG][fU][fC][mA][fA][mC][mU][fG][mG][mU][mU][fU][mG][fU][mA][mG][fA][mCs][mGs][mG]	882
MAPT-2301	Modified 22mer antisense strand	2301-2378 (Hs-Mf)	[MePhosphonate-4O-mUs][fCs][fC][fA][fC][mA][fC][mU][mU][fG][mG][mA][mG][fG][mU][fC][mA][mC][fC][mUs][mGs][mG]	883
MAPT-2347	Modified 22mer antisense strand	2347-2424-1172 (Hs-Mf-Mm)	[MePhosphonate-4O-mUs][fUs][fU][fC][fC][mA][fC][mC][mU][fG][mG][mC][mC][fA][mC][fC][mU][mC][fC][mUs][mGs][mG]	884
MAPT-2357	Modified 22mer antisense strand	2357-2434 (Hs-Mf)	[MePhosphonate-4O-mUs][fCs][fA][fG][fA][mU][fU][mU][mU][fA][mC][mU][mU][fC][mC][fA][mC][mC][fU][mGs][mGs][mG]	885
MAPT-2358	Modified 22mer antisense strand	2358-2435 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fC][fA][fG][mA][fU][mU][mU][fU][mA][mC][mU][fU][mC][fC][mA][mC][fC][mUs][mGs][mG]	886

MAPT-2364	Modified 22mer antisense strand	2364-2441 (Hs-Mf)	[MePhosphonate-4O-mUs][fAs][fG][fC][fU][mU][fC][mU][mC][fA][mG][mA][mU][fU][mU][fU][mA][mC][fU][mUs][mGs][mG]	887
MAPT-2378	Modified 22mer antisense strand	2378 (Hs)	[MePhosphonate-4O-mUs][fUs][fG][fU][fC][mC][fU][mU][mG][fA][mA][mG][mU][fC][mA][fA][mG][mC][fU][mUs][mGs][mG]	888
MAPT-2459	Modified 22mer antisense strand	2459-2536-1284 (Hs-Mf-Mm)	[MePhosphonate-4O-mUs][fGs][fC][fU][fU][mG][fU][mG][mG][fG][mU][mU][mU][fC][mA][fA][mU][mC][fU][mUs][mGs][mG]	889
MAPT-2461	Modified 22mer antisense strand	2461-2538-1286 (Hs-Mf-Mm)	[MePhosphonate-4O-mUs][fCs][fA][fG][fC][mU][fU][mG][mU][fG][mG][mG][mU][fU][mU][fC][mA][mA][fU][mCs][mGs][mG]	890
MAPT-2460	Modified 22mer antisense strand	2460-2537-1285 (Hs-Mf-Mm)	[MePhosphonate-4O-mUs][fAs][fGs][fC][fU][mU][fG][mU][mG][fG][mG][mU][mU][fU][mC][mA][mA][mU][mC][mUs][mGs][mG]	891
MAPT-1479	Modified 22mer antisense strand	1479-1556 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fC][fU][fU][mU][fG][mC][mU][fU][mU][mU][mA][fC][mU][fG][mA][mC][fC][mAs][mGs][mG]	892
MAPT-1505	Modified 22mer antisense strand	1505-1582 (Hs-Mf)	[MePhosphonate-4O-mUs][fCs][fU][fU][fU][mU][fU][mU][mG][fU][mC][mA][mU][fC][mG][fC][mU][mU][fC][mCs][mGs][mG]	893
MAPT-2096	Modified 22mer antisense strand	2096-2173 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fC][fU][fU][mC][fA][mG][mG][fU][mC][mU][mG][fG][mC][fA][mU][mG][fG][mGs][mGs][mG]	894
MAPT-2270	Modified 22mer antisense strand	2270-2347 (Hs-Mf)	[MePhosphonate-4O-mUs][fCs][fU][fG][fG][mU][fU][mU][mG][fU][mA][mG][mA][fC][mU][fA][mU][mU][fU][mGs][mGs][mG]	895
MAPT-2279	Modified 22mer antisense strand	2279-2356 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fC][fA][fG][mG][fU][mC][mA][fA][mC][mU][mG][fG][mU][fU][mU][mG][fU][mAs][mGs][mG]	896
MAPT-2281	Modified 22mer	2281-2358 (Hs-Mf)	[MePhosphonate-4O-mUs][fGs][fC][fU][fC][mA][fG][mG][mU][fC][	897

	antisense strand		mA][mA][mC][fU][mG][fG][mU][mU][fU][mGs][mGs][mG]	
MAPT-2284	Modified 22mer antisense strand	2284-2361 (Hs-Mf)	[MePhosphonate-4O-mUs][fCs][fU][fU][fG][mC][fU][mC][mA][fG][mG][mU][mC][fA][mA][fC][mU][mG][fG][mUs][mGs][mG]	898
MAPT-2299	Modified 22mer antisense strand	2299-2376 (Hs-Mf)	[MePhosphonate-4O-mUs][fAs][fC][fA][fC][mU][fU][mG][mG][fA][mG][mG][mU][fC][mA][fC][mC][mU][fU][mGs][mGs][mG]	899
MAPT-2376	Modified 22mer antisense strand	2376 (Hs)	[MePhosphonate-4O-mUs][fUs][fC][fC][fU][mU][fG][mA][mA][fG][mU][mC][mA][fA][mG][fC][mU][mU][fC][mUs][mGs][mG]	900
MAPT-2379	Modified 22mer antisense strand	2379 (Hs)	[MePhosphonate-4O-mUs][fCs][fU][fG][fU][mC][fC][mU][mU][fG][mA][mA][mG][fU][mC][fA][mA][mG][fC][mUs][mGs][mG]	901
MAPT-2382	Modified 22mer antisense strand	2382 (Hs)	[MePhosphonate-4O-mUs][fAs][fC][fU][fC][mU][fG][mU][mC][fC][mU][mU][mG][fA][mA][fG][mU][mC][fA][mAs][mGs][mG]	902
MAPT-2449	Modified 22mer antisense strand	2449-2526 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fU][fC][fA][mA][fU][mC][mU][fU][mU][mU][mU][fA][mU][fU][mU][mC][fC][mUs][mGs][mG]	903
MAPT-2450	Modified 22mer antisense strand	2450-2527 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fU][fU][fC][mA][fA][mU][mC][fU][mU][mU][mU][fU][mA][fU][mU][mU][fC][mCs][mGs][mG]	904
MAPT-2451	Modified 22mer antisense strand	2451-2528 (Hs-Mf)	[MePhosphonate-4O-mUs][fGs][fU][fU][fU][mC][fA][mA][mU][fC][mU][mU][mU][fU][mU][fA][mU][mU][fU][mCs][mGs][mG]	905
MAPT-2452	Modified 22mer antisense strand	2452-2529 (Hs-Mf)	[MePhosphonate-4O-mUs][fGs][fG][fU][fU][mU][fC][mA][mA][fU][mC][mU][mU][fU][mU][fU][mA][mU][fU][mUs][mGs][mG]	906
MAPT-2453	Modified 22mer antisense strand	2453-2530 (Hs-Mf)	[MePhosphonate-4O-mUs][fGs][fG][fG][fU][mU][fU][mC][mA][fA][mU][mC][mU][fU][mU][fU][mU][mA][fU][mUs][mGs][mG]	907

MAPT-2454	Modified 22mer antisense strand	2454-2531 (Hs-Mf)	[MePhosphonate-4O-mUs][fUs][fG][fG][fG][mU][fU][mU][mC][fA][mA][mU][mC][fU][mU][fU][mU][mU][fA][mUs][mGs][mG]	908
Human MAPT RefSeq	NM_001123066.3	N/A	ATGGCTGAGCCCCGCCAGGAGTTCGAAG TGATGGAAGATCACGCTGGGACGTACGG GTTGGGGGACAGGAAAGATCAGGGGGGC TACACCATGCACCAAGACCAAGAGGGTG ACACGGACGCTGGCCTGAAAGAATCTCC CCTGCAGACCCCCACTGAGGACGGATCT GAGGAACCGGGCTCTGAAACCTCTGATG CTAAGAGCACTCCAACAGCGGAAGATGT GACAGCACCCTTAGTGGATGAGGGAGCT CCCGGCAAGCAGGCTGCCGCGCAGCCCC ACACGGAGATCCCAGAAGGAACCACAGC TGAAGAAGCAGGCATTGGAGACACCCCC AGCCTGGAAGACGAAGCTGCTGGTCACG TGACCCAAGAGCCTGAAAGTGGTAAGGT GGTCCAGGAAGGCTTCCTCCGAGAGCCA GGCCCCCCAGGTCTGAGCCACCAGCTCA TGTCCGGCATGCCTGGGGCTCCCCTCCTG CCTGAGGGCCCCAGAGAGGCCACACGCC AACCTTCGGGGACAGGACCTGAGGACAC AGAGGGCGGCCGCCACGCCCCTGAGCTG CTCAAGCACCAGCTTCTAGGAGACCTGC ACCAGGAGGGGCCGCCGCTGAAGGGGGC AGGGGGCAAAGAGAGGCCGGGGAGCAA GGAGGAGGTGGATGAAGACCGCGACGTC GATGAGTCCTCCCCCCAAGACTCCCCTCC CTCCAAGGCCTCCCCAGCCCAAGATGGG CGGCCTCCCCAGACAGCCGCCAGAGAAG CCACCAGCATCCCAGGCTTCCCAGCGGA GGGTGCCATCCCCCTCCCTGTGGATTTCC TCTCCAAAGTTTCCACAGAGATCCCAGCC TCAGAGCCCGACGGGCCCAGTGTAGGGC GGGCCAAAGGGCAGGATGCCCCCCTGGA GTTCACGTTTCACGTGGAAATCACACCCA ACGTGCAGAAGGAGCAGGCGCACTCGGA GGAGCATTTGGGAAGGGCTGCATTTCCA GGGGCCCCTGGAGAGGGGCCAGAGGCCC GGGGCCCCTCTTTGGGAGAGGACACAAA AGAGGCTGACCTTCCAGAGCCCTCTGAA AAGCAGCCTGCTGCTGCTCCGCGGGGGA AGCCCGTCAGCCGGGTCCCTCAACTCAA	909

			AGCTCGCATGGTCAGTAAAAGCAAAGAC GGGACTGGAAGCGATGACAAAAAAGCCA AGACATCCACACGTTCCTCTGCTAAAACC TTGAAAAATAGGCCTTGCCTTAGCCCCAA ACACCCCACTCCTGGTAGCTCAGACCCTC TGATCCAACCCTCCAGCCCTGCTGTGTGC CCAGAGCCACCTTCCTCTCCTAAATACGT CTCTTCTGTCACTTCCCGAACTGGCAGTT CTGGAGCAAAGGAGATGAAACTCAAGGG GGCTGATGGTAAAACGAAGATCGCCACA CCGCGGGGAGCAGCCCCTCCAGGCCAGA AGGGCCAGGCCAACGCCACCAGGATTCC AGCAAAAACCCCGCCCGCTCCAAAGACA CCACCCAGCTCTGCGACTAAGCAAGTCC AGAGAAGACCACCCCCTGCAGGGCCCAG ATCTGAGAGAGGTGAACCTCCAAAATCA GGGGATCGCAGCGGCTACAGCAGCCCCG GCTCCCCAGGCACTCCCGGCAGCCGCTC CCGCACCCCGTCCCTTCCAACCCCACCCA CCCGGGAGCCCAAGAAGGTGGCAGTGGT CCGTACTCCACCCAAGTCGCCGTCTTCCG CCAAGAGCCGCCTGCAGACAGCCCCCGT GCCCATGCCAGACCTGAAGAATGTCAAG TCCAAGATCGGCTCCACTGAGAACCTGA AGCACCAGCCGGGAGGCGGGAAGGTGCA GATAATTAATAAGAAGCTGGATCTTAGC AACGTCCAGTCCAAGTGTGGCTCAAAGG ATAATATCAAACACGTCCCGGGAGGCGG CAGTGTGCAAATAGTCTACAAACCAGTT GACCTGAGCAAGGTGACCTCCAAGTGTG GCTCATTAGGCAACATCCATCATAAACC AGGAGGTGGCCAGGTGGAAGTAAAATCT GAGAAGCTTGACTTCAAGGACAGAGTCC AGTCGAAGATTGGGTCCCTGGACAATAT CACCCACGTCCCTGGCGGAGGAAATAAA AAGATTGAAACCCACAAGCTGACCTTCC GCGAGAACGCCAAAGCCAAGACAGACCA CGGGGCGGAGATCGTGTACAAGTCGCCA GTGGTGTCTGGGGACACGTCTCCACGGC ATCTCAGCAATGTCTCCTCCACCGGCAGC ATCGACATGGTAGACTCGCCCCAGCTCG CCACGCTAGCTGACGAGGTGTCTGCCTCC CTGGCCAAGCAGGGTTTGTGA	

Mouse MAPT RefSeq	NM_001 038609	N/A	ATGGCTGACCCTCGCCAGGAGTTTGACA CAATGGAAGACCATGCTGGAGATTACAC TCTGCTCCAAGACCAAGAAGGAGACATG GACCATGGCTTAAAAGAGTCTCCCCCAC AGCCCCCCGCCGATGATGGAGCGGAGGA ACCAGGGTCGGAGACCTCCGATGCTAAG AGCACTCCAACTGCTGAAGACGTGACTG CGCCCCTAGTGGATGAGAGAGCTCCCGA CAAGCAGGCCGCTGCCCAGCCCCACACG GAGATCCCAGAAGGAATTACAGCCGAAG AAGCAGGCATCGGAGACACCCCGAACCA GGAGGACCAAGCCGCTGGGCATGTGACT CAAGCTCGTGTGGCCAGCAAAGACAGGA CAGGAAATGACGAGAAGAAAGCCAAGG GCGCTGATGGCAAAACCGGGGCGAAGAT CGCCACACCTCGGGGAGCAGCCTCTCCG GCCCAGAAGGGCACGTCCAACGCCACCA GGATCCCGGCCAAGACCACGCCCAGCCC TAAGACTCCTCCAGGGTCAGGTGAACCA CCAAAATCCGGAGAACGAAGCGGCTACA GCAGCCCCGGCTCTCCCGGAACGCCTGG CAGTCGCTCGCGCACCCCATCCCTACCAA CACCGCCCACCCGGGAGCCCAAGAAGGT GGCAGTGGTCCGCACTCCCCCTAAGTCAC CATCAGCTAGTAAGAGCCGCCTGCAGAC TGCCCCTGTGCCCATGCCAGACCTAAAG AATGTCAGGTCGAAGATTGGCTCTACTG AGAACCTGAAGCACCAGCCAGGAGGTGG CAAGGTGCAGATAATTAATAAGAAGCTG GATCTTAGCAACGTCCAGTCCAAGTGTG GCTCGAAGGATAATATCAAACACGTCCC GGGTGGAGGCAGTGTGCAAATAGTCTAC AAGCCGGTGGACCTGAGCAAAGTGACCT CCAAGTGTGGCTCGTTAGGGAACATCCA TCACAAGCCAGGAGGTGGCCAGGTGGAA GTAAAATCAGAGAAGCTGGACTTCAAGG ACAGAGTCCAGTCGAAGATTGGCTCCTT GGATAATATCACCCACGTCCCTGGAGGA GGGAATAAGAAGATTGAAACCCACAAGC TGACCTTCAGGGAGAATGCCAAAGCCAA GACAGACCATGGAGCAGAAATTGTGTAT AAGTCACCCGTGGTGTCTGGGGACACAT CTCCACGGCACCTCAGCAATGTGTCTTCC ACGGGCAGCATCGACATGGTGGACTCAC	910

			CACAGCTTGCCACACTAGCCGATGAAGT GTCTGCTTCCTTGGCCAAGCAGGGTTTGT GA	
Monkey MAPT RefSEQ	XM_005 584531	N/A	ATGGCTGAGCCCCGCCAGGAGTTCGATG TGATGGAAGATCACGCTGGGACGTACGG GTTGGGGGACAGGAAAGATCAAGAGGGC TACACCATGCTCCAAGACCAAGAGGGTG ACACGGACGCTGGCCTGAAAGAATCTCC CCTGCAGACCCCCGCTGAGGATGGATCT GAGGAACTGGGCTCTGAAACCTCTGATG CTAAGAGCACTCCAACGGCGGAAGCTGA GGAAGCAGGCATCGGAGACACCCCCAGC CTGGAAGACGAAGCTGCTGGTCACGTGA CCCAAGAGGAGTTGAGAGTTCCGGGCCA GCAGAGGAAGGCACCTGAAAGGCCCCTG GCCAATGAGATTAGTGCTCACGTCCAGC CTGGACCCTGCAAAGAGGCCTCTGGGGT CTCTGGGCTGTGCATGGGGGAGAAAGAG CCAGAAGCTCCCATCCCACTGACCGCGA GCCTTCCTCAGCACCGTCCCATTTGCTCA GCGCCTCCTCCAACAGGAGGCCCTCGAG AGCCCTCCCAGGAGTGGGGACGAAAAGG TGGGGACTGGGCCGAGAAGGGTCCGACC TTTCCGAAGTCCGCCACCCCTGCGTATCT CCACACAGAGCCTGAAAGTGGTAAGGTG GTCCAGGAAGTCTTCCTCGGAGAGCCAG GCCCCCCAGGTCTGAGCCACCAGCTCGT GTCCAGCATGCCTGGGGCTCCCCTCCTGC CTGAGGGCCCCAGAGAGGCCACACGCCA GCCTTCAGGGACAGGACCTGAGGACACA GAGGGTGGCCAACACGCCCCTGAGCTGC TCAAGCACCAGCTTCTGGGAGACCTGCA CCAGGAGGGGCCGCCACTGAAGGGAGCC GGGGGCAAAGAGAGGCTGGGGAGCAAG GAGGAGGTGGATGAAGACCGCGACGTCG ATGAGTCCTCCCCGCAAGACTCCCCTCCA TCCAGGGTCTCCCCAGTCCAAGATGGGC AGCCTCCCCAGACAGCCGCCAGAGAAGC CACCAGCGTCCCAGGCTTCCCAGCGGAG GGTGCCATTGCCCTCCCTGTGGATTTCCT CTCCAGAGTTTCCACAGAGATCCCAGCCT CTGAGCCCGAGGGGCCCAGTGCAGGGTG GGCTGAAGGGCAGGACATGCCCCCTGAG TTCACGTTCCACGTGGAAATCACACCCAA	911

			CGTGCAGAAGGAGCAGGCGCACCCGGAG GAGGATTCGGGAAGGGCTGCATTTCCAG GGGCTCCTGGAGAGGAGCCAGAGGCCCG GGGCCCCTCTTTGGGAGAGGACACAAAA GAGGCTGAGCTTCCAGAGCCCACTGAAA AGCAGCCTGCTGCTGCTCCGCGGGGAAA ACCCGTCAGCCGGGTCCCTCAACTCAAA GCTCGCATGGTCAGTAAAAGCAAAGACG GGACTGGAAGCGATGACAAAAAAGCCAA GACATCCACACGTTCCTCTGCTAAAACCT TGAAAAATAGGCCTTGCCTTAGCCCCAA ACACCCCACTCCTGGTAGCTCAGACCCTC TGATCCAACCCTCCAGCCCTGCCGTGTGC CCAGAGCCACCTTCCTCTCCTAAATACGT CTCTTCTGTCACTCCCCGAACTGGCAGTT CTGGAGCAAAGGAGATGAAACTCAAGGG GGCTGATGGGAAAACGAAGATCGCCACA CCCCGGGGAGCGGCCCCTCCAGGCCAGA AGGGCCAAGCCAACGCCACCAGGATTCC AGCAAAAACCCCGCCCGCCCCAAAGACA CCACCCAGCTCTGCGACCAAGCAAGTGC AGAGAAAACCACCCCCTGCAGAGCCCAC ATCTGAGAGAGGTGAACCTCCAAAATCA GGGGATCGCAGTGGCTACAGCAGCCCCG GCTCCCCGGGCACTCCCGGCAGCCGCTC CCGCACCCCGTCCCTTCCAACCCCTCCAG CCCGGGAGCCCAAGAAGGTGGCGGTGGT CCGTACTCCACCTAAGTCGCCGTCTTCCG CCAAGAGCCGCCTGCAGACAGCCCCCGT GCCCATGCCAGACCTGAAGAACGTCAAG TCCAAGATCGGCTCCACCGAGAACCTGA AGCACCAGCCGGGAGGCGGGAAGGTGCA GATAATTAATAAGAAGCTGGATCTTAGC AACGTCCAGTCCAAGTGTGGCTCAAAGG ATAATATCAAACACGTCCCGGGAGGCGG CAGTGTGCAAATAGTCTACAAACCAGTT GACCTGAGCAAGGTGACCTCCAAGTGTG GCTCATTAGGCAACATCCATCATAAACC AGGAGGTGGCCAGGTGGAAGTAAAATCT GAGAAGCTGGACTTCAAGGACAGAGTGC AGTCGAAGATCGGGTCCCTGGACAATAT CACCCATGTCCCTGGCGGAGGAAATAAA AAGATTGAAACCCACAAGCTGACCTTCC GCGAGAACGCCAAAGCCAAGACAGACCA	

			CGGGGCGGAAATCGTGTACAAGTCGCCG GTGGTGTCTGGGGACACGTCTCCACGGC ACCTCAGCAATGTCTCCTCCACCGGCAGC ATCGACATGGTAGACTCGCCCCAGCTCG CCACGCTAGCCGACGAGGTGTCTGCCTCC CTGGCCAAGCAGGGTTTGTGA	
MAPT-2141	19mer sense strand	2141-2218-966 (Hs-Mf-Mm)	GAGAACCUGAAGCACCAGC	912
MAPT-2142	19mer sense strand	2142-2219-967 (Hs-Mf-Mm)	AGAACCUGAAGCACCAGCC	913
MAPT-2303	19mer sense strand	2303-2380-1128 (Hs-Mf-Mm)	GUGACCUCCAAGUGUGGCU	914
MAPT-2347	19mer sense strand	2347-2424-1172 (Hs-Mf-Mm)	AGGAGGUGGCCAGGUGGAA	915
MAPT-2349	19mer sense strand	2349-2426-1174 (Hs-Mf-Mm)	GAGGUGGCCAGGUGGAAGU	916
MAPT-2350	19mer sense strand	2350-2427-1175 (Hs-Mf-Mm)	AGGUGGCCAGGUGGAAGUA	917
MAPT-2351	19mer sense strand	2351-2428-1176 (Hs-Mf-Mm)	GGUGGCCAGGUGGAAGUAA	918
MAPT-2352	19mer sense strand	2352-2429-1177 (Hs-Mf-Mm)	GUGGCCAGGUGGAAGUAAA	919
MAPT-2353	19mer sense strand	2353-2430-1178 (Hs-Mf-Mm)	UGGCCAGGUGGAAGUAAAA	920
MAPT-2354	19mer sense strand	2354-2431-1179 (Hs-Mf-Mm)	GGCCAGGUGGAAGUAAAAU	921
MAPT-2355	19mer sense strand	2355-2432-1180 (Hs-Mf-Mm)	GCCAGGUGGAAGUAAAAUC	922
MAPT-2459	19mer sense strand	2459-2536-1284 (Hs-Mf-Mm)	AAGAUUGAAACCCACAAGC	923

MAPT-2460	19mer sense strand	2460-2537-1285 (Hs-Mf-Mm)	AGAUUGAAACCCACAAGCU	924
MAPT-2461	19mer sense strand	2461-2538-1286 (Hs-Mf-Mm)	GAUUGAAACCCACAAGCUG	925
MAPT-2462	19mer sense strand	2462-2539-1287 (Hs-Mf-Mm)	AUUGAAACCCACAAGCUGA	926
MAPT-2463	19mer sense strand	2463-2540-1288 (Hs-Mf-Mm)	UUGAAACCCACAAGCUGAC	927
MAPT-2464	19mer sense strand	2464-2541-1289 (Hs-Mf-Mm)	UGAAACCCACAAGCUGACC	928
MAPT-2465	19mer sense strand	2465-2542-1290 (Hs-Mf-Mm)	GAAACCCACAAGCUGACCU	929
MAPT-2466	19mer sense strand	2466-2543-1291 (Hs-Mf-Mm)	AAACCCACAAGCUGACCUU	930
MAPT-2467	19mer sense strand	2467-2544-1292 (Hs-Mf-Mm)	AACCCACAAGCUGACCUUC	931
MAPT-2495	19mer sense strand	2495-2572-1320 (Hs-Mf-Mm)	GCCAAAGCCAAGACAGACC	932
MAPT-2496	19mer sense strand	2496-2573-1321 (Hs-Mf-Mm)	CCAAAGCCAAGACAGACCA	933
MAPT-3686	19mer sense strand	3686-3758-2505 (Hs-Mf-Mm)	UCUUUGUAAGGACUUGUGC	934
MAPT-3687	19mer sense strand	3687-3759-2506 (Hs-Mf-Mm)	CUUUGUAAGGACUUGUGCC	935
MAPT-3688	19mer sense strand	3688-3760-2507 (Hs-Mf-Mm)	UUUGUAAGGACUUGUGCCU	936
MAPT-3691	19mer sense strand	3691-3763-2510 (Hs-Mf-Mm)	GUAAGGACUUGUGCCUCUU	937

MAPT-3692	19mer sense strand	3692-3764-2511 (Hs-Mf-Mm)	UAAGGACUUGUGCCUCUUG	938
MAPT-3693	19mer sense strand	3693-3765-2512 (Hs-Mf-Mm)	AAGGACUUGUGCCUCUUGG	939
MAPT-4534	19mer sense strand	4534-4605-3332 (Hs-Mf-Mm)	GUUGUAGUUGGAUUUGUCU	940
MAPT-4535	19mer sense strand	4535-4606-3333 (Hs-Mf-Mm)	UUGUAGUUGGAUUUGUCUG	941
MAPT-4536	19mer sense strand	4536-4607-3334 (Hs-Mf-Mm)	UGUAGUUGGAUUUGUCUGU	942
MAPT-4537	19mer sense strand	4537-4608-3335 (Hs-Mf-Mm)	GUAGUUGGAUUUGUCUGUU	943
MAPT-4538	19mer sense strand	4538-4609-3336 (Hs-Mf-Mm)	UAGUUGGAUUUGUCUGUUU	944
MAPT-4566	19mer sense strand	4566-4637-3362 (Hs-Mf-Mm)	UUCACCAGAGUGACUAUGA	945
MAPT-4567	19mer sense strand	4567-4638-3363 (Hs-Mf-Mm)	UCACCAGAGUGACUAUGAU	946
MAPT-4568	19mer sense strand	4568-4639-3364 (Hs-Mf-Mm)	CACCAGAGUGACUAUGAUA	947
MAPT-4569	19mer sense strand	4569-4640-3365 (Hs-Mf-Mm)	ACCAGAGUGACUAUGAUAG	948
MAPT-4570	19mer sense strand	4570-4641-3366 (Hs-Mf-Mm)	CCAGAGUGACUAUGAUAGU	949
MAPT-4571	19mer sense strand	4571-4642-3367 (Hs-Mf-Mm)	CAGAGUGACUAUGAUAGUG	950
MAPT-4572	19mer sense strand	4572-4643-3368 (Hs-Mf-Mm)	AGAGUGACUAUGAUAGUGA	951

MAPT-4573	19mer sense strand	4573-4644-3369 (Hs-Mf-Mm)	GAGUGACUAUGAUAGUGAA	952
MAPT-4574	19mer sense strand	4574-4645-3370 (Hs-Mf-Mm)	AGUGACUAUGAUAGUGAAA	953
MAPT-4575	19mer sense strand	4575-4646-3371 (Hs-Mf-Mm)	GUGACUAUGAUAGUGAAAA	954
MAPT-4576	19mer sense strand	4576-4647-3372 (Hs-Mf-Mm)	UGACUAUGAUAGUGAAAAG	955
MAPT-4577	19mer sense strand	4577-4648-3373 (Hs-Mf-Mm)	GACUAUGAUAGUGAAAAGA	956
MAPT-4578	19mer sense strand	4578-4649-3374 (Hs-Mf-Mm)	ACUAUGAUAGUGAAAAGAA	957
MAPT-4579	19mer sense strand	4579-4650-3375 (Hs-Mf-Mm)	CUAUGAUAGUGAAAAGAAA	958
MAPT-4580	19mer sense strand	4580-4651-3376 (Hs-Mf-Mm)	UAUGAUAGUGAAAAGAAAA	959
MAPT-4605	19mer sense strand	4605-4677-3439 (Hs-Mf-Mm)	AAAAAAAAGGACGCAUGUA	960
MAPT-4606	19mer sense strand	4606-4678-3440 (Hs-Mf-Mm)	AAAAAAAGGACGCAUGUAU	961
MAPT-4607	19mer sense strand	4607-4679-3441 (Hs-Mf-Mm)	AAAAAAGGACGCAUGUAUC	962
MAPT-4608	19mer sense strand	4608-4680-3442 (Hs-Mf-Mm)	AAAAAGGACGCAUGUAUCU	963
MAPT-4609	19mer sense strand	4609-4681-3443 (Hs-Mf-Mm)	AAAAGGACGCAUGUAUCUU	964
MAPT-4610	19mer sense strand	4610-4682-3444 (Hs-Mf-Mm)	AAAGGACGCAUGUAUCUUG	965

MAPT-4611	19mer sense strand	4611-4683-3445 (Hs-Mf-Mm)	AAGGACGCAUGUAUCUUGA	966
MAPT-4612	19mer sense strand	4612-4684-3446 (Hs-Mf-Mm)	AGGACGCAUGUAUCUUGAA	967
MAPT-4613	19mer sense strand	4613-4685-3447 (Hs-Mf-Mm)	GGACGCAUGUAUCUUGAAA	968
MAPT-4614	19mer sense strand	4614-4686-3448 (Hs-Mf-Mm)	GACGCAUGUAUCUUGAAAU	969
MAPT-5969	19mer sense strand	5969-6024-4540 (Hs-Mf-Mm)	UCACUUUAUCAAUAGUUCC	970
MAPT-5970	19mer sense strand	5970-6025-4541 (Hs-Mf-Mm)	CACUUUAUCAAUAGUUCCA	971
MAPT-5971	19mer sense strand	5971-6026-4542 (Hs-Mf-Mm)	ACUUUAUCAAUAGUUCCAU	972
MAPT-5972	19mer sense strand	5972-6027-4543 (Hs-Mf-Mm)	CUUUAUCAAUAGUUCCAUU	973
MAPT-5973	19mer sense strand	5973-6028-4544 (Hs-Mf-Mm)	UUUAUCAAUAGUUCCAUUU	974
MAPT-5974	19mer sense strand	5974-6029-4545 (Hs-Mf-Mm)	UUAUCAAUAGUUCCAUUUA	975
MAPT-5975	19mer sense strand	5975-6030-4546 (Hs-Mf-Mm)	UAUCAAUAGUUCCAUUUAA	976
MAPT-5976	19mer sense strand	5976-6031-4547 (Hs-Mf-Mm)	AUCAAUAGUUCCAUUUAAA	977
MAPT-5977	19mer sense strand	5977-6032-4548 (Hs-Mf-Mm)	UCAAUAGUUCCAUUUAAAU	978
MAPT-5978	19mer sense strand	5978-6033-4549 (Hs-Mf-Mm)	CAAUAGUUCCAUUUAAAUU	979

MAPT-5979	19mer sense strand	5979-6034-4550 (Hs-Mf-Mm)	AAUAGUUCCAUUUAAAUUG	980
MAPT-5980	19mer sense strand	5980-6035-4551 (Hs-Mf-Mm)	AUAGUUCCAUUUAAAUUGA	981
MAPT-5981	19mer sense strand	5981-6036-4552 (Hs-Mf-Mm)	UAGUUCCAUUUAAAUUGAC	982
MAPT-5982	19mer sense strand	5982-6037-4553 (Hs-Mf-Mm)	AGUUCCAUUUAAAUUGACU	983
MAPT-5983	19mer sense strand	5983-6038-4554 (Hs-Mf-Mm)	GUUCCAUUUAAAUUGACUU	984
MAPT-5984	19mer sense strand	5984-6039-4555 (Hs-Mf-Mm)	UUCCAUUUAAAUUGACUUC	985
MAPT-5985	19mer sense strand	5985-6040-4556 (Hs-Mf-Mm)	UCCAUUUAAAUUGACUUCA	986
MAPT-6662	19mer sense strand	6662-6723-5230 (Hs-Mf-Mm)	CUUGCAAGUCCCAUGAUUU	987
MAPT-6663	19mer sense strand	6663-6724-5231 (Hs-Mf-Mm)	UUGCAAGUCCCAUGAUUUC	988
MAPT-6664	19mer sense strand	6664-6725-5232 (Hs-Mf-Mm)	UGCAAGUCCCAUGAUUUCU	989
MAPT-6665	19mer sense strand	6665-6726-5233 (Hs-Mf-Mm)	GCAAGUCCCAUGAUUUCUU	990
MAPT-6800	19mer sense strand	6800-6861-5365 (Hs-Mf-Mm)	GUAAAAGUGAAUUUGGAAA	991
MAPT-6801	19mer sense strand	6801-6862-5366 (Hs-Mf-Mm)	UAAAAGUGAAUUUGGAAAU	992
MAPT-6802	19mer sense strand	6802-6863-5367 (Hs-Mf-Mm)	AAAAGUGAAUUUGGAAAUA	993

MAPT-6803	19mer sense strand	6803-6864-5368 (Hs-Mf-Mm)	AAAGUGAAUUUGGAAAUAA	994
MAPT-6804	19mer sense strand	6804-6865-5369 (Hs-Mf-Mm)	AAGUGAAUUUGGAAAUAAA	995
MAPT-6805	19mer sense strand	6805-6866-5370 (Hs-Mf-Mm)	AGUGAAUUUGGAAAUAAAG	996
MAPT-6806	19mer sense strand	6806-6867-5371 (Hs-Mf-Mm)	GUGAAUUUGGAAAUAAAGU	997
MAPT-6807	19mer sense strand	6807-6868-5372 (Hs-Mf-Mm)	UGAAUUUGGAAAUAAAGUU	998
MAPT-6808	19mer sense strand	6808-6869-5373 (Hs-Mf-Mm)	GAAUUUGGAAAUAAAGUUA	999
MAPT-6809	19mer sense strand	6809-6870-5374 (Hs-Mf-Mm)	AAUUUGGAAAUAAAGUUAU	1000
MAPT-6810	19mer sense strand	6810-6871-5375 (Hs-Mf-Mm)	AUUUGGAAAUAAAGUUAUU	1001
MAPT-6811	19mer sense strand	6811-6872-5376 (Hs-Mf-Mm)	UUUGGAAAUAAAGUUAUUA	1002
MAPT-6812	19mer sense strand	6812-6873-5377 (Hs-Mf-Mm)	UUGGAAAUAAAGUUAUUAC	1003
MAPT-6813	19mer sense strand	6813-6874-5378 (Hs-Mf-Mm)	UGGAAAUAAAGUUAUUACU	1004
MAPT-6814	19mer sense strand	6814-6875-5379 (Hs-Mf-Mm)	GGAAAUAAAGUUAUUACUC	1005
MAPT-6815	19mer sense strand	6815-6876-5380 (Hs-Mf-Mm)	GAAAUAAAGUUAUUACUCU	1006
MAPT-6816	19mer sense strand	6816-6877-5381 (Hs-Mf-Mm)	AAAUAAAGUUAUUACUCUG	1007

MAPT-363	19mer sense strand	363 (Hs)	AGGAGUUCGAAGUGAUGGA	1008
MAPT-364	19mer sense strand	364 (Hs)	GGAGUUCGAAGUGAUGGAA	1009
MAPT-365	19mer sense strand	365 (Hs)	GAGUUCGAAGUGAUGGAAG	1010
MAPT-367	19mer sense strand	367 (Hs)	GUUCGAAGUGAUGGAAGAU	1011
MAPT-369	19mer sense strand	369 (Hs)	UCGAAGUGAUGGAAGAUCA	1012
MAPT-374	19mer sense strand	374-226 (Hs-Mf)	GUGAUGGAAGAUCACGCUG	1013
MAPT-395	19mer sense strand	395-247 (Hs-Mf)	ACGUACGGGUUGGGGGACA	1014
MAPT-400	19mer sense strand	400-252 (Hs-Mf)	CGGGUUGGGGGACAGGAAA	1015
MAPT-443	19mer sense strand	443-295 (Hs-Mf)	CAAGACCAAGAGGGUGACA	1016
MAPT-688	19mer sense strand	688-453 (Hs-Mf)	GGAAGACGAAGCUGCUGGU	1017
MAPT-689	19mer sense strand	689-454 (Hs-Mf)	GAAGACGAAGCUGCUGGUC	1018
MAPT-690	19mer sense strand	690-455 (Hs-Mf)	AAGACGAAGCUGCUGGUCA	1019
MAPT-693	19mer sense strand	693-458 (Hs-Mf)	ACGAAGCUGCUGGUCACGU	1020
MAPT-695	19mer sense strand	695-460 (Hs-Mf)	GAAGCUGCUGGUCACGUGA	1021

MAPT-696	19mer sense strand	696-461 (Hs-Mf)	AAGCUGCUGGUCACGUGAC	1022
MAPT-1475	19mer sense strand	1475-1552 (Hs-Mf)	CGCAUGGUCAGUAAAAGCA	1023
MAPT-1476	19mer sense strand	1476-1553 (Hs-Mf)	GCAUGGUCAGUAAAAGCAA	1024
MAPT-1479	19mer sense strand	1479-1556 (Hs-Mf)	UGGUCAGUAAAAGCAAAGA	1025
MAPT-1480	19mer sense strand	1480-1557 (Hs-Mf)	GGUCAGUAAAAGCAAAGAC	1026
MAPT-1481	19mer sense strand	1481-1558 (Hs-Mf)	GUCAGUAAAAGCAAAGACG	1027
MAPT-1484	19mer sense strand	1484-1561 (Hs-Mf)	AGUAAAAGCAAAGACGGGA	1028
MAPT-1485	19mer sense strand	1485-1562 (Hs-Mf)	GUAAAAGCAAAGACGGGAC	1029
MAPT-1492	19mer sense strand	1492-1569 (Hs-Mf)	CAAAGACGGGACUGGAAGC	1030
MAPT-1494	19mer sense strand	1494-1571 (Hs-Mf)	AAGACGGGACUGGAAGCGA	1031
MAPT-1495	19mer sense strand	1495-1572 (Hs-Mf)	AGACGGGACUGGAAGCGAU	1032
MAPT-1498	19mer sense strand	1498-1575 (Hs-Mf)	CGGGACUGGAAGCGAUGAC	1033
MAPT-1499	19mer sense strand	1499-1576 (Hs-Mf)	GGGACUGGAAGCGAUGACA	1034
MAPT-1500	19mer sense strand	1500-1577 (Hs-Mf)	GGACUGGAAGCGAUGACAA	1035

MAPT-1502	19mer sense strand	1502-1579 (Hs-Mf)	ACUGGAAGCGAUGACAAAA	1036
MAPT-1503	19mer sense strand	1503-1580 (Hs-Mf)	CUGGAAGCGAUGACAAAAA	1037
MAPT-1504	19mer sense strand	1504-1581 (Hs-Mf)	UGGAAGCGAUGACAAAAAA	1038
MAPT-1505	19mer sense strand	1505-1582 (Hs-Mf)	GGAAGCGAUGACAAAAAAG	1039
MAPT-1506	19mer sense strand	1506-1583 (Hs-Mf)	GAAGCGAUGACAAAAAAGC	1040
MAPT-1507	19mer sense strand	1507-1584 (Hs-Mf)	AAGCGAUGACAAAAAAGCC	1041
MAPT-1508	19mer sense strand	1508-1585 (Hs-Mf)	AGCGAUGACAAAAAAGCCA	1042
MAPT-1509	19mer sense strand	1509-1586 (Hs-Mf)	GCGAUGACAAAAAAGCCAA	1043
MAPT-1733	19mer sense strand	1733 (Hs)	GAUGGUAAAACGAAGAUCG	1044
MAPT-1796	19mer sense strand	1796-1873 (Hs-Mf)	AACGCCACCAGGAUUCCAG	1045
MAPT-1835	19mer sense strand	1835-1912 (Hs-Mf)	AAGACACCACCCAGCUCUG	1046
MAPT-1912	19mer sense strand	1912-1989 (Hs-Mf)	ACCUCCAAAAUCAGGGGAU	1047
MAPT-2094	19mer sense strand	2094-2171 (Hs-Mf)	UGCCCAUGCCAGACCUGAA	1048
MAPT-2096	19mer sense strand	2096-2173 (Hs-Mf)	CCCAUGCCAGACCUGAAGA	1049

MAPT-2097	19mer sense strand	2097-2174 (Hs-Mf)	CCAUGCCAGACCUGAAGAA	1050
MAPT-2098	19mer sense strand	2098 (Hs)	CAUGCCAGACCUGAAGAAU	1051
MAPT-2105	19mer sense strand	2105 (Hs)	GACCUGAAGAAUGUCAAGU	1052
MAPT-2106	19mer sense strand	2106 (Hs)	ACCUGAAGAAUGUCAAGUC	1053
MAPT-2107	19mer sense strand	2107 (Hs)	CCUGAAGAAUGUCAAGUCC	1054
MAPT-2108	19mer sense strand	2108 (Hs)	CUGAAGAAUGUCAAGUCCA	1055
MAPT-2109	19mer sense strand	2109 (Hs)	UGAAGAAUGUCAAGUCCAA	1056
MAPT-2117	19mer sense strand	2117-2194 (Hs-Mf)	GUCAAGUCCAAGAUCGGCU	1057
MAPT-2136	19mer sense strand	2136 (Hs)	CCACUGAGAACCUGAAGCA	1058
MAPT-2137	19mer sense strand	2137 (Hs)	CACUGAGAACCUGAAGCAC	1059
MAPT-2269	19mer sense strand	2269-2346 (Hs-Mf)	GCAAAUAGUCUACAAACCA	1060
MAPT-2270	19mer sense strand	2270-2347 (Hs-Mf)	CAAAUAGUCUACAAACCAG	1061
MAPT-2271	19mer sense strand	2271-2348 (Hs-Mf)	AAAUAGUCUACAAACCAGU	1062
MAPT-2272	19mer sense strand	2272-2349 (Hs-Mf)	AAUAGUCUACAAACCAGUU	1063

MAPT-2273	19mer sense strand	2273-2350 (Hs-Mf)	AUAGUCUACAAACCAGUUG	1064
MAPT-2274	19mer sense strand	2274-2351 (Hs-Mf)	UAGUCUACAAACCAGUUGA	1065
MAPT-2275	19mer sense strand	2275-2352 (Hs-Mf)	AGUCUACAAACCAGUUGAC	1066
MAPT-2276	19mer sense strand	2276-2353 (Hs-Mf)	GUCUACAAACCAGUUGACC	1067
MAPT-2277	19mer sense strand	2277-2354 (Hs-Mf)	UCUACAAACCAGUUGACCU	1068
MAPT-2278	19mer sense strand	2278-2355 (Hs-Mf)	CUACAAACCAGUUGACCUG	1069
MAPT-2279	19mer sense strand	2279-2356 (Hs-Mf)	UACAAACCAGUUGACCUGA	1070
MAPT-2280	19mer sense strand	2280-2357 (Hs-Mf)	ACAAACCAGUUGACCUGAG	1071
MAPT-2281	19mer sense strand	2281-2358 (Hs-Mf)	CAAACCAGUUGACCUGAGC	1072
MAPT-2282	19mer sense strand	2282-2359 (Hs-Mf)	AAACCAGUUGACCUGAGCA	1073
MAPT-2283	19mer sense strand	2283-2360 (Hs-Mf)	AACCAGUUGACCUGAGCAA	1074
MAPT-2284	19mer sense strand	2284-2361 (Hs-Mf)	ACCAGUUGACCUGAGCAAG	1075
MAPT-2286	19mer sense strand	2286-2363 (Hs-Mf)	CAGUUGACCUGAGCAAGGU	1076
MAPT-2288	19mer sense strand	2288-2365 (Hs-Mf)	GUUGACCUGAGCAAGGUGA	1077

MAPT-2289	19mer sense strand	2289-2366 (Hs-Mf)	UUGACCUGAGCAAGGUGAC	1078
MAPT-2291	19mer sense strand	2291-2368 (Hs-Mf)	GACCUGAGCAAGGUGACCU	1079
MAPT-2294	19mer sense strand	2294-2371 (Hs-Mf)	CUGAGCAAGGUGACCUCCA	1080
MAPT-2299	19mer sense strand	2299-2376 (Hs-Mf)	CAAGGUGACCUCCAAGUGU	1081
MAPT-2300	19mer sense strand	2300-2377 (Hs-Mf)	AAGGUGACCUCCAAGUGUG	1082
MAPT-2301	19mer sense strand	2301-2378 (Hs-Mf)	AGGUGACCUCCAAGUGUGG	1083
MAPT-2308	19mer sense strand	2308-2385 (Hs-Mf)	CUCCAAGUGUGGCUCAUUA	1084
MAPT-2316	19mer sense strand	2316-2393 (Hs-Mf)	GUGGCUCAUUAGGCAACAU	1085
MAPT-2317	19mer sense strand	2317-2394 (Hs-Mf)	UGGCUCAUUAGGCAACAUC	1086
MAPT-2319	19mer sense strand	2319-2396 (Hs-Mf)	GCUCAUUAGGCAACAUCCA	1087
MAPT-2320	19mer sense strand	2320-2397 (Hs-Mf)	CUCAUUAGGCAACAUCCAU	1088
MAPT-2322	19mer sense strand	2322-2399 (Hs-Mf)	CAUUAGGCAACAUCCAUCA	1089
MAPT-2323	19mer sense strand	2323-2400 (Hs-Mf)	AUUAGGCAACAUCCAUCAU	1090
MAPT-2324	19mer sense strand	2324-2401 (Hs-Mf)	UUAGGCAACAUCCAUCAUA	1091

MAPT-2326	19mer sense strand	2326-2403 (Hs-Mf)	AGGCAACAUCCAUCAUAAA	1092
MAPT-2330	19mer sense strand	2330-2407 (Hs-Mf)	AACAUCCAUCAUAAACCAG	1093
MAPT-2356	19mer sense strand	2356-2433 (Hs-Mf)	CCAGGUGGAAGUAAAAUCU	1094
MAPT-2357	19mer sense strand	2357-2434 (Hs-Mf)	CAGGUGGAAGUAAAAUCUG	1095
MAPT-2358	19mer sense strand	2358-2435 (Hs-Mf)	AGGUGGAAGUAAAAUCUGA	1096
MAPT-2359	19mer sense strand	2359-2436 (Hs-Mf)	GGUGGAAGUAAAAUCUGAG	1097
MAPT-2360	19mer sense strand	2360-2437 (Hs-Mf)	GUGGAAGUAAAAUCUGAGA	1098
MAPT-2361	19mer sense strand	2361-2438 (Hs-Mf)	UGGAAGUAAAAUCUGAGAA	1099
MAPT-2362	19mer sense strand	2362-2439 (Hs-Mf)	GGAAGUAAAAUCUGAGAAG	1100
MAPT-2363	19mer sense strand	2363-2440 (Hs-Mf)	GAAGUAAAAUCUGAGAAGC	1101
MAPT-2364	19mer sense strand	2364-2441 (Hs-Mf)	AAGUAAAAUCUGAGAAGCU	1102
MAPT-2365	19mer sense strand	2365 (Hs)	AGUAAAAUCUGAGAAGCUU	1103
MAPT-2372	19mer sense strand	2372 (Hs)	UCUGAGAAGCUUGACUUCA	1104
MAPT-2373	19mer sense strand	2373 (Hs)	CUGAGAAGCUUGACUUCAA	1105

MAPT-2374	19mer sense strand	2374 (Hs)	UGAGAAGCUUGACUUCAAG	1106
MAPT-2375	19mer sense strand	2375 (Hs)	GAGAAGCUUGACUUCAAGG	1107
MAPT-2376	19mer sense strand	2376 (Hs)	AGAAGCUUGACUUCAAGGA	1108
MAPT-2377	19mer sense strand	2377 (Hs)	GAAGCUUGACUUCAAGGAC	1109
MAPT-2378	19mer sense strand	2378 (Hs)	AAGCUUGACUUCAAGGACA	1110
MAPT-2379	19mer sense strand	2379 (Hs)	AGCUUGACUUCAAGGACAG	1111
MAPT-2380	19mer sense strand	2380 (Hs)	GCUUGACUUCAAGGACAGA	1112
MAPT-2381	19mer sense strand	2381 (Hs)	CUUGACUUCAAGGACAGAG	1113
MAPT-2382	19mer sense strand	2382 (Hs)	UUGACUUCAAGGACAGAGU	1114
MAPT-2390	19mer sense strand	2390 (Hs)	AAGGACAGAGUCCAGUCGA	1115
MAPT-2391	19mer sense strand	2391 (Hs)	AGGACAGAGUCCAGUCGAA	1116
MAPT-2414	19mer sense strand	2414-2491 (Hs-Mf)	GGGUCCCUGGACAAUAUCA	1117
MAPT-2448	19mer sense strand	2448-2525 (Hs-Mf)	GAGGAAAUAAAAAGAUUGA	1118
MAPT-2449	19mer sense strand	2449-2526 (Hs-Mf)	AGGAAAUAAAAAGAUUGAA	1119

MAPT-2450	19mer sense strand	2450-2527 (Hs-Mf)	GGAAAUAAAAAGAUUGAAA	1120
MAPT-2451	19mer sense strand	2451-2528 (Hs-Mf)	GAAAUAAAAAGAUUGAAAC	1121
MAPT-2452	19mer sense strand	2452-2529 (Hs-Mf)	AAAUAAAAAGAUUGAAACC	1122
MAPT-2453	19mer sense strand	2453-2530 (Hs-Mf)	AAUAAAAAGAUUGAAACCC	1123
MAPT-2454	19mer sense strand	2454-2531 (Hs-Mf)	AUAAAAAGAUUGAAACCCA	1124
MAPT-2456	19mer sense strand	2456-2533 (Hs-Mf)	AAAAAGAUUGAAACCCACA	1125
MAPT-2457	19mer sense strand	2457-2534 (Hs-Mf)	AAAAGAUUGAAACCCACAA	1126
MAPT-2567	19mer sense strand	2567 (Hs)	CGGCAUCUCAGCAAUGUCU	1127
MAPT-2598	19mer sense strand	2598-2675 (Hs-Mf)	GCAUCGACAUGGUAGACUC	1128
MAPT-2657	19mer sense strand	2657-2734 (Hs-Mf)	CUGGCCAAGCAGGGUUUGU	1129
MAPT-2723	19mer sense strand	2723-2800 (Hs-Mf)	AGAGUGUGGAAAAAAAAAG	1130
MAPT-2724	19mer sense strand	2724-2801 (Hs-Mf)	GAGUGUGGAAAAAAAAAGA	1131
MAPT-2726	19mer sense strand	2726-2803 (Hs-Mf)	GUGUGGAAAAAAAAAGAAU	1132
MAPT-2784	19mer sense strand	2784-2860-1 mismatch (Hs-Mf)	GCAGUUCGGUUAAUUGGUU	1133

MAPT-2963	19mer sense strand	2963-3039 (Hs-Mf)	GGCAAUUCCUUUUGAUUCU	1134
MAPT-3110	19mer sense strand	3110-3186 (Hs-Mf)	AGCAACAAAGGAUUUGAAA	1135
MAPT-3114	19mer sense strand	3114-3190 (Hs-Mf)	ACAAAGGAUUUGAAACUUG	1136
MAPT-3116	19mer sense strand	3116-3192 (Hs-Mf)	AAAGGAUUUGAAACUUGGU	1137
MAPT-3118	19mer sense strand	3118-3194 (Hs-Mf)	AGGAUUUGAAACUUGGUGU	1138
MAPT-3158	19mer sense strand	3158-3234 (Hs-Mf)	CGAUGUCAACCUUGUGUGA	1139
MAPT-3503	19mer sense strand	3503-3576 (Hs-Mf)	AAAGACUGACCUUGAUGUC	1140
MAPT-3589	19mer sense strand	3589-3661 (Hs-Mf)	CUCCACAGAAACCCUGUUU	1141
MAPT-3591	19mer sense strand	3591-3663 (Hs-Mf)	CCACAGAAACCCUGUUUUA	1142
MAPT-3592	19mer sense strand	3592-3664 (Hs-Mf)	CACAGAAACCCUGUUUUAU	1143
MAPT-3593	19mer sense strand	3593-3665 (Hs-Mf)	ACAGAAACCCUGUUUUAUU	1144
MAPT-3594	19mer sense strand	3594-3666 (Hs-Mf)	CAGAAACCCUGUUUUAUUG	1145
MAPT-3595	19mer sense strand	3595-3667 (Hs-Mf)	AGAAACCCUGUUUUAUUGA	1146
MAPT-3596	19mer sense strand	3596-3668 (Hs-Mf)	GAAACCCUGUUUUAUUGAG	1147

MAPT-3597	19mer sense strand	3597-3669 (Hs-Mf)	AAACCCUGUUUUAUUGAGU	1148
MAPT-3598	19mer sense strand	3598-3670 (Hs-Mf)	AACCCUGUUUUAUUGAGUU	1149
MAPT-3599	19mer sense strand	3599-3671 (Hs-Mf)	ACCCUGUUUUAUUGAGUUC	1150
MAPT-3600	19mer sense strand	3600-3672 (Hs-Mf)	CCCUGUUUUAUUGAGUUCU	1151
MAPT-3601	19mer sense strand	3601-3673 (Hs-Mf)	CCUGUUUUAUUGAGUUCUG	1152
MAPT-3602	19mer sense strand	3602-3674 (Hs-Mf)	CUGUUUUAUUGAGUUCUGA	1153
MAPT-3603	19mer sense strand	3603-3675 (Hs-Mf)	UGUUUUAUUGAGUUCUGAA	1154
MAPT-3605	19mer sense strand	3605-3677 (Hs-Mf)	UUUUAUUGAGUUCUGAAGG	1155
MAPT-3607	19mer sense strand	3607-3679 (Hs-Mf)	UUAUUGAGUUCUGAAGGUU	1156
MAPT-3609	19mer sense strand	3609-3681 (Hs-Mf)	AUUGAGUUCUGAAGGUUGG	1157
MAPT-3610	19mer sense strand	3610-3682 (Hs-Mf)	UUGAGUUCUGAAGGUUGGA	1158
MAPT-3677	19mer sense strand	3677-3749 (Hs-Mf)	AACCAGUUCUCUUUGUAAG	1159
MAPT-3678	19mer sense strand	3678-3750 (Hs-Mf)	ACCAGUUCUCUUUGUAAGG	1160
MAPT-3679	19mer sense strand	3679-3751 (Hs-Mf)	CCAGUUCUCUUUGUAAGGA	1161

MAPT-3680	19mer sense strand	3680-3752 (Hs-Mf)	CAGUUCUCUUUGUAAGGAC	1162
MAPT-3958	19mer sense strand	3958-4030 (Hs-Mf)	CUACUCCAUACUGAGGGUG	1163
MAPT-3959	19mer sense strand	3959-4031 (Hs-Mf)	UACUCCAUACUGAGGGUGA	1164
MAPT-3960	19mer sense strand	3960-4032 (Hs-Mf)	ACUCCAUACUGAGGGUGAA	1165
MAPT-3961	19mer sense strand	3961-4033 (Hs-Mf)	CUCCAUACUGAGGGUGAAA	1166
MAPT-3965	19mer sense strand	3965-4037 (Hs-Mf)	AUACUGAGGGUGAAAUUAA	1167
MAPT-3970	19mer sense strand	3970-4042 (Hs-Mf)	GAGGGUGAAAUUAAGGGAA	1168
MAPT-4146	19mer sense strand	4146-4218 (Hs-Mf)	GGUGUUUCUGCCUUGUUGA	1169
MAPT-4474	19mer sense strand	4474-4545 (Hs-Mf)	CUGGAGCAGCUGAACAUAU	1170
MAPT-4475	19mer sense strand	4475-4546 (Hs-Mf)	UGGAGCAGCUGAACAUAUA	1171
MAPT-4477	19mer sense strand	4477-4548 (Hs-Mf)	GAGCAGCUGAACAUAUACA	1172
MAPT-4478	19mer sense strand	4478-4549 (Hs-Mf)	AGCAGCUGAACAUAUACAU	1173
MAPT-4479	19mer sense strand	4479-4550 (Hs-Mf)	GCAGCUGAACAUAUACAUA	1174
MAPT-4480	19mer sense strand	4480-4551 (Hs-Mf)	CAGCUGAACAUAUACAUAG	1175

MAPT-4481	19mer sense strand	4481-4552 (Hs-Mf)	AGCUGAACAUAUACAUAGA	1176
MAPT-4482	19mer sense strand	4482-4553 (Hs-Mf)	GCUGAACAUAUACAUAGAU	1177
MAPT-4485	19mer sense strand	4485-4556 (Hs-Mf)	GAACAUAUACAUAGAUGUU	1178
MAPT-4486	19mer sense strand	4486-4557 (Hs-Mf)	AACAUAUACAUAGAUGUUG	1179
MAPT-4532	19mer sense strand	4532 (Hs)	GAGUUGUAGUUGGAUUUGU	1180
MAPT-4533	19mer sense strand	4533 (Hs)	AGUUGUAGUUGGAUUUGUC	1181
MAPT-4539	19mer sense strand	4539-4610 (Hs-Mf)	AGUUGGAUUUGUCUGUUUA	1182
MAPT-4540	19mer sense strand	4540-4611 (Hs-Mf)	GUUGGAUUUGUCUGUUUAU	1183
MAPT-4541	19mer sense strand	4541-4612 (Hs-Mf)	UUGGAUUUGUCUGUUUAUG	1184
MAPT-4543	19mer sense strand	4543-4614 (Hs-Mf)	GGAUUUGUCUGUUUAUGCU	1185
MAPT-4544	19mer sense strand	4544-4615 (Hs-Mf)	GAUUUGUCUGUUUAUGCUU	1186
MAPT-4545	19mer sense strand	4545-4616 (Hs-Mf)	AUUUGUCUGUUUAUGCUUG	1187
MAPT-4546	19mer sense strand	4546-4617 (Hs-Mf)	UUUGUCUGUUUAUGCUUGG	1188
MAPT-4547	19mer sense strand	4547-4618 (Hs-Mf)	UUGUCUGUUUAUGCUUGGA	1189

MAPT-4548	19mer sense strand	4548-4619 (Hs-Mf)	UGUCUGUUUAUGCUUGGAU	1190
MAPT-4549	19mer sense strand	4549-4620 (Hs-Mf)	GUCUGUUUAUGCUUGGAUU	1191
MAPT-4550	19mer sense strand	4550-4621 (Hs-Mf)	UCUGUUUAUGCUUGGAUUC	1192
MAPT-4551	19mer sense strand	4551-4622 (Hs-Mf)	CUGUUUAUGCUUGGAUUCA	1193
MAPT-4552	19mer sense strand	4552-4623 (Hs-Mf)	UGUUUAUGCUUGGAUUCAC	1194
MAPT-4554	19mer sense strand	4554-4625 (Hs-Mf)	UUUAUGCUUGGAUUCACCA	1195
MAPT-4556	19mer sense strand	4556-4627 (Hs-Mf)	UAUGCUUGGAUUCACCAGA	1196
MAPT-4557	19mer sense strand	4557-4628 (Hs-Mf)	AUGCUUGGAUUCACCAGAG	1197
MAPT-4558	19mer sense strand	4558-4629 (Hs-Mf)	UGCUUGGAUUCACCAGAGU	1198
MAPT-4559	19mer sense strand	4559-4630 (Hs-Mf)	GCUUGGAUUCACCAGAGUG	1199
MAPT-4560	19mer sense strand	4560-4631 (Hs-Mf)	CUUGGAUUCACCAGAGUGA	1200
MAPT-4561	19mer sense strand	4561-4632 (Hs-Mf)	UUGGAUUCACCAGAGUGAC	1201
MAPT-4562	19mer sense strand	4562-4633 (Hs-Mf)	UGGAUUCACCAGAGUGACU	1202
MAPT-4563	19mer sense strand	4563-4634 (Hs-Mf)	GGAUUCACCAGAGUGACUA	1203

MAPT-4564	19mer sense strand	4564-4635 (Hs-Mf)	GAUUCACCAGAGUGACUAU	1204
MAPT-4615	19mer sense strand	4615-4687 (Hs-Mf)	ACGCAUGUAUCUUGAAAUG	1205
MAPT-4616	19mer sense strand	4616-4688 (Hs-Mf)	CGCAUGUAUCUUGAAAUGC	1206
MAPT-4617	19mer sense strand	4617-4689 (Hs-Mf)	GCAUGUAUCUUGAAAUGCU	1207
MAPT-4618	19mer sense strand	4618-4690 (Hs-Mf)	CAUGUAUCUUGAAAUGCUU	1208
MAPT-4619	19mer sense strand	4619-4691 (Hs-Mf)	AUGUAUCUUGAAAUGCUUG	1209
MAPT-4620	19mer sense strand	4620-4692 (Hs-Mf)	UGUAUCUUGAAAUGCUUGU	1210
MAPT-4621	19mer sense strand	4621-4693 (Hs-Mf)	GUAUCUUGAAAUGCUUGUA	1211
MAPT-4622	19mer sense strand	4622-4694 (Hs-Mf)	UAUCUUGAAAUGCUUGUAA	1212
MAPT-4623	19mer sense strand	4623-4695 (Hs-Mf)	AUCUUGAAAUGCUUGUAAA	1213
MAPT-4625	19mer sense strand	4625-4697 (Hs-Mf)	CUUGAAAUGCUUGUAAAGA	1214
MAPT-4627	19mer sense strand	4627-4699 (Hs-Mf)	UGAAAUGCUUGUAAAGAGG	1215
MAPT-4628	19mer sense strand	4628-4700 (Hs-Mf)	GAAAUGCUUGUAAAGAGGU	1216
MAPT-4629	19mer sense strand	4629-4701 (Hs-Mf)	AAAUGCUUGUAAAGAGGUU	1217

MAPT-4630	19mer sense strand	4630-4702 (Hs-Mf)	AAUGCUUGUAAAGAGGUUU	1218
MAPT-4632	19mer sense strand	4632-4704 (Hs-Mf)	UGCUUGUAAAGAGGUUUCU	1219
MAPT-4633	19mer sense strand	4633-4705 (Hs-Mf)	GCUUGUAAAGAGGUUUCUA	1220
MAPT-4825	19mer sense strand	4825-4897 (Hs-Mf)	ACAGGAUUAGGACUGAAGC	1221
MAPT-4828	19mer sense strand	4828-4900 (Hs-Mf)	GGAUUAGGACUGAAGCGAU	1222
MAPT-5682	19mer sense strand	5682-5743 (Hs-Mf)	GAAGUUCUUGUGCCCUGCU	1223
MAPT-5958	19mer sense strand	5958 (Hs)	AAGCUGCUGACUCACUUUA	1224
MAPT-5959	19mer sense strand	5959 (Hs)	AGCUGCUGACUCACUUUAU	1225
MAPT-5961	19mer sense strand	5961 (Hs)	CUGCUGACUCACUUUAUCA	1226
MAPT-5963	19mer sense strand	5963 (Hs)	GCUGACUCACUUUAUCAAU	1227
MAPT-5964	19mer sense strand	5964 (Hs)	CUGACUCACUUUAUCAAUA	1228
MAPT-5965	19mer sense strand	5965 (Hs)	UGACUCACUUUAUCAAUAG	1229
MAPT-5966	19mer sense strand	5966-6021 (Hs-Mf)	GACUCACUUUAUCAAUAGU	1230
MAPT-5967	19mer sense strand	5967-6022 (Hs-Mf)	ACUCACUUUAUCAAUAGUU	1231

MAPT-5968	19mer sense strand	5968-6023 (Hs-Mf)	CUCACUUUAUCAAUAGUUC	1232
MAPT-6006	19mer sense strand	6006-6061 (Hs-Mf)	GGUGAGACUGUAUCCUGUU	1233
MAPT-6007	19mer sense strand	6007-6062 (Hs-Mf)	GUGAGACUGUAUCCUGUUU	1234
MAPT-6008	19mer sense strand	6008-6063 (Hs-Mf)	UGAGACUGUAUCCUGUUUG	1235
MAPT-6009	19mer sense strand	6009-6064 (Hs-Mf)	GAGACUGUAUCCUGUUUGC	1236
MAPT-6010	19mer sense strand	6010-6065 (Hs-Mf)	AGACUGUAUCCUGUUUGCU	1237
MAPT-6011	19mer sense strand	6011-6066 (Hs-Mf)	GACUGUAUCCUGUUUGCUA	1238
MAPT-6012	19mer sense strand	6012-6067 (Hs-Mf)	ACUGUAUCCUGUUUGCUAU	1239
MAPT-6013	19mer sense strand	6013-6068 (Hs-Mf)	CUGUAUCCUGUUUGCUAUU	1240
MAPT-6014	19mer sense strand	6014-6069 (Hs-Mf)	UGUAUCCUGUUUGCUAUUG	1241
MAPT-6015	19mer sense strand	6015-6070 (Hs-Mf)	GUAUCCUGUUUGCUAUUGC	1242
MAPT-6017	19mer sense strand	6017-6072 (Hs-Mf)	AUCCUGUUUGCUAUUGCUU	1243
MAPT-6119	19mer sense strand	6119-6174 (Hs-Mf)	GCCUCGUAACCCUUUUCAU	1244
MAPT-6628	19mer sense strand	6628-6689 (Hs-Mf)	GAGUUUGCCAUGUUGAGCA	1245

MAPT-6629	19mer sense strand	6629-6690 (Hs-Mf)	AGUUUGCCAUGUUGAGCAG	1246
MAPT-6631	19mer sense strand	6631-6692 (Hs-Mf)	UUUGCCAUGUUGAGCAGGA	1247
MAPT-6672	19mer sense strand	6672-6733 (Hs-Mf)	CCAUGAUUUCUUCGGUAAU	1248
MAPT-6731	19mer sense strand	6731 (Hs)	GCUUUCUGUCUGUGAAUGU	1249
MAPT-6732	19mer sense strand	6732 (Hs)	CUUUCUGUCUGUGAAUGUC	1250
MAPT-6738	19mer sense strand	6738-6799 (Hs-Mf)	GUCUGUGAAUGUCUAUAUA	1251
MAPT-6739	19mer sense strand	6739-6800 (Hs-Mf)	UCUGUGAAUGUCUAUAUAG	1252
MAPT-6740	19mer sense strand	6740-6801 (Hs-Mf)	CUGUGAAUGUCUAUAUAGU	1253
MAPT-6741	19mer sense strand	6741-6802 (Hs-Mf)	UGUGAAUGUCUAUAUAGUG	1254
MAPT-6742	19mer sense strand	6742-6803 (Hs-Mf)	GUGAAUGUCUAUAUAGUGU	1255
MAPT-6743	19mer sense strand	6743-6804 (Hs-Mf)	UGAAUGUCUAUAUAGUGUA	1256
MAPT-6745	19mer sense strand	6745-6806 (Hs-Mf)	AAUGUCUAUAUAGUGUAUU	1257
MAPT-6748	19mer sense strand	6748-6809 (Hs-Mf)	GUCUAUAUAGUGUAUUGUG	1258
MAPT-6749	19mer sense strand	6749-6810 (Hs-Mf)	UCUAUAUAGUGUAUUGUGU	1259

MAPT-6750	19mer sense strand	6750-6811 (Hs-Mf)	CUAUAUAGUGUAUUGUGUG	1260
MAPT-6751	19mer sense strand	6751-6812 (Hs-Mf)	UAUAUAGUGUAUUGUGUGU	1261
MAPT-6752	19mer sense strand	6752-6813 (Hs-Mf)	AUAUAGUGUAUUGUGUGUU	1262
MAPT-6753	19mer sense strand	6753-6814 (Hs-Mf)	UAUAGUGUAUUGUGUGUUU	1263
MAPT-6754	19mer sense strand	6754-6815 (Hs-Mf)	AUAGUGUAUUGUGUGUUUU	1264
MAPT-6755	19mer sense strand	6755-6816 (Hs-Mf)	UAGUGUAUUGUGUGUUUUA	1265
MAPT-6756	19mer sense strand	6756-6817 (Hs-Mf)	AGUGUAUUGUGUGUUUUAA	1266
MAPT-6757	19mer sense strand	6757-6818 (Hs-Mf)	GUGUAUUGUGUGUUUUAAC	1267
MAPT-6758	19mer sense strand	6758-6819 (Hs-Mf)	UGUAUUGUGUGUUUUAACA	1268
MAPT-6759	19mer sense strand	6759-6820 (Hs-Mf)	GUAUUGUGUGUUUUAACAA	1269
MAPT-6760	19mer sense strand	6760-6821 (Hs-Mf)	UAUUGUGUGUUUUAACAAA	1270
MAPT-6761	19mer sense strand	6761-6822 (Hs-Mf)	AUUGUGUGUUUUAACAAAU	1271
MAPT-6762	19mer sense strand	6762-6823 (Hs-Mf)	UUGUGUGUUUUAACAAAUG	1272
MAPT-6763	19mer sense strand	6763-6824 (Hs-Mf)	UGUGUGUUUUAACAAAUGA	1273

MAPT-6764	19mer sense strand	6764-6825 (Hs-Mf)	GUGUGUUUUAACAAAUGAU	1274
MAPT-6765	19mer sense strand	6765-6826 (Hs-Mf)	UGUGUUUUAACAAAUGAUU	1275
MAPT-6766	19mer sense strand	6766-6827 (Hs-Mf)	GUGUUUUAACAAAUGAUUU	1276
MAPT-6767	19mer sense strand	6767-6828 (Hs-Mf)	UGUUUUAACAAAUGAUUUA	1277
MAPT-6768	19mer sense strand	6768-6829 (Hs-Mf)	GUUUUAACAAAUGAUUUAC	1278
MAPT-6769	19mer sense strand	6769-6830 (Hs-Mf)	UUUUAACAAAUGAUUUACA	1279
MAPT-6772	19mer sense strand	6772-6833 (Hs-Mf)	UAACAAAUGAUUUACACUG	1280
MAPT-6773	19mer sense strand	6773-6834 (Hs-Mf)	AACAAAUGAUUUACACUGA	1281
MAPT-6774	19mer sense strand	6774-6835 (Hs-Mf)	ACAAAUGAUUUACACUGAC	1282
MAPT-6775	19mer sense strand	6775-6836 (Hs-Mf)	CAAAUGAUUUACACUGACU	1283
MAPT-6777	19mer sense strand	6777-6838 (Hs-Mf)	AAUGAUUUACACUGACUGU	1284
MAPT-6778	19mer sense strand	6778-6839 (Hs-Mf)	AUGAUUUACACUGACUGUU	1285
MAPT-6779	19mer sense strand	6779-6840 (Hs-Mf)	UGAUUUACACUGACUGUUG	1286
MAPT-6780	19mer sense strand	6780-6841 (Hs-Mf)	GAUUUACACUGACUGUUGC	1287

MAPT-6781	19mer sense strand	6781 (Hs)	AUUUACACUGACUGUUGCU	1288
MAPT-6789	19mer sense strand	6789 (Hs)	UGACUGUUGCUGUAAAAGU	1289
MAPT-6792	19mer sense strand	6792 (Hs)	CUGUUGCUGUAAAAGUGAA	1290
MAPT-6793	19mer sense strand	6793 (Hs)	UGUUGCUGUAAAAGUGAAU	1291
MAPT-6795	19mer sense strand	6795 (Hs)	UUGCUGUAAAAGUGAAUUU	1292
MAPT-6796	19mer sense strand	6796 (Hs)	UGCUGUAAAAGUGAAUUUG	1293
MAPT-6797	19mer sense strand	6797 (Hs)	GCUGUAAAAGUGAAUUUGG	1294
MAPT-6798	19mer sense strand	6798 (Hs)	CUGUAAAAGUGAAUUUGGA	1295
MAPT-2141	19mer anti-sense strand	2141-2218-966 (Hs-Mf-Mm)	GCUGGUGCUUCAGGUUCUC	1296
MAPT-2142	19mer anti-sense strand	2142-2219-967 (Hs-Mf-Mm)	GGCUGGUGCUUCAGGUUCU	1297
MAPT-2303	19mer anti-sense strand	2303-2380-1128 (Hs-Mf-Mm)	AGCCACACUUGGAGGUCAC	1298
MAPT-2347	19mer anti-sense strand	2347-2424-1172 (Hs-Mf-Mm)	UUCCACCUGGCCACCUCCU	1299
MAPT-2349	19mer anti-	2349-2426-1174 (Hs-Mf-Mm)	ACUUCCACCUGGCCACCUC	1300

	sense strand			
MAPT-2350	19mer anti-sense strand	2350-2427-1175 (Hs-Mf-Mm)	UACUUCCACCUGGCCACCU	1301
MAPT-2351	19mer anti-sense strand	2351-2428-1176 (Hs-Mf-Mm)	UUACUUCCACCUGGCCACC	1302
MAPT-2352	19mer anti-sense strand	2352-2429-1177 (Hs-Mf-Mm)	UUUACUUCCACCUGGCCAC	1303
MAPT-2353	19mer anti-sense strand	2353-2430-1178 (Hs-Mf-Mm)	UUUUACUUCCACCUGGCCA	1304
MAPT-2354	19mer anti-sense strand	2354-2431-1179 (Hs-Mf-Mm)	AUUUUACUUCCACCUGGCC	1305
MAPT-2355	19mer anti-sense strand	2355-2432-1180 (Hs-Mf-Mm)	GAUUUUACUUCCACCUGGC	1306
MAPT-2459	19mer anti-sense strand	2459-2536-1284 (Hs-Mf-Mm)	GCUUGUGGGUUUCAAUCUU	1307
MAPT-2460	19mer anti-sense strand	2460-2537-1285 (Hs-Mf-Mm)	AGCUUGUGGGUUUCAAUCU	1308
MAPT-2461	19mer anti-sense strand	2461-2538-1286 (Hs-Mf-Mm)	CAGCUUGUGGGUUUCAAUC	1309
MAPT-2462	19mer anti-sense strand	2462-2539-1287 (Hs-Mf-Mm)	UCAGCUUGUGGGUUUCAAU	1310

MAPT-2463	19mer anti-sense strand	2463-2540-1288 (Hs-Mf-Mm)	GUCAGCUUGUGGGUUUCAA	1311
MAPT-2464	19mer anti-sense strand	2464-2541-1289 (Hs-Mf-Mm)	GGUCAGCUUGUGGGUUUCA	1312
MAPT-2465	19mer anti-sense strand	2465-2542-1290 (Hs-Mf-Mm)	AGGUCAGCUUGUGGGUUUC	1313
MAPT-2466	19mer anti-sense strand	2466-2543-1291 (Hs-Mf-Mm)	AAGGUCAGCUUGUGGGUUU	1314
MAPT-2467	19mer anti-sense strand	2467-2544-1292 (Hs-Mf-Mm)	GAAGGUCAGCUUGUGGGUU	1315
MAPT-2495	19mer anti-sense strand	2495-2572-1320 (Hs-Mf-Mm)	GGUCUGUCUUGGCUUUGGC	1316
MAPT-2496	19mer anti-sense strand	2496-2573-1321 (Hs-Mf-Mm)	UGGUCUGUCUUGGCUUUGG	1317
MAPT-3686	19mer anti-sense strand	3686-3758-2505 (Hs-Mf-Mm)	GCACAAGUCCUUACAAAGA	1318
MAPT-3687	19mer anti-sense strand	3687-3759-2506 (Hs-Mf-Mm)	GGCACAAGUCCUUACAAAG	1319
MAPT-3688	19mer anti-sense strand	3688-3760-2507 (Hs-Mf-Mm)	AGGCACAAGUCCUUACAAA	1320
MAPT-3691	19mer anti-	3691-3763-2510 (Hs-Mf-Mm)	AAGAGGCACAAGUCCUUAC	1321

	sense strand			
MAPT-3692	19mer anti-sense strand	3692-3764-2511 (Hs-Mf-Mm)	CAAGAGGCACAAGUCCUUA	1322
MAPT-3693	19mer anti-sense strand	3693-3765-2512 (Hs-Mf-Mm)	CCAAGAGGCACAAGUCCUU	1323
MAPT-4534	19mer anti-sense strand	4534-4605-3332 (Hs-Mf-Mm)	AGACAAAUCCAACUACAAC	1324
MAPT-4535	19mer anti-sense strand	4535-4606-3333 (Hs-Mf-Mm)	CAGACAAAUCCAACUACAA	1325
MAPT-4536	19mer anti-sense strand	4536-4607-3334 (Hs-Mf-Mm)	ACAGACAAAUCCAACUACA	1326
MAPT-4537	19mer anti-sense strand	4537-4608-3335 (Hs-Mf-Mm)	AACAGACAAAUCCAACUAC	1327
MAPT-4538	19mer anti-sense strand	4538-4609-3336 (Hs-Mf-Mm)	AAACAGACAAAUCCAACUA	1328
MAPT-4566	19mer anti-sense strand	4566-4637-3362 (Hs-Mf-Mm)	UCAUAGUCACUCUGGUGAA	1329
MAPT-4567	19mer anti-sense strand	4567-4638-3363 (Hs-Mf-Mm)	AUCAUAGUCACUCUGGUGA	1330
MAPT-4568	19mer anti-sense strand	4568-4639-3364 (Hs-Mf-Mm)	UAUCAUAGUCACUCUGGUG	1331

MAPT-4569	19mer anti-sense strand	4569-4640-3365 (Hs-Mf-Mm)	CUAUCAUAGUCACUCUGGU	1332
MAPT-4570	19mer anti-sense strand	4570-4641-3366 (Hs-Mf-Mm)	ACUAUCAUAGUCACUCUGG	1333
MAPT-4571	19mer anti-sense strand	4571-4642-3367 (Hs-Mf-Mm)	CACUAUCAUAGUCACUCUG	1334
MAPT-4572	19mer anti-sense strand	4572-4643-3368 (Hs-Mf-Mm)	UCACUAUCAUAGUCACUCU	1335
MAPT-4573	19mer anti-sense strand	4573-4644-3369 (Hs-Mf-Mm)	UUCACUAUCAUAGUCACUC	1336
MAPT-4574	19mer anti-sense strand	4574-4645-3370 (Hs-Mf-Mm)	UUUCACUAUCAUAGUCACU	1337
MAPT-4575	19mer anti-sense strand	4575-4646-3371 (Hs-Mf-Mm)	UUUUCACUAUCAUAGUCAC	1338
MAPT-4576	19mer anti-sense strand	4576-4647-3372 (Hs-Mf-Mm)	CUUUUCACUAUCAUAGUCA	1339
MAPT-4577	19mer anti-sense strand	4577-4648-3373 (Hs-Mf-Mm)	UCUUUUCACUAUCAUAGUC	1340
MAPT-4578	19mer anti-sense strand	4578-4649-3374 (Hs-Mf-Mm)	UUCUUUUCACUAUCAUAGU	1341
MAPT-4579	19mer anti-	4579-4650-3375 (Hs-Mf-Mm)	UUUCUUUUCACUAUCAUAG	1342

	sense strand			
MAPT-4580	19mer anti-sense strand	4580-4651-3376 (Hs-Mf-Mm)	UUUUCUUUUCACUAUCAUA	1343
MAPT-4605	19mer anti-sense strand	4605-4677-3439 (Hs-Mf-Mm)	UACAUGCGUCCUUUUUUUU	1344
MAPT-4606	19mer anti-sense strand	4606-4678-3440 (Hs-Mf-Mm)	AUACAUGCGUCCUUUUUUU	1345
MAPT-4607	19mer anti-sense strand	4607-4679-3441 (Hs-Mf-Mm)	GAUACAUGCGUCCUUUUUU	1346
MAPT-4608	19mer anti-sense strand	4608-4680-3442 (Hs-Mf-Mm)	AGAUACAUGCGUCCUUUUU	1347
MAPT-4609	19mer anti-sense strand	4609-4681-3443 (Hs-Mf-Mm)	AAGAUACAUGCGUCCUUUU	1348
MAPT-4610	19mer anti-sense strand	4610-4682-3444 (Hs-Mf-Mm)	CAAGAUACAUGCGUCCUUU	1349
MAPT-4611	19mer anti-sense strand	4611-4683-3445 (Hs-Mf-Mm)	UCAAGAUACAUGCGUCCUU	1350
MAPT-4612	19mer anti-sense strand	4612-4684-3446 (Hs-Mf-Mm)	UUCAAGAUACAUGCGUCCU	1351
MAPT-4613	19mer anti-sense strand	4613-4685-3447 (Hs-Mf-Mm)	UUUCAAGAUACAUGCGUCC	1352

MAPT-4614	19mer anti-sense strand	4614-4686-3448 (Hs-Mf-Mm)	AUUUCAAGAUACAUGCGUC	1353
MAPT-5969	19mer anti-sense strand	5969-6024-4540 (Hs-Mf-Mm)	GGAACUAUUGAUAAAGUGA	1354
MAPT-5970	19mer anti-sense strand	5970-6025-4541 (Hs-Mf-Mm)	UGGAACUAUUGAUAAAGUG	1355
MAPT-5971	19mer anti-sense strand	5971-6026-4542 (Hs-Mf-Mm)	AUGGAACUAUUGAUAAAGU	1356
MAPT-5972	19mer anti-sense strand	5972-6027-4543 (Hs-Mf-Mm)	AAUGGAACUAUUGAUAAAG	1357
MAPT-5973	19mer anti-sense strand	5973-6028-4544 (Hs-Mf-Mm)	AAAUGGAACUAUUGAUAAA	1358
MAPT-5974	19mer anti-sense strand	5974-6029-4545 (Hs-Mf-Mm)	UAAAUGGAACUAUUGAUAA	1359
MAPT-5975	19mer anti-sense strand	5975-6030-4546 (Hs-Mf-Mm)	UUAAAUGGAACUAUUGAUA	1360
MAPT-5976	19mer anti-sense strand	5976-6031-4547 (Hs-Mf-Mm)	UUUAAAUGGAACUAUUGAU	1361
MAPT-5977	19mer anti-sense strand	5977-6032-4548 (Hs-Mf-Mm)	AUUUAAAUGGAACUAUUGA	1362
MAPT-5978	19mer anti-	5978-6033-4549 (Hs-Mf-Mm)	AAUUUAAAUGGAACUAUUG	1363

	sense strand			
MAPT-5979	19mer anti-sense strand	5979-6034-4550 (Hs-Mf-Mm)	CAAUUUAAAUGGAACUAUU	1364
MAPT-5980	19mer anti-sense strand	5980-6035-4551 (Hs-Mf-Mm)	UCAAUUUAAAUGGAACUAU	1365
MAPT-5981	19mer anti-sense strand	5981-6036-4552 (Hs-Mf-Mm)	GUCAAUUUAAAUGGAACUA	1366
MAPT-5982	19mer anti-sense strand	5982-6037-4553 (Hs-Mf-Mm)	AGUCAAUUUAAAUGGAACU	1367
MAPT-5983	19mer anti-sense strand	5983-6038-4554 (Hs-Mf-Mm)	AAGUCAAUUUAAAUGGAAC	1368
MAPT-5984	19mer anti-sense strand	5984-6039-4555 (Hs-Mf-Mm)	GAAGUCAAUUUAAAUGGAA	1369
MAPT-5985	19mer anti-sense strand	5985-6040-4556 (Hs-Mf-Mm)	UGAAGUCAAUUUAAAUGGA	1370
MAPT-6662	19mer anti-sense strand	6662-6723-5230 (Hs-Mf-Mm)	AAAUCAUGGGACUUGCAAG	1371
MAPT-6663	19mer anti-sense strand	6663-6724-5231 (Hs-Mf-Mm)	GAAAUCAUGGGACUUGCAA	1372
MAPT-6664	19mer anti-sense strand	6664-6725-5232 (Hs-Mf-Mm)	AGAAAUCAUGGGACUUGCA	1373

MAPT-6665	19mer anti-sense strand	6665-6726-5233 (Hs-Mf-Mm)	AAGAAAUCAUGGGACUUGC	1374
MAPT-6800	19mer anti-sense strand	6800-6861-5365 (Hs-Mf-Mm)	UUUCCAAAUUCACUUUUAC	1375
MAPT-6801	19mer anti-sense strand	6801-6862-5366 (Hs-Mf-Mm)	AUUUCCAAAUUCACUUUUA	1376
MAPT-6802	19mer anti-sense strand	6802-6863-5367 (Hs-Mf-Mm)	UAUUUCCAAAUUCACUUUU	1377
MAPT-6803	19mer anti-sense strand	6803-6864-5368 (Hs-Mf-Mm)	UUAUUUCCAAAUUCACUUU	1378
MAPT-6804	19mer anti-sense strand	6804-6865-5369 (Hs-Mf-Mm)	UUUAUUUCCAAAUUCACUU	1379
MAPT-6805	19mer anti-sense strand	6805-6866-5370 (Hs-Mf-Mm)	CUUUAUUUCCAAAUUCACU	1380
MAPT-6806	19mer anti-sense strand	6806-6867-5371 (Hs-Mf-Mm)	ACUUUAUUUCCAAAUUCAC	1381
MAPT-6807	19mer anti-sense strand	6807-6868-5372 (Hs-Mf-Mm)	AACUUUAUUUCCAAAUUCA	1382
MAPT-6808	19mer anti-sense strand	6808-6869-5373 (Hs-Mf-Mm)	UAACUUUAUUUCCAAAUUC	1383
MAPT-6809	19mer anti-	6809-6870-5374 (Hs-Mf-Mm)	AUAACUUUAUUUCCAAAUU	1384

	sense strand			
MAPT-6810	19mer anti-sense strand	6810-6871-5375 (Hs-Mf-Mm)	AAUAACUUUAUUUCCAAAU	1385
MAPT-6811	19mer anti-sense strand	6811-6872-5376 (Hs-Mf-Mm)	UAAUAACUUUAUUUCCAAA	1386
MAPT-6812	19mer anti-sense strand	6812-6873-5377 (Hs-Mf-Mm)	GUAAUAACUUUAUUUCCAA	1387
MAPT-6813	19mer anti-sense strand	6813-6874-5378 (Hs-Mf-Mm)	AGUAAUAACUUUAUUUCCA	1388
MAPT-6814	19mer anti-sense strand	6814-6875-5379 (Hs-Mf-Mm)	GAGUAAUAACUUUAUUUCC	1389
MAPT-6815	19mer anti-sense strand	6815-6876-5380 (Hs-Mf-Mm)	AGAGUAAUAACUUUAUUUC	1390
MAPT-6816	19mer anti-sense strand	6816-6877-5381 (Hs-Mf-Mm)	CAGAGUAAUAACUUUAUUU	1391
MAPT-363	19mer anti-sense strand	363 (Hs)	UCCAUCACUUCGAACUCCU	1392
MAPT-364	19mer anti-sense strand	364 (Hs)	UUCCAUCACUUCGAACUCC	1393
MAPT-365	19mer anti-sense strand	365 (Hs)	CUUCCAUCACUUCGAACUC	1394

MAPT-367	19mer anti-sense strand	367 (Hs)	AUCUUCCAUCACUUCGAAC	1395
MAPT-369	19mer anti-sense strand	369 (Hs)	UGAUCUUCCAUCACUUCGA	1396
MAPT-374	19mer anti-sense strand	374-226 (Hs-Mf)	CAGCGUGAUCUUCCAUCAC	1397
MAPT-395	19mer anti-sense strand	395-247 (Hs-Mf)	UGUCCCCCAACCCGUACGU	1398
MAPT-400	19mer anti-sense strand	400-252 (Hs-Mf)	UUUCCUGUCCCCCAACCCG	1399
MAPT-443	19mer anti-sense strand	443-295 (Hs-Mf)	UGUCACCCUCUUGGUCUUG	1400
MAPT-688	19mer anti-sense strand	688-453 (Hs-Mf)	ACCAGCAGCUUCGUCUUCC	1401
MAPT-689	19mer anti-sense strand	689-454 (Hs-Mf)	GACCAGCAGCUUCGUCUUC	1402
MAPT-690	19mer anti-sense strand	690-455 (Hs-Mf)	UGACCAGCAGCUUCGUCUU	1403
MAPT-693	19mer anti-sense strand	693-458 (Hs-Mf)	ACGUGACCAGCAGCUUCGU	1404
MAPT-695	19mer anti-	695-460 (Hs-Mf)	UCACGUGACCAGCAGCUUC	1405

	sense strand			
MAPT-696	19mer anti-sense strand	696-461 (Hs-Mf)	GUCACGUGACCAGCAGCUU	1406
MAPT-1475	19mer anti-sense strand	1475-1552 (Hs-Mf)	UGCUUUUACUGACCAUGCG	1407
MAPT-1476	19mer anti-sense strand	1476-1553 (Hs-Mf)	UUGCUUUUACUGACCAUGC	1408
MAPT-1479	19mer anti-sense strand	1479-1556 (Hs-Mf)	UCUUUGCUUUUACUGACCA	1409
MAPT-1480	19mer anti-sense strand	1480-1557 (Hs-Mf)	GUCUUUGCUUUUACUGACC	1410
MAPT-1481	19mer anti-sense strand	1481-1558 (Hs-Mf)	CGUCUUUGCUUUUACUGAC	1411
MAPT-1484	19mer anti-sense strand	1484-1561 (Hs-Mf)	UCCCGUCUUUGCUUUUACU	1412
MAPT-1485	19mer anti-sense strand	1485-1562 (Hs-Mf)	GUCCCGUCUUUGCUUUUAC	1413
MAPT-1492	19mer anti-sense strand	1492-1569 (Hs-Mf)	GCUUCCAGUCCCGUCUUUG	1414
MAPT-1494	19mer anti-sense strand	1494-1571 (Hs-Mf)	UCGCUUCCAGUCCCGUCUU	1415

MAPT-1495	19mer anti-sense strand	1495-1572 (Hs-Mf)	AUCGCUUCCAGUCCCGUCU	1416
MAPT-1498	19mer anti-sense strand	1498-1575 (Hs-Mf)	GUCAUCGCUUCCAGUCCCG	1417
MAPT-1499	19mer anti-sense strand	1499-1576 (Hs-Mf)	UGUCAUCGCUUCCAGUCCC	1418
MAPT-1500	19mer anti-sense strand	1500-1577 (Hs-Mf)	UUGUCAUCGCUUCCAGUCC	1419
MAPT-1502	19mer anti-sense strand	1502-1579 (Hs-Mf)	UUUUGUCAUCGCUUCCAGU	1420
MAPT-1503	19mer anti-sense strand	1503-1580 (Hs-Mf)	UUUUUGUCAUCGCUUCCAG	1421
MAPT-1504	19mer anti-sense strand	1504-1581 (Hs-Mf)	UUUUUUGUCAUCGCUUCCA	1422
MAPT-1505	19mer anti-sense strand	1505-1582 (Hs-Mf)	CUUUUUUGUCAUCGCUUCC	1423
MAPT-1506	19mer anti-sense strand	1506-1583 (Hs-Mf)	GCUUUUUUGUCAUCGCUUC	1424
MAPT-1507	19mer anti-sense strand	1507-1584 (Hs-Mf)	GGCUUUUUUGUCAUCGCUU	1425
MAPT-1508	19mer anti-	1508-1585 (Hs-Mf)	UGGCUUUUUUGUCAUCGCU	1426

	sense strand			
MAPT-1509	19mer anti-sense strand	1509-1586 (Hs-Mf)	UUGGCUUUUUUGUCAUCGC	1427
MAPT-1733	19mer anti-sense strand	1733 (Hs)	CGAUCUUCGUUUUACCAUC	1428
MAPT-1796	19mer anti-sense strand	1796-1873 (Hs-Mf)	CUGGAAUCCUGGUGGCGUU	1429
MAPT-1835	19mer anti-sense strand	1835-1912 (Hs-Mf)	CAGAGCUGGGUGGUGUCUU	1430
MAPT-1912	19mer anti-sense strand	1912-1989 (Hs-Mf)	AUCCCCUGAUUUUGGAGGU	1431
MAPT-2094	19mer anti-sense strand	2094-2171 (Hs-Mf)	UUCAGGUCUGGCAUGGGCA	1432
MAPT-2096	19mer anti-sense strand	2096-2173 (Hs-Mf)	UCUUCAGGUCUGGCAUGGG	1433
MAPT-2097	19mer anti-sense strand	2097-2174 (Hs-Mf)	UUCUUCAGGUCUGGCAUGG	1434
MAPT-2098	19mer anti-sense strand	2098 (Hs)	AUUCUUCAGGUCUGGCAUG	1435
MAPT-2105	19mer anti-sense strand	2105 (Hs)	ACUUGACAUUCUUCAGGUC	1436

MAPT-2106	19mer anti-sense strand	2106 (Hs)	GACUUGACAUUCUUCAGGU	1437
MAPT-2107	19mer anti-sense strand	2107 (Hs)	GGACUUGACAUUCUUCAGG	1438
MAPT-2108	19mer anti-sense strand	2108 (Hs)	UGGACUUGACAUUCUUCAG	1439
MAPT-2109	19mer anti-sense strand	2109 (Hs)	UUGGACUUGACAUUCUUCA	1440
MAPT-2117	19mer anti-sense strand	2117-2194 (Hs-Mf)	AGCCGAUCUUGGACUUGAC	1441
MAPT-2136	19mer anti-sense strand	2136 (Hs)	UGCUUCAGGUUCUCAGUGG	1442
MAPT-2137	19mer anti-sense strand	2137 (Hs)	GUGCUUCAGGUUCUCAGUG	1443
MAPT-2269	19mer anti-sense strand	2269-2346 (Hs-Mf)	UGGUUUGUAGACUAUUUGC	1444
MAPT-2270	19mer anti-sense strand	2270-2347 (Hs-Mf)	CUGGUUUGUAGACUAUUUG	1445
MAPT-2271	19mer anti-sense strand	2271-2348 (Hs-Mf)	ACUGGUUUGUAGACUAUUU	1446
MAPT-2272	19mer anti-	2272-2349 (Hs-Mf)	AACUGGUUUGUAGACUAUU	1447

	sense strand			
MAPT-2273	19mer anti-sense strand	2273-2350 (Hs-Mf)	CAACUGGUUUGUAGACUAU	1448
MAPT-2274	19mer anti-sense strand	2274-2351 (Hs-Mf)	UCAACUGGUUUGUAGACUA	1449
MAPT-2275	19mer anti-sense strand	2275-2352 (Hs-Mf)	GUCAACUGGUUUGUAGACU	1450
MAPT-2276	19mer anti-sense strand	2276-2353 (Hs-Mf)	GGUCAACUGGUUUGUAGAC	1451
MAPT-2277	19mer anti-sense strand	2277-2354 (Hs-Mf)	AGGUCAACUGGUUUGUAGA	1452
MAPT-2278	19mer anti-sense strand	2278-2355 (Hs-Mf)	CAGGUCAACUGGUUUGUAG	1453
MAPT-2279	19mer anti-sense strand	2279-2356 (Hs-Mf)	UCAGGUCAACUGGUUUGUA	1454
MAPT-2280	19mer anti-sense strand	2280-2357 (Hs-Mf)	CUCAGGUCAACUGGUUUGU	1455
MAPT-2281	19mer anti-sense strand	2281-2358 (Hs-Mf)	GCUCAGGUCAACUGGUUUG	1456
MAPT-2282	19mer anti-sense strand	2282-2359 (Hs-Mf)	UGCUCAGGUCAACUGGUUU	1457

MAPT-2283	19mer anti-sense strand	2283-2360 (Hs-Mf)	UUGCUCAGGUCAACUGGUU	1458
MAPT-2284	19mer anti-sense strand	2284-2361 (Hs-Mf)	CUUGCUCAGGUCAACUGGU	1459
MAPT-2286	19mer anti-sense strand	2286-2363 (Hs-Mf)	ACCUUGCUCAGGUCAACUG	1460
MAPT-2288	19mer anti-sense strand	2288-2365 (Hs-Mf)	UCACCUUGCUCAGGUCAAC	1461
MAPT-2289	19mer anti-sense strand	2289-2366 (Hs-Mf)	GUCACCUUGCUCAGGUCAA	1462
MAPT-2291	19mer anti-sense strand	2291-2368 (Hs-Mf)	AGGUCACCUUGCUCAGGUC	1463
MAPT-2294	19mer anti-sense strand	2294-2371 (Hs-Mf)	UGGAGGUCACCUUGCUCAG	1464
MAPT-2299	19mer anti-sense strand	2299-2376 (Hs-Mf)	ACACUUGGAGGUCACCUUG	1465
MAPT-2300	19mer anti-sense strand	2300-2377 (Hs-Mf)	CACACUUGGAGGUCACCUU	1466
MAPT-2301	19mer anti-sense strand	2301-2378 (Hs-Mf)	CCACACUUGGAGGUCACCU	1467
MAPT-2308	19mer anti-	2308-2385 (Hs-Mf)	UAAUGAGCCACACUUGGAG	1468

	sense strand			
MAPT-2316	19mer anti-sense strand	2316-2393 (Hs-Mf)	AUGUUGCCUAAUGAGCCAC	1469
MAPT-2317	19mer anti-sense strand	2317-2394 (Hs-Mf)	GAUGUUGCCUAAUGAGCCA	1470
MAPT-2319	19mer anti-sense strand	2319-2396 (Hs-Mf)	UGGAUGUUGCCUAAUGAGC	1471
MAPT-2320	19mer anti-sense strand	2320-2397 (Hs-Mf)	AUGGAUGUUGCCUAAUGAG	1472
MAPT-2322	19mer anti-sense strand	2322-2399 (Hs-Mf)	UGAUGGAUGUUGCCUAAUG	1473
MAPT-2323	19mer anti-sense strand	2323-2400 (Hs-Mf)	AUGAUGGAUGUUGCCUAAU	1474
MAPT-2324	19mer anti-sense strand	2324-2401 (Hs-Mf)	UAUGAUGGAUGUUGCCUAA	1475
MAPT-2326	19mer anti-sense strand	2326-2403 (Hs-Mf)	UUUAUGAUGGAUGUUGCCU	1476
MAPT-2330	19mer anti-sense strand	2330-2407 (Hs-Mf)	CUGGUUUAUGAUGGAUGUU	1477
MAPT-2356	19mer anti-sense strand	2356-2433 (Hs-Mf)	AGAUUUUACUUCCACCUGG	1478

MAPT-2357	19mer anti-sense strand	2357-2434 (Hs-Mf)	CAGAUUUUACUUCCACCUG	1479
MAPT-2358	19mer anti-sense strand	2358-2435 (Hs-Mf)	UCAGAUUUUACUUCCACCU	1480
MAPT-2359	19mer anti-sense strand	2359-2436 (Hs-Mf)	CUCAGAUUUUACUUCCACC	1481
MAPT-2360	19mer anti-sense strand	2360-2437 (Hs-Mf)	UCUCAGAUUUUACUUCCAC	1482
MAPT-2361	19mer anti-sense strand	2361-2438 (Hs-Mf)	UUCUCAGAUUUUACUUCCA	1483
MAPT-2362	19mer anti-sense strand	2362-2439 (Hs-Mf)	CUUCUCAGAUUUUACUUCC	1484
MAPT-2363	19mer anti-sense strand	2363-2440 (Hs-Mf)	GCUUCUCAGAUUUUACUUC	1485
MAPT-2364	19mer anti-sense strand	2364-2441 (Hs-Mf)	AGCUUCUCAGAUUUUACUU	1486
MAPT-2365	19mer anti-sense strand	2365 (Hs)	AAGCUUCUCAGAUUUUACU	1487
MAPT-2372	19mer anti-sense strand	2372 (Hs)	UGAAGUCAAGCUUCUCAGA	1488
MAPT-2373	19mer anti-	2373 (Hs)	UUGAAGUCAAGCUUCUCAG	1489

	sense strand			
MAPT-2374	19mer anti-sense strand	2374 (Hs)	CUUGAAGUCAAGCUUCUCA	1490
MAPT-2375	19mer anti-sense strand	2375 (Hs)	CCUUGAAGUCAAGCUUCUC	1491
MAPT-2376	19mer anti-sense strand	2376 (Hs)	UCCUUGAAGUCAAGCUUCU	1492
MAPT-2377	19mer anti-sense strand	2377 (Hs)	GUCCUUGAAGUCAAGCUUC	1493
MAPT-2378	19mer anti-sense strand	2378 (Hs)	UGUCCUUGAAGUCAAGCUU	1494
MAPT-2379	19mer anti-sense strand	2379 (Hs)	CUGUCCUUGAAGUCAAGCU	1495
MAPT-2380	19mer anti-sense strand	2380 (Hs)	UCUGUCCUUGAAGUCAAGC	1496
MAPT-2381	19mer anti-sense strand	2381 (Hs)	CUCUGUCCUUGAAGUCAAG	1497
MAPT-2382	19mer anti-sense strand	2382 (Hs)	ACUCUGUCCUUGAAGUCAA	1498
MAPT-2390	19mer anti-sense strand	2390 (Hs)	UCGACUGGACUCUGUCCUU	1499

MAPT-2391	19mer anti-sense strand	2391 (Hs)	UUCGACUGGACUCUGUCCU	1500
MAPT-2414	19mer anti-sense strand	2414-2491 (Hs-Mf)	UGAUAUUGUCCAGGGACCC	1501
MAPT-2448	19mer anti-sense strand	2448-2525 (Hs-Mf)	UCAAUCUUUUUAUUUCCUC	1502
MAPT-2449	19mer anti-sense strand	2449-2526 (Hs-Mf)	UUCAAUCUUUUUAUUUCCU	1503
MAPT-2450	19mer anti-sense strand	2450-2527 (Hs-Mf)	UUUCAAUCUUUUUAUUUCC	1504
MAPT-2451	19mer anti-sense strand	2451-2528 (Hs-Mf)	GUUUCAAUCUUUUUAUUUC	1505
MAPT-2452	19mer anti-sense strand	2452-2529 (Hs-Mf)	GGUUUCAAUCUUUUUAUUU	1506
MAPT-2453	19mer anti-sense strand	2453-2530 (Hs-Mf)	GGGUUUCAAUCUUUUUAUU	1507
MAPT-2454	19mer anti-sense strand	2454-2531 (Hs-Mf)	UGGGUUUCAAUCUUUUUAU	1508
MAPT-2456	19mer anti-sense strand	2456-2533 (Hs-Mf)	UGUGGGUUUCAAUCUUUUU	1509
MAPT-2457	19mer anti-	2457-2534 (Hs-Mf)	UUGUGGGUUUCAAUCUUUU	1510

	sense strand			
MAPT-2567	19mer anti-sense strand	2567 (Hs)	AGACAUUGCUGAGAUGCCG	1511
MAPT-2598	19mer anti-sense strand	2598-2675 (Hs-Mf)	GAGUCUACCAUGUCGAUGC	1512
MAPT-2657	19mer anti-sense strand	2657-2734 (Hs-Mf)	ACAAACCCUGCUUGGCCAG	1513
MAPT-2723	19mer anti-sense strand	2723-2800 (Hs-Mf)	CUUUUUUUUUCCACACUCU	1514
MAPT-2724	19mer anti-sense strand	2724-2801 (Hs-Mf)	UCUUUUUUUUUCCACACUC	1515
MAPT-2726	19mer anti-sense strand	2726-2803 (Hs-Mf)	AUUCUUUUUUUUUCCACAC	1516
MAPT-2784	19mer anti-sense strand	2784-2860-1 mismatch (Hs-Mf)	AACCAAUUAACCGAACUGC	1517
MAPT-2963	19mer anti-sense strand	2963-3039 (Hs-Mf)	AGAAUCAAAAGGAAUUGCC	1518
MAPT-3110	19mer anti-sense strand	3110-3186 (Hs-Mf)	UUUCAAAUCCUUUGUUGCU	1519
MAPT-3114	19mer anti-sense strand	3114-3190 (Hs-Mf)	CAAGUUUCAAAUCCUUUGU	1520

MAPT-3116	19mer anti-sense strand	3116-3192 (Hs-Mf)	ACCAAGUUUCAAAUCCUUU	1521
MAPT-3118	19mer anti-sense strand	3118-3194 (Hs-Mf)	ACACCAAGUUUCAAAUCCU	1522
MAPT-3158	19mer anti-sense strand	3158-3234 (Hs-Mf)	UCACACAAGGUUGACAUCG	1523
MAPT-3503	19mer anti-sense strand	3503-3576 (Hs-Mf)	GACAUCAAGGUCAGUCUUU	1524
MAPT-3589	19mer anti-sense strand	3589-3661 (Hs-Mf)	AAACAGGGUUUCUGUGGAG	1525
MAPT-3591	19mer anti-sense strand	3591-3663 (Hs-Mf)	UAAAACAGGGUUUCUGUGG	1526
MAPT-3592	19mer anti-sense strand	3592-3664 (Hs-Mf)	AUAAAACAGGGUUUCUGUG	1527
MAPT-3593	19mer anti-sense strand	3593-3665 (Hs-Mf)	AAUAAAACAGGGUUUCUGU	1528
MAPT-3594	19mer anti-sense strand	3594-3666 (Hs-Mf)	CAAUAAAACAGGGUUUCUG	1529
MAPT-3595	19mer anti-sense strand	3595-3667 (Hs-Mf)	UCAAUAAAACAGGGUUUCU	1530
MAPT-3596	19mer anti-	3596-3668 (Hs-Mf)	CUCAAUAAAACAGGGUUUC	1531

	sense strand			
MAPT-3597	19mer anti-sense strand	3597-3669 (Hs-Mf)	ACUCAAUAAAACAGGGUUU	1532
MAPT-3598	19mer anti-sense strand	3598-3670 (Hs-Mf)	AACUCAAUAAAACAGGGUU	1533
MAPT-3599	19mer anti-sense strand	3599-3671 (Hs-Mf)	GAACUCAAUAAAACAGGGU	1534
MAPT-3600	19mer anti-sense strand	3600-3672 (Hs-Mf)	AGAACUCAAUAAAACAGGG	1535
MAPT-3601	19mer anti-sense strand	3601-3673 (Hs-Mf)	CAGAACUCAAUAAAACAGG	1536
MAPT-3602	19mer anti-sense strand	3602-3674 (Hs-Mf)	UCAGAACUCAAUAAAACAG	1537
MAPT-3603	19mer anti-sense strand	3603-3675 (Hs-Mf)	UUCAGAACUCAAUAAAACA	1538
MAPT-3605	19mer anti-sense strand	3605-3677 (Hs-Mf)	CCUUCAGAACUCAAUAAAA	1539
MAPT-3607	19mer anti-sense strand	3607-3679 (Hs-Mf)	AACCUUCAGAACUCAAUAA	1540
MAPT-3609	19mer anti-sense strand	3609-3681 (Hs-Mf)	CCAACCUUCAGAACUCAAU	1541

MAPT-3610	19mer anti-sense strand	3610-3682 (Hs-Mf)	UCCAACCUUCAGAACUCAA	1542
MAPT-3677	19mer anti-sense strand	3677-3749 (Hs-Mf)	CUUACAAAGAGAACUGGUU	1543
MAPT-3678	19mer anti-sense strand	3678-3750 (Hs-Mf)	CCUUACAAAGAGAACUGGU	1544
MAPT-3679	19mer anti-sense strand	3679-3751 (Hs-Mf)	UCCUUACAAAGAGAACUGG	1545
MAPT-3680	19mer anti-sense strand	3680-3752 (Hs-Mf)	GUCCUUACAAAGAGAACUG	1546
MAPT-3958	19mer anti-sense strand	3958-4030 (Hs-Mf)	CACCCUCAGUAUGGAGUAG	1547
MAPT-3959	19mer anti-sense strand	3959-4031 (Hs-Mf)	UCACCCUCAGUAUGGAGUA	1548
MAPT-3960	19mer anti-sense strand	3960-4032 (Hs-Mf)	UUCACCCUCAGUAUGGAGU	1549
MAPT-3961	19mer anti-sense strand	3961-4033 (Hs-Mf)	UUUCACCCUCAGUAUGGAG	1550
MAPT-3965	19mer anti-sense strand	3965-4037 (Hs-Mf)	UUAAUUUCACCCUCAGUAU	1551
MAPT-3970	19mer anti-	3970-4042 (Hs-Mf)	UUCCCUUAAUUUCACCCUC	1552

	sense strand			
MAPT-4146	19mer anti-sense strand	4146-4218 (Hs-Mf)	UCAACAAGGCAGAAACACC	1553
MAPT-4474	19mer anti-sense strand	4474-4545 (Hs-Mf)	AUAUGUUCAGCUGCUCCAG	1554
MAPT-4475	19mer anti-sense strand	4475-4546 (Hs-Mf)	UAUAUGUUCAGCUGCUCCA	1555
MAPT-4477	19mer anti-sense strand	4477-4548 (Hs-Mf)	UGUAUAUGUUCAGCUGCUC	1556
MAPT-4478	19mer anti-sense strand	4478-4549 (Hs-Mf)	AUGUAUAUGUUCAGCUGCU	1557
MAPT-4479	19mer anti-sense strand	4479-4550 (Hs-Mf)	UAUGUAUAUGUUCAGCUGC	1558
MAPT-4480	19mer anti-sense strand	4480-4551 (Hs-Mf)	CUAUGUAUAUGUUCAGCUG	1559
MAPT-4481	19mer anti-sense strand	4481-4552 (Hs-Mf)	UCUAUGUAUAUGUUCAGCU	1560
MAPT-4482	19mer anti-sense strand	4482-4553 (Hs-Mf)	AUCUAUGUAUAUGUUCAGC	1561
MAPT-4485	19mer anti-sense strand	4485-4556 (Hs-Mf)	AACAUCUAUGUAUAUGUUC	1562

MAPT-4486	19mer anti-sense strand	4486-4557 (Hs-Mf)	CAACAUCUAUGUAUAUGUU	1563
MAPT-4532	19mer anti-sense strand	4532 (Hs)	ACAAAUCCAACUACAACUC	1564
MAPT-4533	19mer anti-sense strand	4533 (Hs)	GACAAAUCCAACUACAACU	1565
MAPT-4539	19mer anti-sense strand	4539-4610 (Hs-Mf)	UAAACAGACAAAUCCAACU	1566
MAPT-4540	19mer anti-sense strand	4540-4611 (Hs-Mf)	AUAAACAGACAAAUCCAAC	1567
MAPT-4541	19mer anti-sense strand	4541-4612 (Hs-Mf)	CAUAAACAGACAAAUCCAA	1568
MAPT-4543	19mer anti-sense strand	4543-4614 (Hs-Mf)	AGCAUAAACAGACAAAUCC	1569
MAPT-4544	19mer anti-sense strand	4544-4615 (Hs-Mf)	AAGCAUAAACAGACAAAUC	1570
MAPT-4545	19mer anti-sense strand	4545-4616 (Hs-Mf)	CAAGCAUAAACAGACAAAU	1571
MAPT-4546	19mer anti-sense strand	4546-4617 (Hs-Mf)	CCAAGCAUAAACAGACAAA	1572
MAPT-4547	19mer anti-	4547-4618 (Hs-Mf)	UCCAAGCAUAAACAGACAA	1573

	sense strand			
MAPT-4548	19mer anti-sense strand	4548-4619 (Hs-Mf)	AUCCAAGCAUAAACAGACA	1574
MAPT-4549	19mer anti-sense strand	4549-4620 (Hs-Mf)	AAUCCAAGCAUAAACAGAC	1575
MAPT-4550	19mer anti-sense strand	4550-4621 (Hs-Mf)	GAAUCCAAGCAUAAACAGA	1576
MAPT-4551	19mer anti-sense strand	4551-4622 (Hs-Mf)	UGAAUCCAAGCAUAAACAG	1577
MAPT-4552	19mer anti-sense strand	4552-4623 (Hs-Mf)	GUGAAUCCAAGCAUAAACA	1578
MAPT-4554	19mer anti-sense strand	4554-4625 (Hs-Mf)	UGGUGAAUCCAAGCAUAAA	1579
MAPT-4556	19mer anti-sense strand	4556-4627 (Hs-Mf)	UCUGGUGAAUCCAAGCAUA	1580
MAPT-4557	19mer anti-sense strand	4557-4628 (Hs-Mf)	CUCUGGUGAAUCCAAGCAU	1581
MAPT-4558	19mer anti-sense strand	4558-4629 (Hs-Mf)	ACUCUGGUGAAUCCAAGCA	1582
MAPT-4559	19mer anti-sense strand	4559-4630 (Hs-Mf)	CACUCUGGUGAAUCCAAGC	1583

MAPT-4560	19mer anti-sense strand	4560-4631 (Hs-Mf)	UCACUCUGGUGAAUCCAAG	1584
MAPT-4561	19mer anti-sense strand	4561-4632 (Hs-Mf)	GUCACUCUGGUGAAUCCAA	1585
MAPT-4562	19mer anti-sense strand	4562-4633 (Hs-Mf)	AGUCACUCUGGUGAAUCCA	1586
MAPT-4563	19mer anti-sense strand	4563-4634 (Hs-Mf)	UAGUCACUCUGGUGAAUCC	1587
MAPT-4564	19mer anti-sense strand	4564-4635 (Hs-Mf)	AUAGUCACUCUGGUGAAUC	1588
MAPT-4615	19mer anti-sense strand	4615-4687 (Hs-Mf)	CAUUUCAAGAUACAUGCGU	1589
MAPT-4616	19mer anti-sense strand	4616-4688 (Hs-Mf)	GCAUUUCAAGAUACAUGCG	1590
MAPT-4617	19mer anti-sense strand	4617-4689 (Hs-Mf)	AGCAUUUCAAGAUACAUGC	1591
MAPT-4618	19mer anti-sense strand	4618-4690 (Hs-Mf)	AAGCAUUUCAAGAUACAUG	1592
MAPT-4619	19mer anti-sense strand	4619-4691 (Hs-Mf)	CAAGCAUUUCAAGAUACAU	1593
MAPT-4620	19mer anti-	4620-4692 (Hs-Mf)	ACAAGCAUUUCAAGAUACA	1594

	sense strand			
MAPT-4621	19mer anti-sense strand	4621-4693 (Hs-Mf)	UACAAGCAUUUCAAGAUAC	1595
MAPT-4622	19mer anti-sense strand	4622-4694 (Hs-Mf)	UUACAAGCAUUUCAAGAUA	1596
MAPT-4623	19mer anti-sense strand	4623-4695 (Hs-Mf)	UUUACAAGCAUUUCAAGAU	1597
MAPT-4625	19mer anti-sense strand	4625-4697 (Hs-Mf)	UCUUUACAAGCAUUUCAAG	1598
MAPT-4627	19mer anti-sense strand	4627-4699 (Hs-Mf)	CCUCUUUACAAGCAUUUCA	1599
MAPT-4628	19mer anti-sense strand	4628-4700 (Hs-Mf)	ACCUCUUUACAAGCAUUUC	1600
MAPT-4629	19mer anti-sense strand	4629-4701 (Hs-Mf)	AACCUCUUUACAAGCAUUU	1601
MAPT-4630	19mer anti-sense strand	4630-4702 (Hs-Mf)	AAACCUCUUUACAAGCAUU	1602
MAPT-4632	19mer anti-sense strand	4632-4704 (Hs-Mf)	AGAAACCUCUUUACAAGCA	1603
MAPT-4633	19mer anti-sense strand	4633-4705 (Hs-Mf)	UAGAAACCUCUUUACAAGC	1604

MAPT-4825	19mer anti-sense strand	4825-4897 (Hs-Mf)	GCUUCAGUCCUAAUCCUGU	1605
MAPT-4828	19mer anti-sense strand	4828-4900 (Hs-Mf)	AUCGCUUCAGUCCUAAUCC	1606
MAPT-5682	19mer anti-sense strand	5682-5743 (Hs-Mf)	AGCAGGGCACAAGAACUUC	1607
MAPT-5958	19mer anti-sense strand	5958 (Hs)	UAAAGUGAGUCAGCAGCUU	1608
MAPT-5959	19mer anti-sense strand	5959 (Hs)	AUAAAGUGAGUCAGCAGCU	1609
MAPT-5961	19mer anti-sense strand	5961 (Hs)	UGAUAAAGUGAGUCAGCAG	1610
MAPT-5963	19mer anti-sense strand	5963 (Hs)	AUUGAUAAAGUGAGUCAGC	1611
MAPT-5964	19mer anti-sense strand	5964 (Hs)	UAUUGAUAAAGUGAGUCAG	1612
MAPT-5965	19mer anti-sense strand	5965 (Hs)	CUAUUGAUAAAGUGAGUCA	1613
MAPT-5966	19mer anti-sense strand	5966-6021 (Hs-Mf)	ACUAUUGAUAAAGUGAGUC	1614
MAPT-5967	19mer anti-	5967-6022 (Hs-Mf)	AACUAUUGAUAAAGUGAGU	1615

	sense strand			
MAPT-5968	19mer anti-sense strand	5968-6023 (Hs-Mf)	GAACUAUUGAUAAAGUGAG	1616
MAPT-6006	19mer anti-sense strand	6006-6061 (Hs-Mf)	AACAGGAUACAGUCUCACC	1617
MAPT-6007	19mer anti-sense strand	6007-6062 (Hs-Mf)	AAACAGGAUACAGUCUCAC	1618
MAPT-6008	19mer anti-sense strand	6008-6063 (Hs-Mf)	CAAACAGGAUACAGUCUCA	1619
MAPT-6009	19mer anti-sense strand	6009-6064 (Hs-Mf)	GCAAACAGGAUACAGUCUC	1620
MAPT-6010	19mer anti-sense strand	6010-6065 (Hs-Mf)	AGCAAACAGGAUACAGUCU	1621
MAPT-6011	19mer anti-sense strand	6011-6066 (Hs-Mf)	UAGCAAACAGGAUACAGUC	1622
MAPT-6012	19mer anti-sense strand	6012-6067 (Hs-Mf)	AUAGCAAACAGGAUACAGU	1623
MAPT-6013	19mer anti-sense strand	6013-6068 (Hs-Mf)	AAUAGCAAACAGGAUACAG	1624
MAPT-6014	19mer anti-sense strand	6014-6069 (Hs-Mf)	CAAUAGCAAACAGGAUACA	1625

MAPT-6015	19mer anti-sense strand	6015-6070 (Hs-Mf)	GCAAUAGCAAACAGGAUAC	1626
MAPT-6017	19mer anti-sense strand	6017-6072 (Hs-Mf)	AAGCAAUAGCAAACAGGAU	1627
MAPT-6119	19mer anti-sense strand	6119-6174 (Hs-Mf)	AUGAAAAGGGUUACGAGGC	1628
MAPT-6628	19mer anti-sense strand	6628-6689 (Hs-Mf)	UGCUCAACAUGGCAAACUC	1629
MAPT-6629	19mer anti-sense strand	6629-6690 (Hs-Mf)	CUGCUCAACAUGGCAAACU	1630
MAPT-6631	19mer anti-sense strand	6631-6692 (Hs-Mf)	UCCUGCUCAACAUGGCAAA	1631
MAPT-6672	19mer anti-sense strand	6672-6733 (Hs-Mf)	AUUACCGAAGAAAUCAUGG	1632
MAPT-6731	19mer anti-sense strand	6731 (Hs)	ACAUUCACAGACAGAAAGC	1633
MAPT-6732	19mer anti-sense strand	6732 (Hs)	GACAUUCACAGACAGAAAG	1634
MAPT-6738	19mer anti-sense strand	6738-6799 (Hs-Mf)	UAUAUAGACAUUCACAGAC	1635
MAPT-6739	19mer anti-	6739-6800 (Hs-Mf)	CUAUAUAGACAUUCACAGA	1636

	sense strand			
MAPT-6740	19mer anti-sense strand	6740-6801 (Hs-Mf)	ACUAUAUAGACAUUCACAG	1637
MAPT-6741	19mer anti-sense strand	6741-6802 (Hs-Mf)	CACUAUAUAGACAUUCACA	1638
MAPT-6742	19mer anti-sense strand	6742-6803 (Hs-Mf)	ACACUAUAUAGACAUUCAC	1639
MAPT-6743	19mer anti-sense strand	6743-6804 (Hs-Mf)	UACACUAUAUAGACAUUCA	1640
MAPT-6745	19mer anti-sense strand	6745-6806 (Hs-Mf)	AAUACACUAUAUAGACAUU	1641
MAPT-6748	19mer anti-sense strand	6748-6809 (Hs-Mf)	CACAAUACACUAUAUAGAC	1642
MAPT-6749	19mer anti-sense strand	6749-6810 (Hs-Mf)	ACACAAUACACUAUAUAGA	1643
MAPT-6750	19mer anti-sense strand	6750-6811 (Hs-Mf)	CACACAAUACACUAUAUAG	1644
MAPT-6751	19mer anti-sense strand	6751-6812 (Hs-Mf)	ACACACAAUACACUAUAUA	1645
MAPT-6752	19mer anti-sense strand	6752-6813 (Hs-Mf)	AACACACAAUACACUAUAU	1646

MAPT-6753	19mer anti-sense strand	6753-6814 (Hs-Mf)	AAACACACAAUACACUAUA	1647
MAPT-6754	19mer anti-sense strand	6754-6815 (Hs-Mf)	AAAACACACAAUACACUAU	1648
MAPT-6755	19mer anti-sense strand	6755-6816 (Hs-Mf)	UAAAACACACAAUACACUA	1649
MAPT-6756	19mer anti-sense strand	6756-6817 (Hs-Mf)	UUAAAACACACAAUACACU	1650
MAPT-6757	19mer anti-sense strand	6757-6818 (Hs-Mf)	GUUAAAACACACAAUACAC	1651
MAPT-6758	19mer anti-sense strand	6758-6819 (Hs-Mf)	UGUUAAAACACACAAUACA	1652
MAPT-6759	19mer anti-sense strand	6759-6820 (Hs-Mf)	UUGUUAAAACACACAAUAC	1653
MAPT-6760	19mer anti-sense strand	6760-6821 (Hs-Mf)	UUUGUUAAAACACACAAUA	1654
MAPT-6761	19mer anti-sense strand	6761-6822 (Hs-Mf)	AUUUGUUAAAACACACAAU	1655
MAPT-6762	19mer anti-sense strand	6762-6823 (Hs-Mf)	CAUUUGUUAAAACACACAA	1656
MAPT-6763	19mer anti-	6763-6824 (Hs-Mf)	UCAUUUGUUAAAACACACA	1657

	sense strand			
MAPT-6764	19mer anti-sense strand	6764-6825 (Hs-Mf)	AUCAUUUGUUAAAACACAC	1658
MAPT-6765	19mer anti-sense strand	6765-6826 (Hs-Mf)	AAUCAUUUGUUAAAACACA	1659
MAPT-6766	19mer anti-sense strand	6766-6827 (Hs-Mf)	AAAUCAUUUGUUAAAACAC	1660
MAPT-6767	19mer anti-sense strand	6767-6828 (Hs-Mf)	UAAAUCAUUUGUUAAAACA	1661
MAPT-6768	19mer anti-sense strand	6768-6829 (Hs-Mf)	GUAAAUCAUUUGUUAAAAC	1662
MAPT-6769	19mer anti-sense strand	6769-6830 (Hs-Mf)	UGUAAAUCAUUUGUUAAAA	1663
MAPT-6772	19mer anti-sense strand	6772-6833 (Hs-Mf)	CAGUGUAAAUCAUUUGUUA	1664
MAPT-6773	19mer anti-sense strand	6773-6834 (Hs-Mf)	UCAGUGUAAAUCAUUUGUU	1665
MAPT-6774	19mer anti-sense strand	6774-6835 (Hs-Mf)	GUCAGUGUAAAUCAUUUGU	1666
MAPT-6775	19mer anti-sense strand	6775-6836 (Hs-Mf)	AGUCAGUGUAAAUCAUUUG	1667

MAPT-6777	19mer anti-sense strand	6777-6838 (Hs-Mf)	ACAGUCAGUGUAAAUCAUU	1668
MAPT-6778	19mer anti-sense strand	6778-6839 (Hs-Mf)	AACAGUCAGUGUAAAUCAU	1669
MAPT-6779	19mer anti-sense strand	6779-6840 (Hs-Mf)	CAACAGUCAGUGUAAAUCA	1670
MAPT-6780	19mer anti-sense strand	6780-6841 (Hs-Mf)	GCAACAGUCAGUGUAAAUC	1671
MAPT-6781	19mer anti-sense strand	6781 (Hs)	AGCAACAGUCAGUGUAAAU	1672
MAPT-6789	19mer anti-sense strand	6789 (Hs)	ACUUUUACAGCAACAGUCA	1673
MAPT-6792	19mer anti-sense strand	6792 (Hs)	UUCACUUUUACAGCAACAG	1674
MAPT-6793	19mer anti-sense strand	6793 (Hs)	AUUCACUUUUACAGCAACA	1675
MAPT-6795	19mer anti-sense strand	6795 (Hs)	AAAUUCACUUUUACAGCAA	1676
MAPT-6796	19mer anti-sense strand	6796 (Hs)	CAAAUUCACUUUUACAGCA	1677
MAPT-6797	19mer anti-	6797 (Hs)	CCAAAUUCACUUUUACAGC	1678

	sense strand			
MAPT-6798	19mer anti-sense strand	6798 (Hs)	UCCAAAUUCACUUUUACAG	1679
Stem loop	N/A	N/A	GCAGCCGAAAGGCUGC	1680
MAPT-2357	20mer sense strand	2357-2434 (Hs-Mf)	CAGGUGGAAGUAAAAUCUGA	1681
MAPT-2357	20mer sense strand	2357-2434 (Hs-Mf)	[ademCs-C16][mA][fG][mG][fU][mG][mG][fA][mA][fG][mU][fA][fA][mA][fA][mU][fC][mUs][mGs][mA]	1682
Forward Primer	3' assay		GAAGATTGGGTCCCTGGA	1683
Reverse Primer	3' assay		TGTCTTGGCTTTGGCGTT	1684
Probe	3' assay		6FAM- CGG AAG GTC /ZEN/ AGC TTG TGG GTT TCA	1685
Forward Primer	5' assay		CACCACAGCCACCTTCTC	1686
Reverse Primer	5' assay		CTTCCATCACTTCGAACTCCT	1687
Probe	5' assay		CGT CCT CGC /ZEN/ CTC TGT CGA CTA	1688

CLAIMS

The invention claimed is:

1. An RNAi oligonucleotide for reducing *MAPT* gene expression, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein the antisense strand comprises a region of complementarity to a MAPT mRNA target sequence of any one of SEQ ID NOs: 912-1295, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

2. The RNAi oligonucleotide of claim 1, wherein the sense strand is 15 to 50 nucleotides in length.

3. The RNAi oligonucleotide of claims 1 or 2, wherein the sense strand is 18 to 36 nucleotides in length.

4. The RNAi oligonucleotide of any one of claims 1 to 3, wherein the antisense strand is 15 to 30 nucleotides in length.

5. The RNAi oligonucleotide of any one of claims 1 to 4, wherein the antisense strand is 22 nucleotides in length, and wherein antisense strand and the sense strand form a duplex region of at least 19 nucleotides in length, optionally at least 20 nucleotides in length.

6. The RNAi oligonucleotide of any one of claims 1 to 5, wherein the region of complementarity is at least 19 contiguous nucleotides in length.

7. The RNAi oligonucleotide of any one of claims 1 to 6, wherein the region of complementarity is at least 20 contiguous nucleotides in length.

8. A double stranded RNAi oligonucleotide for reducing *MAPT* gene expression, the oligonucleotide comprising:

(i) an antisense strand of 19-30 nucleotides in length, wherein the antisense strand comprises a nucleotide sequence comprising a region of complementarity to a MAPT mRNA target sequence, wherein the region of complementarity is selected from SEQ ID NOs: 1296-1679, and

(ii) a sense strand of 19-50 nucleotides in length comprising a region of complementarity to the antisense strand, wherein the antisense and sense strands are separate strands that form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

9. The RNAi oligonucleotide of any one of claims 1-8, wherein the 3' end of the sense strand comprises a stem-loop set forth as S1-L-S2, wherein S1 is complementary to S2, and wherein L forms a loop between S1 and S2 of 3-5 nucleotides in length.

10. The RNAi oligonucleotide of claim 9, wherein L is a triloop or a tetraloop.

11. The RNAi oligonucleotide of claim 10, wherein L is a tetraloop.

12. The RNAi oligonucleotide of claim 11, wherein the tetraloop comprises the sequence 5'-GAAA-3'.

13. The RNAi oligonucleotide of any one of claims 9-12, wherein the S1 and S2 are 1-10 nucleotides in length and have the same length.

14. The RNAi oligonucleotide of claim 13, wherein S1 and S2 are 1 nucleotide, 2 nucleotides, 3 nucleotides, 4 nucleotides, 5 nucleotides, 6 nucleotides, 7 nucleotides, 8 nucleotides, 9 nucleotides, or 10 nucleotides in length.

15. The RNAi oligonucleotide of claim 14, wherein S1 and S2 are 6 nucleotides in length.

16. The RNAi oligonucleotide of any one of claims 9-15, wherein the stem-loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 1680).

17. The RNAi oligonucleotide of any one of claims 1-8, wherein the oligonucleotide comprises a blunt end.

18. The RNAi oligonucleotide of claim 17, wherein the blunt end comprises the 3' end of the sense strand.

19. The RNAi oligonucleotide of claims 17 or 18, wherein the sense strand is 20-22 nucleotides.

20. The RNAi oligonucleotide of claim 19, wherein the sense strand is 20 nucleotides.

21. The RNAi oligonucleotide of any one of claims 1 to 20, wherein the antisense strand comprises a 3' overhang sequence of one or more nucleotides in length.

22. The RNAi oligonucleotide of claim 21, wherein the overhang comprises purine nucleotides.

23. The RNAi oligonucleotide of claim 21 or 22, wherein the 3' overhang sequence is 2 nucleotides in length.

24. The RNAi oligonucleotide of claim 23, wherein the 3' overhang is selected from AA, GG, AG, and GA.

25. The RNAi oligonucleotide of claim 24, wherein the 3' overhang is GG or AA.

26. The RNAi oligonucleotide of claim 25, wherein the 3' overhang is GG.

27. The RNAi oligonucleotide of any one of the preceding claims, wherein the oligonucleotide comprises at least one modified nucleotide.

28. The RNAi oligonucleotide of claim 27, wherein the modified nucleotide comprises a 2'-modification.

29. The RNAi oligonucleotide of claim 28, wherein the 2'-modification is a modification selected from 2'-aminoethyl, 2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl, and 2'-deoxy-2'-fluoro-β-d-arabinonucleic acid.

30. The RNAi oligonucleotide of any one of claims 28-29, wherein the modification is a 2'-modification selected from 2'-fluoro and 2'-O-methyl.

31. The RNAi oligonucleotide of any one of claims 29-30, wherein about 18-23%, 18%, 19%, 20%, 21%, 22%, or 23% of the nucleotides of the sense strand comprise a 2'-fluoro modification.

32. The RNAi oligonucleotide of any one of claims 29-30, wherein about 38-43%, 38%, 39%, 40%, 41%, 42%, or 43% of the nucleotides of the sense strand comprise a 2'-fluoro modification.

33. The RNAi oligonucleotide of any one of claims 29-32, wherein about 25-35%, 25%, 26%, 27%, 28%, 29%, 30%, 31%, 32%, 33%, 34%, or 35% of the nucleotides of the antisense strand comprise a 2'-fluoro modification.

34. The RNAi oligonucleotide of any one of claims 29-33, wherein about 25-35%, 25%, 26%, 27%, 28%, 29%, 30%, 31%, 32%, 33%, 34%, or 35% of the nucleotides of the oligonucleotide comprise a 2'-fluoro modification.

35. The RNAi oligonucleotide of any one of claims 29-33, wherein about 35-45%, 35%, 36%, 37%, 38%, 39%, 40%, 41%, 42%, 43%, 44%, or 45% of the nucleotides of the oligonucleotide comprise a 2'-fluoro modification.

36. The RNAi oligonucleotide of any one of claims 29-35, wherein the sense strand comprises 36 nucleotides with positions 1-36 from 5' to 3', wherein each of positions 3, 5, 8, 10, 12, 13, 15, and 17 comprise a 2'-fluoro modification.

37. The RNAi oligonucleotide of any one of claims 29-35, wherein the sense strand comprises 20 nucleotides with positions 1-20 from 5' to 3', wherein each of positions 3, 5, 8, 10, 12, 13, 15, and 17 comprise a 2'-fluoro modification.

38. The RNAi oligonucleotide of any one of claims 29-37, wherein the antisense strand comprises 22 nucleotides with positions 1-22 from 5' to 3', and wherein each of positions 2, 3, 4, 5, 7, 10 14, 16, and 19 comprise a 2'-fluoro modification.

39. The RNAi oligonucleotide of any one of claims 31-38, wherein the remaining nucleotides comprise a 2'-O-methyl modification.

40. The RNAi oligonucleotide of any one of the preceding claims, wherein the oligonucleotide comprises at least one modified internucleotide linkage.

41. The RNAi oligonucleotide of claim 40, wherein the at least one modified internucleotide linkage is a phosphorothioate linkage.

42. The RNAi oligonucleotide of claim 41, wherein the antisense strand comprises a phosphorothioate linkage (i) between positions 1 and 2, and between positions 2 and 3; or (ii)

between positions 1 and 2, between positions 2 and 3, and between positions 3 and 4, wherein positions are numbered 1-4 from 5' to 3'.

43. The RNAi oligonucleotide of claim 41 or 42, wherein the antisense strand is 22 nucleotides in length, and wherein the antisense strand comprises a phosphorothioate linkage between positions 20 and 21 and between positions 21 and 22, and wherein positions are numbered 1-22 from 5' to 3'.

44. The RNAi oligonucleotide of any one of claims 41-43, wherein the sense strand comprises a phosphorothioate linkage between positions 1 and 2, and wherein positions are numbered 1-2 from 5' to 3'.

45. The RNAi oligonucleotide of any one of claims 41-43, wherein the sense strand is 20 nucleotides in length, wherein the sense strand comprises a phosphorothioate linkage between positions between positions 1 and 2, between positions 18 and 19 and between positions 19 and 20, and wherein positions are numbered 1-20 from 5' to 3'.

46. The RNAi oligonucleotide of any one of the preceding claims, wherein the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog.

47. The RNAi oligonucleotide of claim 46, wherein the phosphate analog is oxymethyl phosphonate, vinyl phosphonate or malonyl phosphonate, optionally wherein the phosphate analog is a 4'-phosphate analog comprising 4'-oxymethylphosphonate.

48. The RNAi oligonucleotide of any one of the preceding claims, wherein at least one nucleotide of the oligonucleotide is conjugated to one or more targeting ligands.

49. The RNAi oligonucleotide of claim 48, wherein each targeting ligand comprises a carbohydrate, amino sugar, lipid, cholesterol, or polypeptide.

50. The RNAi oligonucleotide of any one of claims 9-16 and 21-49, wherein the stem loop comprises one or more targeting ligands conjugated to one or more nucleotides of the stem loop.

51. The RNAi oligonucleotide of claim 50, wherein the one or more targeting ligands is conjugated to one or more nucleotides of the loop.

52. The RNAi oligonucleotide of claim 51, wherein the loop comprises 4 nucleotides numbered 1-4 from 5' to 3', wherein nucleotides at positions 2, 3, and 4 each comprise one or more targeting ligands, and wherein the targeting ligands are the same or different.

53. The RNAi oligonucleotide of claim 52, wherein each targeting ligand comprises a N-acetylgalactosamine (GalNAc) moiety.

54. The RNAi oligonucleotide of claim 53, wherein the GalNac moiety is a monovalent GalNAc moiety, a bivalent GalNAc moiety, a trivalent GalNAc moiety, or a tetravalent GalNAc moiety.

55. The RNAi oligonucleotide of any one of claims 9-16 and 21-54, wherein up to 4 nucleotides of L of the stem-loop are each conjugated to a monovalent GalNAc moiety.

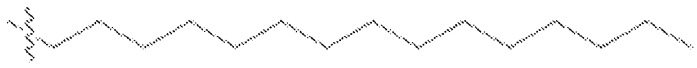
56. The RNAi oligonucleotide of any one of claims 17-48, wherein the one or more targeting ligands is a lipid moiety.

57. The RNAi oligonucleotide of claim 56, wherein the lipid moiety is conjugated to the 5' terminal nucleotide of the sense strand.

58. The RNAi oligonucleotide of claim 56 or 57, wherein the lipid moiety is a hydrocarbon chain.

59. The RNAi oligonucleotide of claim 58, wherein the hydrocarbon chain is a C_8-C_{30} hydrocarbon chain.

60. The RNAi oligonucleotide of claim 58 or 59, wherein the hydrocarbon chain is a C_{16} hydrocarbon chain.

61. The RNAi oligonucleotide of claim 60, wherein the C_{16} hydrocarbon chain is represented by:  .

62. The RNAi oligonucleotide of any one of claims 56-61, wherein the lipid moiety is conjugated to the 2' carbon of the ribose ring of the 5' terminal nucleotide.

63. The RNAi oligonucleotide of any one of claims 1-62, wherein the region of complementarity is fully complementary to the MAPT mRNA target sequence at nucleotide positions 2-8 of the antisense strand, and wherein nucleotide positions are numbered 5' to 3'.

64. The RNAi oligonucleotide of any one of claims 1-62, wherein the region of complementarity is fully complementary to the MAPT mRNA target sequence at nucleotide positions 2-11 of the antisense strand, and wherein nucleotide positions are numbered 5' to 3'.

65. The RNAi oligonucleotide of any one of claims 1 to 64, wherein the sense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 769-803 and 1681.

66. The RNAi oligonucleotide of any one of claims 1 to 65, wherein the antisense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 804-838.

67. The RNAi oligonucleotide of any one of claims 1 to 66, wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 769 and 804, respectively;

b) SEQ ID NOs: 770 and 805, respectively;

c) SEQ ID NOs: 771 and 806, respectively;

d) SEQ ID NOs: 772 and 807, respectively;

e) SEQ ID NOs: 773 and 808, respectively;

f) SEQ ID NOs: 774 and 809, respectively;

g) SEQ ID NOs: 775 and 810, respectively;

h) SEQ ID NOs: 776 and 811, respectively;

i) SEQ ID NOs: 777 and 812, respectively;

j) SEQ ID NOs: 778 and 813, respectively;

k) SEQ ID NOs: 779 and 814, respectively;

l) SEQ ID NOs: 780 and 815, respectively;

m) SEQ ID NOs: 781 and 816, respectively;

n) SEQ ID NOs: 782 and 817, respectively;

o) SEQ ID NOs: 783 and 818, respectively;

p) SEQ ID NOs: 784 and 819, respectively;

q) SEQ ID NOs: 785 and 820, respectively;

r) SEQ ID NOs: 786 and 821, respectively;

s) SEQ ID NOs: 787 and 822, respectively;

t) SEQ ID NOs: 788 and 823, respectively;

u) SEQ ID NOs: 789 and 824, respectively;

v) SEQ ID NOs: 790 and 825, respectively;

w) SEQ ID NOs: 791 and 826, respectively;

x) SEQ ID NOs: 792 and 827, respectively;

y) SEQ ID NOs: 793 and 828, respectively;

z) SEQ ID NOs: 794 and 829, respectively;

aa) SEQ ID NOs: 795 and 830, respectively;

bb) SEQ ID NOs: 796 and 831, respectively;

cc) SEQ ID NOs: 797 and 832, respectively;

dd) SEQ ID NOs: 798 and 833, respectively;

ee) SEQ ID NOs: 799 and 834, respectively;

ff) SEQ ID NOs: 800 and 835, respectively;

gg) SEQ ID NOs: 801 and 836, respectively;

hh) SEQ ID NOs: 802 and 837, respectively;

ii) SEQ ID NOs: 803 and 838, respectively; and

jj) SEQ ID NOs: 1681 and 815, respectively.

68. The RNAi oligonucleotide of any one of claims 1 to 66, wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 776 and 811, respectively;

c) SEQ ID NOs: 780 and 815, respectively;

d) SEQ ID NOs: 781 and 816, respectively;

e) SEQ ID NOs: 782 and 817, respectively;

f) SEQ ID NOs: 790 and 825, respectively;

g) SEQ ID NOs: 795 and 830, respectively;

h) SEQ ID NOs: 798 and 833, respectively;

i) SEQ ID NOs: 799 and 834, respectively;

j) SEQ ID NOs: 803 and 838, respectively; and

k) SEQ ID NOs: 1681 and 815, respectively.

69. The RNAi oligonucleotide of any one of claims 1 to 66, wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 771 and 806, respectively;

b) SEQ ID NOs: 780 and 815, respectively;

c) SEQ ID NOs: 781 and 816, respectively;

d) SEQ ID NOs: 798 and 833, respectively;
e) SEQ ID NOs: 799 and 834, respectively;
f) SEQ ID NOs: 803 and 838, respectively; and
g) SEQ ID NOs: 1681 and 815, respectively.

70. The RNAi oligonucleotide of any one of claims 1 to 66, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 771, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 806.

71. The RNAi oligonucleotide of any one of claims 1 to 66, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 780, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 815.

72. The RNAi oligonucleotide of any one of claims 1 to 66, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 781, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 816.

73. The RNAi oligonucleotide of any one of claims 1 to 66, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 798, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 833.

74. The RNAi oligonucleotide of any one of claims 1 to 66, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 799, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 834.

75. The RNAi oligonucleotide of any one of claims 1 to 66, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 803, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 838.

76. The RNAi oligonucleotide of any one of claims 1 to 66, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 1681, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 815.

77. The RNAi oligonucleotide of any one of claims 1-64, wherein the antisense strand is 22 nucleotides in length.

78. The RNAi oligonucleotide of claim 77, wherein the antisense strand comprises a nucleotide sequence selected from SEQ ID NOs: 806, 815, 816, 833, 834, and 838.

79. The RNAi oligonucleotide of any one of claims 1-64 and 77-78, wherein the sense strand comprises a nucleotide sequence selected from SEQ ID NOs: 1130, 1095, 1096, 1119, 1120, and 1124.

80. The RNAi oligonucleotide of any one of claims 1-64 and 77-79, wherein the sense strand is 36 nucleotides in length.

81. The RNAi oligonucleotide of claim 80, wherein the sense strand comprises a nucleotide sequence selected from SEQ ID NOs: 771, 780, 781, 798, 799, and 803.

82. The RNAi oligonucleotide of any one of claims 1-64, wherein the sense strand comprises the nucleotide sequence of any one of SEQ ID NOs: 839-873 and 1682.

83. The RNAi oligonucleotide of any one of claims 1 to 64 and 82, wherein the antisense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 874-908.

84. The RNAi oligonucleotide of any one of claims 1-64, wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 839 and 874, respectively;

b) SEQ ID NOs: 840 and 875, respectively;
c) SEQ ID NOs: 841 and 876, respectively;
d) SEQ ID NOs: 842 and 877, respectively;
e) SEQ ID NOs: 843 and 878, respectively;
f) SEQ ID NOs: 844 and 879, respectively;
g) SEQ ID NOs: 845 and 880, respectively;
h) SEQ ID NOs: 846 and 881, respectively;
i) SEQ ID NOs: 847 and 882, respectively;
j) SEQ ID NOs: 848 and 883, respectively;
k) SEQ ID NOs: 849 and 884, respectively;
l) SEQ ID NOs: 850 and 885, respectively;
m) SEQ ID NOs: 851 and 886, respectively;
n) SEQ ID NOs: 852 and 887, respectively;
o) SEQ ID NOs: 853 and 888, respectively;
p) SEQ ID NOs: 854 and 889, respectively;
q) SEQ ID NOs: 855 and 890, respectively;
r) SEQ ID NOs: 856 and 891, respectively;
s) SEQ ID NOs: 857 and 892, respectively;
t) SEQ ID NOs: 858 and 893, respectively;
u) SEQ ID NOs: 859 and 894, respectively;
v) SEQ ID NOs: 860 and 895, respectively;
w) SEQ ID NOs: 861 and 896, respectively;
x) SEQ ID NOs: 862 and 897, respectively;
y) SEQ ID NOs: 863 and 898, respectively;
z) SEQ ID NOs: 864 and 899, respectively;
aa) SEQ ID NOs: 865 and 900, respectively;
bb) SEQ ID NOs: 866 and 901, respectively;
cc) SEQ ID NOs: 867 and 902, respectively;
dd) SEQ ID NOs: 868 and 903, respectively;

ee) SEQ ID NOs: 869 and 904, respectively;

ff) SEQ ID NOs: 870 and 905, respectively;

gg) SEQ ID NOs: 871 and 906, respectively;

hh) SEQ ID NOs: 872 and 907, respectively;

ii) SEQ ID NOs: 873 and 908, respectively; and

jj) SEQ ID NOs: 1682 and 885, respectively.

85. The RNAi oligonucleotide of any one of claims 1-64, wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 860 and 895, respectively;

b) SEQ ID NOs: 865 and 900, respectively;

c) SEQ ID NOs: 868 and 903, respectively;

d) SEQ ID NOs: 869 and 904, respectively;

e) SEQ ID NOs: 873 and 908, respectively;

f) SEQ ID NOs: 841 and 876, respectively;

g) SEQ ID NOs: 846 and 881, respectively;

h) SEQ ID NOs: 850 and 885, respectively;

i) SEQ ID NOs: 851 and 886, respectively;

j) SEQ ID NOs: 852 and 887, respectively; and

k) SEQ ID NOs: 1682 and 885, respectively.

86. The RNAi oligonucleotide of any one of claims 1-64, wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

a) SEQ ID NOs: 841 and 876, respectively;

b) SEQ ID NOs: 850 and 885, respectively;

c) SEQ ID NOs: 851 and 886, respectively;

d) SEQ ID NOs: 868 and 903, respectively;

e) SEQ ID NOs: 869 and 904, respectively;

f) SEQ ID NOs: 873 and 908, respectively; and

g) SEQ ID NOs: 1682 and 885, respectively.

87. The RNAi oligonucleotide of any one of claims 1 to 64, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 841, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 876.

88. The RNAi oligonucleotide of any one of claims 1 to 64, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 850, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 885.

89. The RNAi oligonucleotide of any one of claims 1 to 64, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 851, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 886.

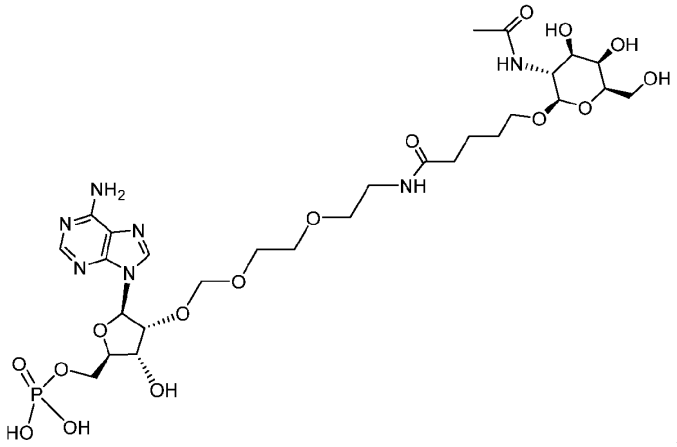
90. The RNAi oligonucleotide of any one of claims 1 to 64, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 868, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 903.

91. The RNAi oligonucleotide of any one of claims 1 to 64, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 869, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 904.

92. The RNAi oligonucleotide of any one of claims 1 to 64, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 873, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 908.

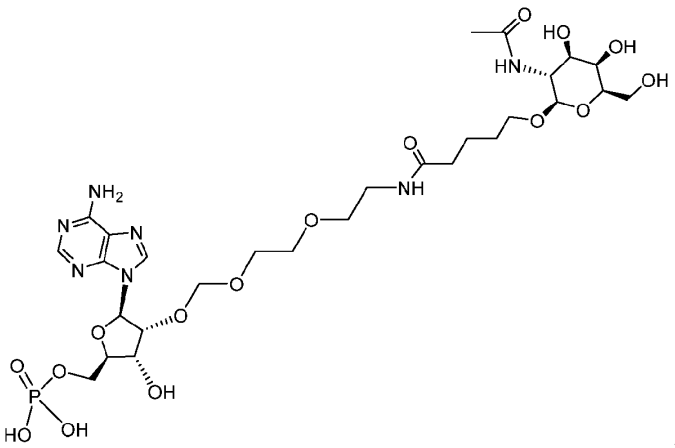
93. The RNAi oligonucleotide of any one of claims 1 to 64, wherein the sense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 1682, and wherein the antisense strand comprises the nucleotide sequence as set forth in SEQ ID NO: 885.

94. The RNAi oligonucleotide of claim 1, wherein the sense strand comprises the sequence and all of the modifications of 5'-[mAs][mG][fA][mG][fU][mG][mU][fG][mG][fA][mA][fA][fA][mA][fA][mA][fA][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 841), wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fCs][fU][fU][fU][mU][fU][mU][mU][fU][mU][mC][mC][fA][mC][fA][mC][mU][fC][mUs][mGs][mG]-3' (SEQ ID NO: 876), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =

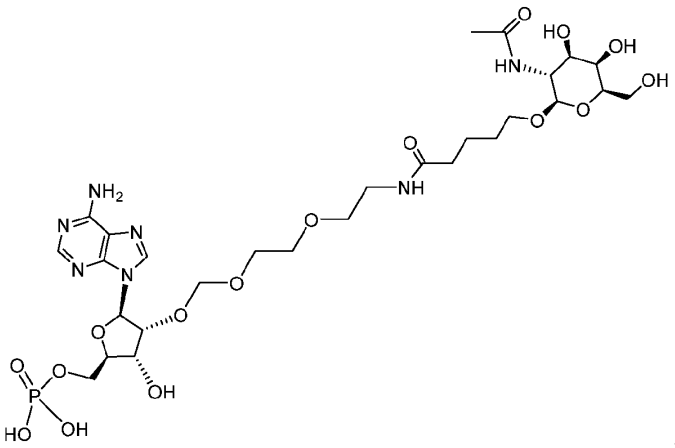


95. The RNAi oligonucleotide of claim 1, wherein the sense strand comprises the sequence and all of the modifications of 5'-[mCs][mA][fG][mG][fU][mG][mG][fA][mA][fG][mU][fA][fA][mA][fA][mU][fC][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 850), wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fCs][fA][fG][fA][mU][fU][mU][mU][fA][mC][mU][mU][fC][mC][fA][mC][mC][fU][mGs][mGs][mG]- 3′ (SEQ ID NO: 885), wherein mC, mA, mG, and mU

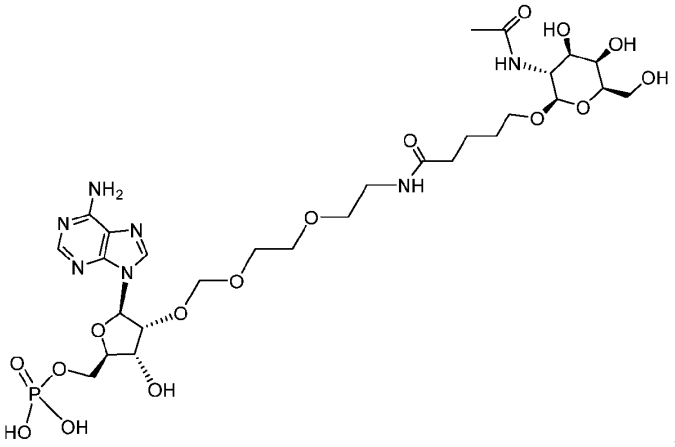
= 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =



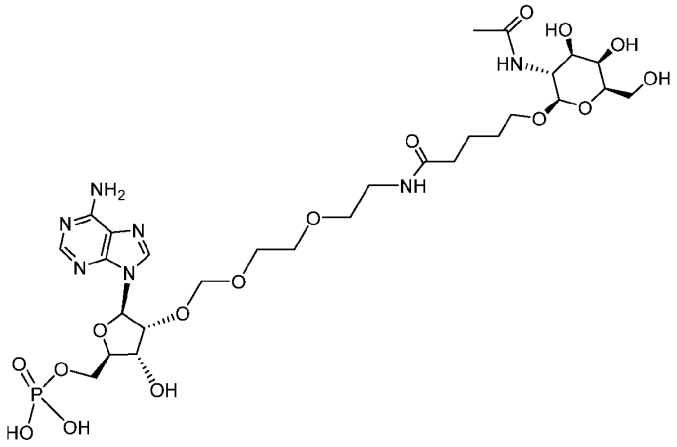
96. The RNAi oligonucleotide of claim 1, wherein the sense strand comprises the sequence and all of the modifications of 5'-[mAs][mG][fG][mU][fG][mG][mA][fA][mG][fU][mA][fA][fA][mA][fU][mC][fU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 851), wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fUs][fC][fA][fG][mA][fU][mU][mU][fU][mA][mC][mU][fU][mC][fC][mA][mC][fC][mUs][mGs][mG]-3' (SEQ ID NO: 886), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =



97. The RNAi oligonucleotide of claim 1, wherein the sense strand comprises the sequence and all of the modifications of 5'-[mAs][mG][fG][mA][fA][mA][mU][fA][mA][fA][mA][fA][fG][mA][fU][mU][fG][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 868), wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fUs][fU][fC][fA][mA][fU][mC][mU][fU][mU][mU][mU][fA][mU][fU][mU][mC][fC][mUs][mGs][mG]-3' (SEQ ID NO: 903), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =

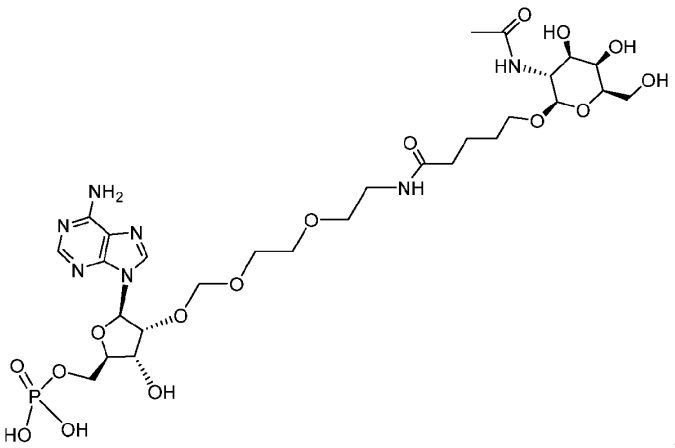


98. The RNAi oligonucleotide of claim 1, wherein the sense strand comprises the sequence and all of the modifications of 5'-[mGs][mG][fA][mA][fA][mU][mA][fA][mA][fA][mA][fG][fA][mU][fU][mG][fA][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 869), wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fUs][fU][fU][fC][mA][fA][mU][mC][fU][mU][mU][mU][fU][mA][fU][mU][mU][fC][mCs][mGs][mG]-3' (SEQ ID NO: 904), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =

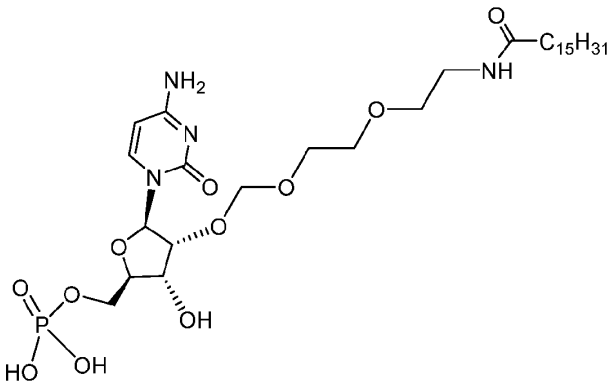


99. The RNAi oligonucleotide of claim 1, wherein the sense strand comprises the sequence and all of the modifications of 5'-[mAs][mU][fA][mA][fA][mA][mA][fG][mA][fU][mU][fG][fA][mA][fA][mC][fC][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]-3' (SEQ ID NO: 873), wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fUs][fG][fG][fG][mU][fU][mU][mC][fA][mA][mU][mC][fU][mU][fU][mU][mU][fA][mUs][mGs][mG]-3' (SEQ ID NO: 908), wherein mC, mA, mG, and mU

= 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =



100. The RNAi oligonucleotide of claim 1, wherein the sense strand comprises the sequence and all of the modifications of 5'-[ademCs-C_{16}][mA][fG][mG][fU][mG][mG][fA][mA][fG][mU][fA][fA][mA][fA][mU][fC][mUs][mGs][mA]-3' (SEQ ID NO: 1682), wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs][fCs][fA][fG][fA][mU][fU][mU][mU][fA][mC][mU][mU][fC][mC][fA][mC][mC][fU][mGs][mGs][mG]- 3' (SEQ ID NO: 885), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s=phosphorothioate, and [ademCs-C16]=cytosine conjugated to C_{16} hydrocarbon chain.



101. A pharmaceutical composition comprising the RNAi oligonucleotide of any one of claims 1 to 100, and a pharmaceutically acceptable carrier, delivery agent or excipient.

102. A method for treating a subject having a disease, disorder, or condition associated with *MAPT* gene expression, the method comprising administering to the subject a therapeutically effective amount of the RNAi oligonucleotide of any one of claim 1-100, or the pharmaceutical composition of claim 101, thereby treating the subject.

103. A method of delivering an oligonucleotide to a subject, the method comprising administering pharmaceutical composition of claim 101 to the subject.

104. A method for reducing *MAPT* gene expression in a cell, a population of cells, or a subject, the method comprising the step of:

i. contacting the cell or the population of cells with the RNAi oligonucleotide of any one of claims 1 to 100, or the pharmaceutical composition of claim 101; or

ii. administering to the subject the RNAi oligonucleotide of any one of claims 1 to 100, or the pharmaceutical composition of claim 101.

105. The method of claim 104, wherein reducing *MAPT* gene expression comprises reducing an amount or level of MAPT mRNA, an amount or level of Tau protein, or both.

106. The method of claim 104 or 105, wherein the subject has a disease, disorder, or condition associated with *MAPT* gene expression.

107. The method of claim 102 or 106, wherein the disease, disorder or condition associated with *MAPT* geme expression is Alzheimer's disease (AD), frontotemporal dementia, progressive supranuclear palsy (PSP), Tau protein associated diseases, primary age-related tauopathy, chronic traumatic encephalopathy, corticobasal degeneration, lytico-bodig disease, ganglioglioma,

meningioangiomatosis, Parkinson's Disease (PD), postencephalitic parkinsonism, or subacute sclerosing panencephalitis.

108. The method of any one of claims 102-107, wherein *MAPT* is reduced in tissue of one or more regions of the central nervous system (CNS), wherein the tissue is associated with AD.

109. The method of claim 108, wherein tissue associated with AD is selected from prefrontal cortex, motor cortex, temporal cortex, parietal cortex, and hippocampus.

110. The method of any one of claims 102-107, wherein *MAPT* is reduced in tissue of one or more regions of the central nervous system (CNS), wherein the tissue is associated with PSP.

111. The method of claim 110, wherein tissue associated with PSP is selected from caudate nucleus, globus pallidus, thalamus, midbrain tegmentum, substantia nigra, pons, cerebellar white matter, cerebellar dentate nucleus, medulla, cervical spinal cord, thoracic spinal cord, and lumbar spinal cord.

112. The method of any one of claims 102-107, wherein *MAPT* is reduced in one or more regions of the CNS selected from cervical spinal cord, thoracic spinal cord, lumbar spinal cord, frontal cortex, temporal cortex, cerebellum, midbrain, occipital cortex, parietal cortex, hippocampus, caudate nucleus, thalamus, brainstem, motor cortex, globus pallidus, midbrain tegmentum, substantia nigra, pons, cerebellar white matter, and cerebellar dentate nucleus.

113. The method of any one of claims 102-112, wherein the RNAi oligonucleotide, or pharmaceutical composition, is administered in combination with a second composition or therapeutic agent.

114. Use of the RNAi oligonucleotide of any one of claims 1 to 100, or the pharmaceutical composition of claim 101, in the manufacture of a medicament for the treatment of a disease, disorder, or condition associated with *MAPT* gene expression.

115. The RNAi oligonucleotide of any one of claims 1 to 100, or the pharmaceutical composition of claim 101, for use, or adaptable for use, in the treatment of a disease, disorder, or condition associated with *MAPT* gene expression.

116. A kit comprising the RNAi oligonucleotide of any one of claims 1 to 100, an optional pharmaceutically acceptable carrier, and a package insert comprising instructions for administration to a subject having a disease, disorder or condition associated with *MAPT* gene expression.

117. The use of claim 114, the RNAi oligonucleotide or pharmaceutical composition for use, or adaptable for use, of claim 115, or the kit of claim 116, wherein the disease, disorder or condition associated with *MAPT* gene expression is Alzheimer's disease (AD), frontotemporal dementia, progressive supranuclear palsy (PSP), Tau protein-associated diseases, primary age-related tauopathy, chronic traumatic encephalopathy, corticobasal degeneration, lytico-bodig disease, ganglioglioma, meningioangiomatosis, Parkinson's Disease (PD), postencephalitic parkinsonism, or subacute sclerosing panencephalitis.