

COMPOSITIONS AND METHODS FOR INHIBITING NUCLEAR RECEPTOR SUBFAMILY 1 GROUP H MEMBER 3 (NR1H3) EXPRESSION

BACKGROUND

The liver plays a critical role in the metabolism of lipids. Abnormalities in normal hepatic lipid metabolism are associated with the development of various liver diseases or disorders such as non-alcoholic fatty liver disease (NAFLD) and its subsequent progression to non-alcoholic steatohepatitis (NASH) and potentially other advanced liver abnormalities.

NAFLD is one of the most common liver diseases, with increasing prevalence worldwide (Loomba R., & Sanyal A.J. NAT. REV. GASTROENTEROL HEPATOL. (2013); 10(11): 686-90). NAFLD is a liver disease characterized by a spectrum of clinical and pathological severity ranging from simple steatosis to nonalcoholic fatty liver (NAFL), nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis, hepatocellular carcinoma (HCC) and liver failure (Bessone F, et al., CELL MOL. LIFE SCI. (2019); 76(1): 99-128). NAFLD is characterized by the presence of fat in the liver in the absence of significant alcohol use and other causes of fat accumulation in the liver such as medications, starvation, and viral disease (Chalasani, N., et al., HEPATOLOGY (Baltimore, Md.), (2012); 55(6): 2005–23). Additionally, as the disease progresses, NASH patients also have an increased risk of developing extra-hepatic complications, particularly cardiovascular diseases (CVD), which are among the most common causes of death in this patient population (Patil R, et al., WORLD J. GASTROINTEST. PATHOPHYSIOL. (2017);8(2): 51–8). The abnormalities in hepatic lipid metabolism that lead to NAFLD also drive the progression of atherogenic dyslipidemia, where elevated plasma triglycerides (TG), cholesterol and lipoprotein particles infiltrate the arterial wall and subsequently develop atherosclerotic plaques (Loomba R & Sanyal AJ NAT. REV. GASTROENTEROL. HEPATOL. (2013); 10(11): 686-90). Thus, there is a significant medical need for the development of disease modifying therapeutics for NAFLD.

SUMMARY OF DISCLOSURE

The disclosure is based in part on the discovery of oligonucleotides (e.g., RNAi oligonucleotides) that reduce *NR1H3* (nuclear receptor subfamily 1, group H, member 3)

expression in the liver. Specifically, target sequences within *NR1H3* mRNA were identified and oligonucleotides that bind to these target sequences and inhibit *NR1H3* mRNA expression were generated. As demonstrated herein, the oligonucleotides inhibited murine, monkey and/or human *NR1H3* expression in the liver. Without being bound by theory, the oligonucleotides described herein are useful for treating a disease, disorder or condition associated with *NR1H3* expression (*e.g.*, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), or systemic lupus erythematosus).

In an aspect, the invention provides an RNAi oligonucleotide for reducing *NR1H3* 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 *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

In an aspect, the invention provides an RNAi oligonucleotide for reducing *NR1H3* 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 *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1125-1511, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

In some embodiments, the RNAi oligonucleotide 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 *NR1H3* mRNA target sequence, wherein the region of complementarity is selected from SEQ ID NOs: 786, 787, 1537 and 813, 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, the RNAi oligonucleotide 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 *NR1H3* mRNA target sequence, wherein the region of complementarity is selected from SEQ ID NOs: 1509, 1510 1409, and 1511 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments of the RNAi oligonucleotide: (i) the sense strand is 15 to 50 or 18 to 36 nucleotides in length, optionally 36 nucleotides in length; optionally (ii) the antisense strand is 15 to 30 nucleotides in length, optionally 22 nucleotides in length; and optionally (iii) the duplex region is at least 19 nucleotides or at least 20 nucleotides in length.

In some embodiments of the RNAi oligonucleotide, the region of complementarity is at least 19 contiguous nucleotides in length, optionally at least 20 contiguous nucleotides in length, optionally 20 contiguous nucleotides, and optionally wherein the region of complementarity is fully complementary to the mRNA target sequence at nucleotide positions 2-8 of the antisense strand or positions 2-11 of the antisense strand, nucleotide numbering 5' to 3'.

In some embodiments of the RNAi oligonucleotide: the 3' end of the sense strand comprises a stem-loop set forth as S1-L-S2, wherein (i) S1 is complementary to S2, L forms a loop between S1 and S2 of 3-5 nucleotides in length, optionally wherein S1 and S2 are each 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides in length, further optionally wherein S1 and S2 are 6 nucleotides in length; and (ii) L forms a loop between S1 and S2 of 3-5 nucleotides in length, optionally wherein L is a triloop or a tetraloop, optionally wherein the tetraloop comprises the sequence 5'-GAAA-3', optionally wherein the stem-loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 1121). In some embodiments of the RNAi oligonucleotide comprises a nicked tetraloop structure or comprises a nick between the 3' terminus of the sense strand and the 5' terminus of the antisense strand.

In some embodiments of the RNAi oligonucleotide: the antisense strand comprises an overhang sequence of one or more nucleotides in length at the 3' terminus, optionally wherein the overhang comprises purine nucleotides, optionally wherein the overhang sequence is 2 nucleotides in length, optionally wherein the overhang is selected from AA, GG, AG, and GA, optionally wherein the overhang is GG.

In some embodiments of the RNAi oligonucleotide: (i) the oligonucleotide comprises at least one modified nucleotide, optionally wherein the modified nucleotide comprises a 2'-modification, optionally wherein: (a) 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, optionally wherein the modification is selected from 2'-fluoro and 2'-O-methyl, optionally wherein all nucleotides of the oligonucleotide are modified, wherein the modification is 2'-fluoro and 2'-O-methyl; (b) about 10-15%, 10%, 11%, 12%, 13%, 14%, or 15% of the nucleotides of the sense strand comprise a 2'-fluoro modification; (c) 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; (d) 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; (e) the sense strand comprises 36 nucleotides with positions 1-36 from 5' to 3', wherein positions 8-11 comprise a 2'-fluoro modification; (f) the antisense strand comprises 22 nucleotides with positions 1-22 from 5' to 3', and wherein positions 2, 3, 4, 5, 7, 10, and 14 comprise a 2'-fluoro modification; and/or (g) the remaining nucleotides comprise a 2'-O-methyl modification, and/or (ii) the oligonucleotide comprises at least one modified internucleotide linkage, optionally wherein the at least one modified internucleotide linkage is a phosphorothioate linkage, optionally wherein: (a) 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'; and/or (b) 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', and/or (iii) the antisense strand comprises a phosphorylated nucleotide at the 5' terminus, wherein the phosphorylated nucleotide is selected from uridine and adenosine, optionally wherein the phosphorylated nucleotide is uridine, and/or (iv) the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog, optionally wherein the phosphate analog is oxymethylphosphonate, vinylphosphonate or malonylphosphonate, optionally wherein the phosphate analog is a 4'-phosphate analog comprising 5'-methoxyphosphonate-4'-oxy, and/or (v) at least one nucleotide of the oligonucleotide is conjugated to one or more targeting ligands, optionally wherein: (a) each targeting ligand comprises a carbohydrate, amino sugar, cholesterol, polypeptide or lipid; (b) the stem loop comprises one or more targeting ligands conjugated to one or more nucleotides of the stem loop; (c) the one or more targeting ligands is conjugated to one or more nucleotides of the loop, optionally 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, wherein the targeting ligands are the same or different; (d) each targeting ligand comprises a N-acetylgalactosamine (GalNAc) moiety, optionally wherein the GalNAc moiety is a monovalent GalNAc moiety, a bivalent GalNAc moiety, a trivalent GalNAc moiety or a tetravalent GalNAc moiety; and/or (e) up to 4 nucleotides of L of the stem-loop are each conjugated to a monovalent GalNAc moiety.

In some embodiments of the RNAi oligonucleotide, the targeting ligand comprises at least one GalNAc moiety and targets human liver cells (e.g., human hepatocytes).

In some embodiments of the RNAi oligonucleotide: (i) the sense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 769-856, SEQ ID NOs: 1519-1552, SEQ ID NOs: 1409, 1509-1511, or SEQ ID NOs: 945-1032, optionally a nucleotide sequence selected from SEQ ID NOs: 786, 787, 813, and 1537; and optionally (ii) the antisense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 857-944 or SEQ ID NOs: 1033-1120, optionally a nucleotide sequence selected from SEQ ID NOs: 874, 875, 901, and 929.

In some embodiments of the RNAi oligonucleotide: the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

- (a) SEQ ID NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;

- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;

(ss) SEQ ID NOs: 813 and 901, respectively;
(tt) SEQ ID NOs: 814 and 902, respectively;
(uu) SEQ ID NOs: 815 and 903, respectively;
(vv) SEQ ID NOs: 816 and 904, respectively;
(ww) SEQ ID NOs: 817 and 905, respectively;
(xx) SEQ ID NOs: 818 and 906, respectively;
(yy) SEQ ID NOs: 819 and 907, respectively;
(zz) SEQ ID NOs: 820 and 908, respectively;
(aaa) SEQ ID NOs: 821 and 909, respectively;
(bbb) SEQ ID NOs: 822 and 910, respectively;
(ccc) SEQ ID NOs: 823 and 911, respectively;
(ddd) SEQ ID NOs: 824 and 912, respectively;
(eee) SEQ ID NOs: 825 and 913, respectively;
(fff) SEQ ID NOs: 826 and 914, respectively;
(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm)SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;
(ooo) SEQ ID NOs: 835 and 923, respectively;
(ppp) SEQ ID NOs: 836 and 924, respectively;
(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;
(uuu) SEQ ID NOs: 1537 and 929, respectively;
(vvv) SEQ ID NOs: 842 and 930, respectively;

(www) SEQ ID NOs: 843 and 931, respectively;
 (xxx) SEQ ID NOs: 844 and 932, respectively;
 (yyy) SEQ ID NOs: 845 and 933, respectively;
 (zzz) SEQ ID NOs: 846 and 934, respectively;
 (aaaa) SEQ ID NOs: 847 and 935, respectively;
 (bbbb) SEQ ID NOs: 848 and 936, respectively;
 (cccc) SEQ ID NOs: 849 and 937, respectively;
 (dddd) SEQ ID NOs: 850 and 938, respectively;
 (eeee) SEQ ID NOs: 851 and 939, respectively;
 (ffff) SEQ ID NOs: 852 and 940, respectively;
 (gggg) SEQ ID NOs: 853 and 941, respectively;
 (hhhh) SEQ ID NOs: 854 and 942, respectively;
 (iiii) SEQ ID NOs: 855 and 943, respectively; and,
 (jjjj) SEQ ID NOs: 856 and 944, respectively.

In some embodiments of the RNAi oligonucleotide: the sense and antisense strands comprise nucleotide sequences selected from the group consisting of:

- (a) SEQ ID NOs: 945 and 1033, respectively;
- (b) SEQ ID NOs: 946 and 1034, respectively;
- (c) SEQ ID NOs: 947 and 1035, respectively;
- (d) SEQ ID NOs: 948 and 1036, respectively;
- (e) SEQ ID NOs: 949 and 1037, respectively;
- (f) SEQ ID NOs: 950 and 1038, respectively;
- (g) SEQ ID NOs: 951 and 1039, respectively;
- (h) SEQ ID NOs: 952 and 1040, respectively;
- (i) SEQ ID NOs: 953 and 1041, respectively;
- (j) SEQ ID NOs: 954 and 1042, respectively;
- (k) SEQ ID NOs: 955 and 1043, respectively;
- (l) SEQ ID NOs: 956 and 1044 respectively;
- (m) SEQ ID NOs: 957 and 1045, respectively;
- (n) SEQ ID NOs: 958 and 1046, respectively;

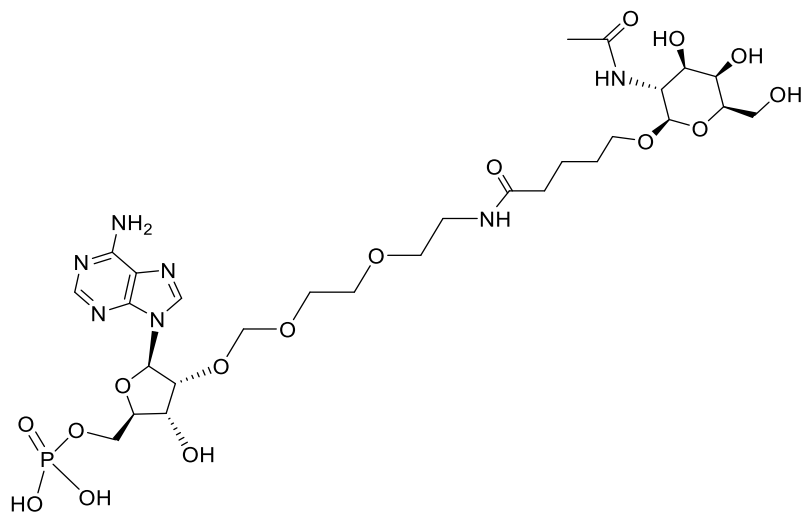
- (o) SEQ ID NOs: 959 and 1047, respectively;
- (p) SEQ ID NOs: 960 and 1048, respectively;
- (q) SEQ ID NOs: 961 and 1049, respectively;
- (r) SEQ ID NOs: 962 and 1050, respectively;
- (s) SEQ ID NOs: 963 and 1051, respectively;
- (t) SEQ ID NOs: 964 and 1052, respectively;
- (u) SEQ ID NOs: 965 and 1053, respectively;
- (v) SEQ ID NOs: 966 and 1054, respectively;
- (w) SEQ ID NOs: 967 and 1055, respectively;
- (x) SEQ ID NOs: 968 and 1056, respectively;
- (y) SEQ ID NOs: 969 and 1057, respectively;
- (z) SEQ ID NOs: 970 and 1058, respectively;
- (aa) SEQ ID NOs: 971 and 1059, respectively;
- (bb) SEQ ID NOs: 972 and 1060, respectively;
- (cc) SEQ ID NOs: 973 and 1061, respectively;
- (dd) SEQ ID NOs: 974 and 1062, respectively;
- (ee) SEQ ID NOs: 975 and 1063, respectively;
- (ff) SEQ ID NOs: 976 and 1064, respectively;
- (gg) SEQ ID NOs: 977 and 1065, respectively;
- (hh) SEQ ID NOs: 978 and 1066, respectively;
- (ii) SEQ ID NOs: 979 and 1067, respectively;
- (jj) SEQ ID NOs: 980 and 1068, respectively;
- (kk) SEQ ID NOs: 981 and 1069, respectively;
- (ll) SEQ ID NOs: 982 and 1070, respectively;
- (mm) SEQ ID NOs: 983 and 1071, respectively;
- (nn) SEQ ID NOs: 984 and 1072, respectively;
- (oo) SEQ ID NOs: 985 and 1073, respectively;
- (pp) SEQ ID NOs: 986 and 1074, respectively;
- (qq) SEQ ID NOs: 987 and 1075, respectively;
- (rr) SEQ ID NOs: 988 and 1076, respectively;

(ss) SEQ ID NOs: 989 and 1077, respectively;
(tt) SEQ ID NOs: 990 and 1078, respectively;
(uu) SEQ ID NOs: 991 and 1079, respectively;
(vv) SEQ ID NOs: 992 and 1080, respectively;
(ww) SEQ ID NOs: 993 and 1081, respectively;
(xx) SEQ ID NOs: 994 and 1082, respectively;
(yy) SEQ ID NOs: 995 and 1083, respectively;
(zz) SEQ ID NOs: 996 and 1084, respectively;
(aaa) SEQ ID NOs: 997 and 1085, respectively;
(bbb) SEQ ID NOs: 998 and 1086, respectively;
(ccc) SEQ ID NOs: 999 and 1087, respectively;
(ddd) SEQ ID NOs: 1000 and 1088, respectively;
(eee) SEQ ID NOs: 1001 and 1089, respectively;
(fff) SEQ ID NOs: 1002 and 1090, respectively;
(ggg) SEQ ID NOs: 1003 and 1091, respectively;
(hhh) SEQ ID NOs: 1004 and 1092 respectively;
(iii) SEQ ID NOs: 1005 and 1093 respectively;
(jjj) SEQ ID NOs: 1006 and 1094, respectively;
(kkk) SEQ ID NOs: 1007 and 1095, respectively;
(lll) SEQ ID NOs: 1008 and 1096, respectively;
(mmm)SEQ ID NOs: 1009 and 1097, respectively;
(nnn) SEQ ID NOs: 1010 and 1098, respectively;
(ooo) SEQ ID NOs: 1011 and 1099, respectively;
(ppp) SEQ ID NOs: 1012 and 1100, respectively;
(qqq) SEQ ID NOs: 1013 and 1101, respectively;
(rrr) SEQ ID NOs: 1014 and 1102 respectively;
(sss) SEQ ID NOs: 1015 and 1103, respectively;
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(vvv) SEQ ID NOs: 1018 and 1106, respectively;

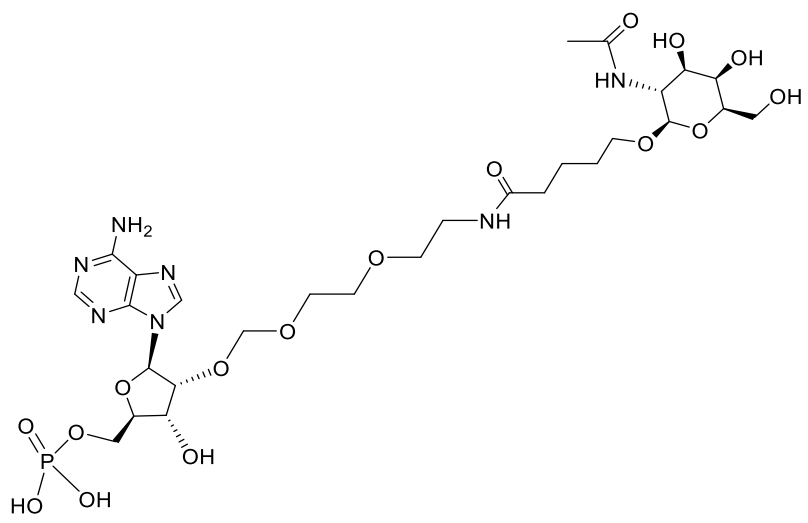
(www) SEQ ID NOs: 1019 and 1107, respectively;
 (xxx) SEQ ID NOs: 1020 and 1108, respectively;
 (yyy) SEQ ID NOs: 1021 and 1109, respectively;
 (zzz) SEQ ID NOs: 1022 and 1110, respectively;
 (aaaa) SEQ ID NOs: 1023 and 1111, respectively;
 (bbbb) SEQ ID NOs: 1024 and 1112, respectively;
 (cccc) SEQ ID NOs: 1025 and 1113, respectively;
 (dddd) SEQ ID NOs: 1026 and 1114, respectively;
 (eeee) SEQ ID NOs: 1027 and 1115, respectively;
 (ffff) SEQ ID NOs: 1028 and 1116, respectively;
 (gggg) SEQ ID NOs: 1029 and 1117, respectively;
 (hhhh) SEQ ID NOs: 1030 and 1118, respectively;
 (iiii) SEQ ID NOs: 1031 and 1119, respectively; and,
 (jjjj) SEQ ID NOs: 1032 and 1120, respectively.

In some embodiments of the RNAi oligonucleotide:

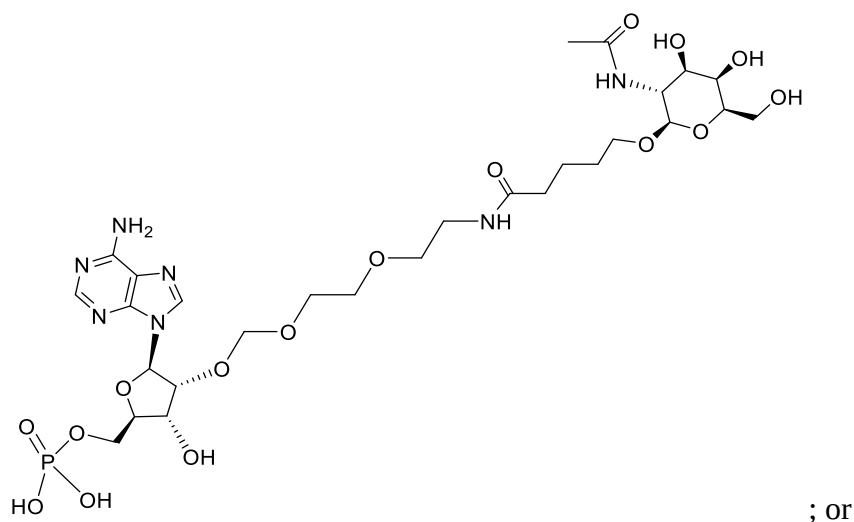
(i) the sense strand comprises the sequence and all of the modifications of 5'-mCs-mU-mC-mA-mA-mG-mG-fA-fU-fU-fU-mC-mA-mG-mU-mU-mA-mU-mA-mA-mG-mC-mA-mG-mC-mC-mG-[ademA-GalNAc]-[ademA-GalNAc]-[ademA-GalNAc]-mG-mG-mC-mU-mG-mC-3' (SEQ ID NO: 963), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs]-fUs-fAs-fU-fA-mA-fC-mU-mG-fA-mA-mA-mU-fC-mC-mU-mU-mG-mA-mGs-mGs-mG-3' (SEQ ID NO: 1051), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc = Chem. formula 5



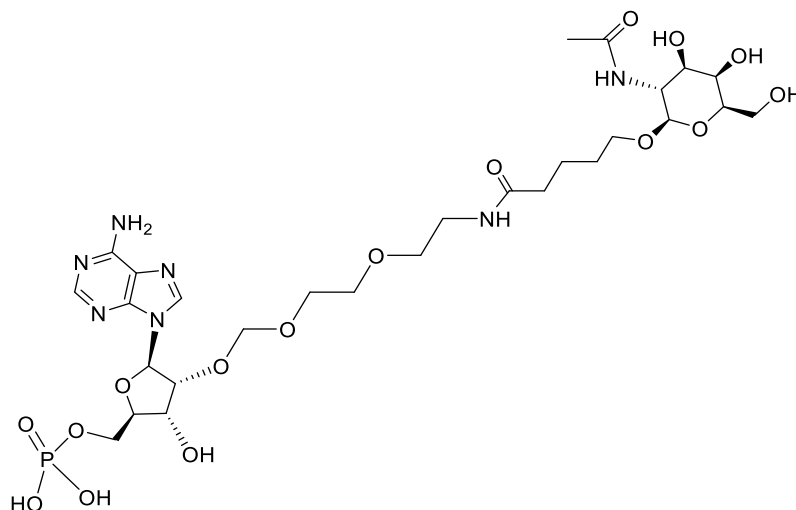
(ii) the sense strand comprises the sequence and all of the modifications of 5'-mUs-mC-mA-mA-mG-mG-mA-fU-fU-fU-fC-mA-mG-mU-mU-mA-mU-mA-mA-mG-mC-mA-mG-mC-mC-mG-[ademA-GalNAc]-[ademA-GalNAc]-[ademA-GalNAc]-mG-mG-mC-mU-mG-mC-3' (SEQ ID NO: 964), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs]-fUs-fUs-fA-fU-mA-fA-mC-mU-fG-mA-mA-mA-fU-mC-mC-mU-mU-mG-mAs-mGs-mG-3' (SEQ ID NO: 1052), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc = Chem. formula 5



(iii) the sense strand comprises the sequence and all of the modifications of 5'-mAs-mG-mC-mA-mG-mC-mG-fU-fC-fC-fA-mC-mU-mC-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: 1006), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs]-fGs-fCs-fU-fC-mU-fG-mA-mG-fU-mG-mG-mA-fC-mG-mC-mU-mG-mC-mUs-mGs-mG-3' (SEQ ID NO: 1094), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc = Chem. formula 5



(iv) the sense strand comprises the sequence and all of the modifications of 5'-mAs-mU-mG-mU-mG-mC-mA-fC-fG-fA-fA-mU-mG-mA-mC-mU-mG-mU-mU-mA-mG-mC-mA-mG-mC-mC-mG-[ademA-GalNAc]-[ademA-GalNAc]-[ademA-GalNAc]-mG-mG-mC-mU-mG-mC-3' (SEQ ID NO: 1018), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs]-fAs-fAs-fC-fA-mG-fU-mC-mA-fU-mU-mC-mG-fU-mG-mC-mA-mC-mA-mUs-mGs-mG-3' (SEQ ID NO: 1106), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc = Chem. formula 5



optionally wherein the oligonucleotide is a Dicer substrate.

In an aspect, the invention provides a pharmaceutical composition comprising the RNAi oligonucleotide according to the invention and a pharmaceutically acceptable carrier, delivery agent or excipient.

In an aspect, the invention provides a kit comprising the RNAi oligonucleotide according to the invention, an optional pharmaceutically acceptable carrier, and a package insert comprising instructions for administration to a subject having a disease, disorder or condition associated with *NR1H3* expression, optionally for the treatment of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), or systemic lupus erythematosus

In an aspect, the invention provides the use of the RNAi oligonucleotide according to the invention, or the pharmaceutical composition according to the invention, in the manufacture of a medicament for the treatment of a disease, disorder or condition associated with *NR1H3* expression, optionally for the treatment of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), or systemic lupus erythematosus, optionally for use in combination with a second composition or therapeutic agent.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1A provides a drawing of an oligonucleotide comprising a nicked tetraloop structure.

FIG. 1B provides a graph depicting the percent (%) remaining human *NR1H3* mRNA in liver of mice exogenously expressing human *NR1H3* (hydrodynamic injection model) after treatment with GalNAc-conjugated *NR1H3* oligonucleotides. Three days post-dose mice were hydrodynamically injected (HDI) with the human *NR1H3* mRNA construct. 18 hours later, livers were collected and human and mouse *NR1H3* mRNA levels were measured. Exons indicate the location on the mRNA where the construct targets. Constructs tested in **FIG. 1B** were selected from the screen described in **Example 2**. White arrows indicate potential constructs for non-human primate (NHP) studies.

FIG. 2 provides graphs depicting the percentage (%) of remaining human or mouse *NR1H3* mRNA in liver of mice exogenously expressing human *NR1H3* (hydrodynamic injection model) after treatment with GalNAc-conjugated *NR1H3* oligonucleotides designed based on sequences identified using the algorithm described in **Example 2**. Mice were dosed subcutaneously with 2 mg/kg of the indicated *NR1H3*-GalNAc construct. Three days post-dose mice were hydrodynamically injected (HDI) with the human *NR1H3* mRNA construct. 18 hours later, livers were collected and human and mouse *NR1H3* mRNA levels were measured. Exons indicate the location on the mRNA where the construct targets. Benchmark constructs (*NR1H3*-769 and *NR1H3*-1469) were selected from prior sequence screening conducted at Dicerna.

FIG. 3 provides a graph depicting the percent (%) remaining human *NR1H3* mRNA in liver of mice exogenously expressing human *NR1H3* (HDI model) after treatment with GalNAc-conjugated *NR1H3* oligonucleotides. Constructs tested in **FIG. 3** are a repeat assay validating the constructs tested in **FIG. 2**. White arrows indicate potential constructs for non-human primate studies.

FIG. 4 provides a graph depicting the percent (%) remaining human *NR1H3* mRNA in liver of mice exogenously expressing human *NR1H3* (HDI model) after treatment with GalNAc-conjugated *NR1H3* oligonucleotides. Constructs tested in **FIG. 1B** and **FIG. 2** were validated and repeated in two assays (experiment 1 and experiment 2) using the same methods. White arrows indicate potential constructs for non-human primate studies.

FIG. 5 provides a schematic depicting the dosing scheme and specimen collection for treatment of non-human primates with GalNAc-conjugated *NR1H3* oligonucleotides. 1 mg/kg or

4 mg/kg are dosed once every 4 weeks for four months (Q4Wx4). Timing for liver biopsies and blood collection is shown.

DETAILED DESCRIPTION

The liver X receptors α (LXR α ; encoded by the *NR1H3 gene*) and β (LXR β ; encoded by *NR1H2 gene*) are nuclear receptors that function in the regulation of lipid and cholesterol homeostasis, as well as inflammation (Venkateswaran, A., et al., PROC. NATL. ACAD. SCI. U. S. A., (2000); 97: 12097–102). LXR α is highly expressed in lipid metabolism-related organs such as the liver, small intestine, kidney, spleen, adrenal gland, and adipose tissue, whereas LXR β expression is distributed ubiquitously. The hypothesis of specific inhibition of LXR α in the hepatocytes to treat NASH-related dyslipidemia is supported by several clinical and pre-clinical observations. Activation of LXR α increases plasma and hepatic TG and plasma LDLc, as was demonstrated in human subjects treated with LXR agonist in a dose-dependent manner (Kirchgessner, T.G., et al., CELL METAB, (2016); 24(2): 223-33). Consistent with this observation, hepatic deletion of LXR α in mice lowers liver fat and reduces plasma triglycerides. (J. CLIN. INVEST. (2012); 122(5): 1688-99.

In addition, hepatic expression of LXR α is significantly upregulated in liver biopsies from NAFLD and NASH patients (Ahn, S.B., et al. DIG. DIS. SCI. (2014);59: 2975–82). However, avoiding inhibition of LXR α in macrophages is desirable as LXR α activation increases reverse cholesterol transport (RCT) which prevents atherosclerosis (CURR. OPIN. INVESTIG. DRUGS. (2003);4(9): 1053-8). Taken together, and without being bound by theory, antagonism/inhibition of LXR α specifically in hepatocytes (*e.g.*, via *NR1H3*-targeted RNAi oligonucleotides) decreases *de novo* lipogenesis with concomitant preservation of LXR α function in macrophages and stellate cells for their positive roles in preventing inflammation and fibrosis respectively, thus representing a promising approach for treatment of NAFLD and/or NASH. (Higuchi, N., et al., HEPATOL. RES. (2008);38: 1122-29) (Repa, J. J.; and, Mangelsdorf, D. J. ANNU. REV. CELL DEV. BIOL. (2000);16: 459–81). This approach may be best managed by a specific and targeted reduction of the *NR1H3* expression in the liver while other organs, tissues or cells expressing *NR1H3* are left essentially alone. In this sense the current invention may provide an improved modality of treatment given its specific targeting of mRNA production in the liver.

According to some aspects, the disclosure provides oligonucleotides (*e.g.*, RNAi oligonucleotides) that reduce *NR1H3* expression in the liver. In some embodiments, the oligonucleotides provided herein are designed to treat diseases associated with *NR1H3* expression in the liver, *e.g.*, non-alcoholic fatty liver disease (NAFLD), or non-alcoholic steatohepatitis (NASH). In some respects, the disclosure provides methods of treating a disease associated with *NR1H3* expression by reducing *NR1H3* expression in cells (*e.g.*, cells of the liver) or in organs (*e.g.*, liver).

Oligonucleotide Inhibitors of *NR1H3* Expression

***NR1H3* Target Sequences**

In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) is targeted to a target sequence comprising a *NR1H3* mRNA. In some embodiments, an oligonucleotide described herein is targeted to a target sequence within a *NR1H3* mRNA sequence. In some embodiments, the oligonucleotide described herein corresponds to a target sequence within a *NR1H3* 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 double-stranded (ds) RNAi oligonucleotide) binds or anneals to a target sequence comprising *NR1H3* mRNA, thereby inhibiting *NR1H3* expression.

In some embodiments, the oligonucleotide is targeted to a *NR1H3* target sequence for the purpose of inhibiting *NR1H3* expression *in vivo*. In some embodiments, the amount or extent of inhibition of *NR1H3* expression by an oligonucleotide targeted to a *NR1H3* target sequence correlates with the potency of the oligonucleotide. In some embodiments, the amount or extent of inhibition of *NR1H3* expression by an oligonucleotide targeted to a *NR1H3* target sequence correlates with the amount or extent of therapeutic benefit in a subject or patient having a disease, disorder or condition associated with *NR1H3* expression treated with the oligonucleotide.

Through examination of the nucleotide sequence of mRNAs encoding *NR1H3*, including mRNAs of multiple different species (*e.g.*, human, cynomolgus monkey, mouse, and rat; *see, e.g.*, Example 2) and as a result of *in vitro* and *in vivo* testing (*see, e.g.*, Examples 2-5), it has been discovered that certain nucleotide sequences of *NR1H3* mRNA are more amenable than others to oligonucleotide-based inhibition and are thus useful as target sequences for the oligonucleotides

herein. In some embodiments, a sense strand of an oligonucleotide (*e.g.*, an RNAi oligonucleotide) described herein comprises a *NR1H3* target sequence. In some embodiments, a portion or region of the sense strand of an oligonucleotide described herein (*e.g.*, an RNAi oligonucleotide) comprises a *NR1H3* target sequence. In some embodiments, a *NR1H3* target sequence comprises, or consists of, a sequence of any one of SEQ ID NOs: 1-384. In some embodiments, a *NR1H3* target sequence can consist of one of the sequences set forth in SEQ ID NO: 92, 285, and/or 354.

NR1H3 Targeting Sequences

In some embodiments, the oligonucleotides herein (*e.g.*, RNAi oligonucleotides) have regions of complementarity to *NR1H3* mRNA (*e.g.*, within a target sequence of *NR1H3* mRNA) for purposes of targeting the *NR1H3* mRNA in cells and inhibiting and/or reducing *NR1H3* expression. In some embodiments, the oligonucleotides herein comprise a *NR1H3* targeting sequence (*e.g.*, an antisense strand or a guide strand of a dsRNAi oligonucleotide) having a region of complementarity that binds or anneals to a *NR1H3* target sequence by complementary (Watson-Crick) base pairing. The targeting sequence or region of complementarity is generally of a suitable length and base content to enable binding or annealing of the oligonucleotide (or a strand thereof) to a *NR1H3* mRNA for purposes of inhibiting and/or reducing *NR1H3* 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 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, an oligonucleotide comprises a target sequence or region of complementarity complementary to a sequence of any one of SEQ ID NOs: 1-384. In some embodiments, an oligonucleotide comprises a target sequence or region of complementarity complementary to a sequence of any one of SEQ ID NOs: 1125-1511 and the targeting sequence or region of complementarity is 18 nucleotides in length. In some embodiments, an 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 19 nucleotides in length. In some embodiments, an oligonucleotide comprises a target sequence or region of complementarity complementary to a sequence of any one of SEQ ID NOs: 1125-1511, and the targeting sequence or region of complementarity is 19 nucleotides in length.

In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) comprises a targeting sequence or a region of complementarity (*e.g.*, an antisense strand or a guide strand of a double-stranded oligonucleotide) that is fully complementary to a *NR1H3* target sequence. In some embodiments, the targeting sequence or region of complementarity is partially complementary to a *NR1H3* target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is fully complementary to a *NR1H3* target sequence. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to a *NR1H3* 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: 1-384. 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: 1125-1511. 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: 1409, 1509, 1510 or 1511. 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: 1-384. 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: 1125-1511. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity that is partially complementary to the sequence set forth in SEQ ID NO: 1409, 1509, 1510 or 1511.

In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) comprises a targeting sequence or region of complementarity that is complementary to a contiguous sequence of nucleotides comprising a *NR1H3* 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 *NR1H3* 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 *NR1H3* 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 *NR1H3* mRNA, wherein the contiguous sequence of nucleotides is 20 nucleotides in length.

In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi 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: 1-384. In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi 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: 1125-1511, 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: 1409, 1509, 1510 or 1511, wherein the contiguous sequence of nucleotides is 19 nucleotides in length.

In some embodiments, a targeting sequence or region of complementarity of an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1-384. In some embodiments, a targeting sequence or region of complementarity of an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1125-1511. In some embodiments, a targeting sequence or region of complementarity of an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) is complementary to a contiguous sequence of nucleotides of any one of SEQ ID NOs: 1-384 and spans the entire length of an antisense strand. In some embodiments, a targeting sequence or region of complementarity of the oligonucleotide is complementary to a contiguous sequence of nucleotides of SEQ ID NOs: 1-384 and spans a portion of the entire length of an antisense strand. In some embodiments, a targeting sequence or region of complementarity of the oligonucleotide is complementary to a contiguous sequence of nucleotides of SEQ ID NOs: 1125-1511 and spans a portion of the entire length of an antisense strand. In some embodiments, a targeting sequence or region of complementarity of the oligonucleotide is complementary to a contiguous sequence of nucleotides of SEQ ID NOs: 1125-1511 and spans a portion of the entire length of an antisense strand. In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) comprises a region of complementarity (*e.g.*, on an antisense strand of a dsRNA) that is at least partially (*e.g.*, fully) complementary to a contiguous stretch of nucleotides spanning nucleotides 1-19 or 1-20 of a sequence as set forth in any one of SEQ ID NOs: 1-384. In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) comprises a region of complementarity (*e.g.*, on an antisense strand of a dsRNA) that is at least partially (*e.g.*, fully) complementary to a contiguous stretch of nucleotides spanning nucleotides 1-19 or 1-20 of a sequence as set forth in any one of SEQ ID NOs: 1125-1511.

In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) comprises a targeting sequence or region of complementarity having one or more base pair (bp) mismatches with the corresponding *NR1H3* 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 *NR1H3* target sequence provided that the ability of the targeting sequence or region of complementarity to bind or anneal to the *NR1H3* mRNA under appropriate hybridization conditions and/or the ability of the oligonucleotide

to inhibit *NR1H3* expression is maintained. Alternatively, 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 *NR1H3* target sequence provided that the ability of the targeting sequence or region of complementarity to bind or anneal to the *NR1H3* mRNA under appropriate hybridization conditions and/or the ability of the oligonucleotide to inhibit *NR1H3* 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 having 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 throughout the targeting sequence or region of complementarity. In some embodiments, the oligonucleotide comprises a targeting sequence or region of complementarity having 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. 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: 1-384, 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 *NR1H3* target sequence. 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: 1125-1511, 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 *NR1H3* target sequence. 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: 1-384, 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 *NR1H3* target sequence. 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: 1125-1511, 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 *NR1H3* target sequence. 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: 1409, 1509, 1510 or 1511, 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 *NR1H3* target sequence. 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: 1409, 1509, 1510 or 1511, 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 *NR1H3* target sequence.

Types of Oligonucleotides

A variety of oligonucleotide types and/or structures are useful for targeting *NR1H3* in the methods herein including, but not limited to, RNAi oligonucleotides, antisense oligonucleotides (ASOs), miRNAs, *etc.* Any of the oligonucleotide types described herein or elsewhere are contemplated for use as a framework to incorporate a *NR1H3* targeting sequence herein for the purposes of inhibiting *NR1H3* expression.

In some embodiments, the oligonucleotides herein inhibit *NR1H3* expression by engaging with RNA interference (RNAi) pathways upstream or downstream of Dicer involvement. For

example, RNAi oligonucleotides have been developed with each strand having sizes of about 19-25 nucleotides with at least one 3'-overhang of 1 to 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 dsRNAs 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 tetraloop 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 double-stranded (ds) extensions.

In some embodiments, the oligonucleotides herein engage with the RNAi pathway downstream of the involvement of Dicer (*e.g.*, Dicer cleavage). In some embodiments, the oligonucleotides described herein are Dicer substrates. In some embodiments, upon endogenous Dicer processing, double-stranded nucleic acids of 19-23 nucleotides in length capable of reducing *NR1H3* expression are produced. 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 (*e.g.*, siRNA) comprises a 21-nucleotide guide strand that is antisense to a target RNA and a complementary passenger 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 available including oligonucleotides having a guide strand of 23 nucleotides and a passenger strand of 21 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 two 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 21 bp duplex region. *See, e.g.*, US Patent Nos. 9,012,138; 9,012,621 and 9,193,753.

In some embodiments, the oligonucleotides herein comprise sense and antisense strands that are both in the range of about 17 to 36 (*e.g.*, 17 to 36, 20 to 25, or 21-23) nucleotides in length. In some embodiments, the oligonucleotides described herein comprise an antisense strand of 19-30 nucleotides in length and a sense strand of 19-50 nucleotides in length, wherein the antisense and sense strands are separate strands which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand. In some embodiments, an

oligonucleotide herein comprises a sense and antisense strand 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, an 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 sense and antisense strands is 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.

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.* METHODS MOL. BIOL. (2010);629: 141-158), blunt siRNAs (*e.g.*, of 19 bps in length; *see, e.g.*, Kraynack & Baker RNA (2006);12: 163-176), asymmetrical siRNAs (aiRNA; *see, e.g.*, Sun *et al.* NAT. BIOTECHNOL. (2008);26: 1379-1382), asymmetric shorter-duplex siRNA (*see, e.g.*, Chang *et al.* MOL. THER. (2009);17: 725-32), fork siRNAs (*see, e.g.*, Hohjoh FEBS LETT. (2004);557: 193-198), ss siRNAs (Elsner NAT. BIOTECHNOL. (2012);30: 1063), dumbbell-shaped circular siRNAs (*see, e.g.*, Abe *et al.* J. AM. CHEM. SOC. (2007);129: 15108-09), and small internally segmented interfering RNA (siRNA; *see, e.g.*, Bramsen *et al.* NUCLEIC ACIDS RES. (2007);35: 5886-97). Further non-limiting examples of an oligonucleotide structures that may be used in some embodiments to reduce or inhibit the expression of *NR1H3* are microRNA (miRNA), short hairpin RNA (shRNA) and short siRNA (*see, e.g.*, Hamilton *et al.* EMBO J. (2002);21: 4671-79; *see also*, US Patent Application Publication No. 2009/0099115).

Still, in some embodiments, an oligonucleotide for reducing or inhibiting *NR1H3* expression herein is single-stranded (ss). Such structures may include but are not limited to single-stranded RNAi molecules. Recent efforts have demonstrated the activity of ss RNAi molecules (*see, e.g.*, Matsui *et al.* MOL. THER. (2016);24: 946-55). However, in some embodiments,

oligonucleotides herein are antisense oligonucleotides (ASOs). An antisense oligonucleotide is a single-stranded oligonucleotide that has a nucleobase sequence which, when written 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.* ANNU. REV. PHARMACOL. (2017);57: 81-105).

In some embodiments, the antisense oligonucleotide shares a region of complementarity with *NR1H3* mRNA. In some embodiments, the antisense oligonucleotide targets the human *NR1H3* mRNA (Homo sapiens NR1H3, mRNA, transcript variant 5, NCBI Reference Sequence: NM_001251935.1). In some embodiments, the antisense oligonucleotide is 15-50 nucleotides in length. In some embodiments, the antisense oligonucleotide is 15-25 nucleotides in length. In some embodiments, the antisense oligonucleotide is 22 nucleotides in length. In some embodiments, the antisense oligonucleotide is complementary to any one of SEQ ID NOs: 1-384. In some embodiments, the antisense oligonucleotide is complementary to any one of SEQ ID NOs: 1125-1511. In some embodiments, the antisense oligonucleotide is at least 15 contiguous nucleotides in length. In some embodiments, the antisense oligonucleotide is at least 19 contiguous nucleotides in length. In some embodiments, the antisense oligonucleotide is at least 20 contiguous nucleotides in length. In some embodiments, the antisense oligonucleotide differs by 1, 2, or 3 nucleotides from the target sequence.

Double-Stranded Oligonucleotides

In some aspects, the disclosure provides double-stranded (ds) RNAi oligonucleotides for targeting *NR1H3* mRNA and inhibiting *NR1H3* 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 antisense strand are covalently linked. In some embodiments, the sense strand and antisense strand form a duplex region, wherein the sense strand and antisense strand, or a portion thereof, binds with one another in a complementary fashion (*e.g.*, by Watson-Crick base pairing).

In some embodiments, the sense strand has a first region (R1) and a second region (R2), wherein R2 comprises a first subregion (S1), a tetraloop (L) or triloop (triL), and a second subregion (S2), wherein L or triL is located between S1 and S2, and wherein S1 and S2 form a second duplex (D2). D2 may have various length. In some embodiments, D2 is about 1-6 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. 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 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 20 nucleotides in length. In some embodiments, D1 comprising sense strand and antisense strand does not span the entire length of the sense strand and/or antisense strand. In some embodiments, D1 comprising the sense strand and antisense strand spans the entire length of either the sense strand or antisense strand or both. In certain embodiments, D1 comprising the sense strand and antisense strand spans the entire length of both the sense strand and the antisense strand.

In some embodiments, an oligonucleotide provided herein 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. In some embodiments, an oligonucleotide provided herein comprises a sense strand having a sequence of any one of SEQ ID NOs: 1125-1511 and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 1512-1515.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand having a sequence of any one of SEQ ID NOs: 769-856 or 1519-1552

and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 857-944 as is arranged in **Tables 3** and **4**.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand and an antisense strand comprising nucleotide sequences selected from:

- (a) SEQ ID NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;

- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;
- (yy) SEQ ID NOs: 819 and 907, respectively;
- (zz) SEQ ID NOs: 820 and 908, respectively;
- (aaa) SEQ ID NOs: 821 and 909, respectively;
- (bbb) SEQ ID NOs: 822 and 910, respectively;
- (ccc) SEQ ID NOs: 823 and 911, respectively;
- (ddd) SEQ ID NOs: 824 and 912, respectively;

(eee) SEQ ID NOs: 825 and 913, respectively;
(fff) SEQ ID NOs: 826 and 914, respectively;
(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm) SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;
(ooo) SEQ ID NOs: 835 and 923, respectively;
(ppp) SEQ ID NOs: 836 and 924, respectively;
(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;
(uuu) SEQ ID NOs: 1537 and 929, respectively;
(vvv) SEQ ID NOs: 842 and 930, respectively;
(www) SEQ ID NOs: 843 and 931, respectively;
(xxx) SEQ ID NOs: 844 and 932, respectively;
(yyy) SEQ ID NOs: 845 and 933, respectively;
(zzz) SEQ ID NOs: 846 and 934, respectively;
(aaaa) SEQ ID NOs: 847 and 935, respectively;
(bbbb) SEQ ID NOs: 848 and 936, respectively;
(cccc) SEQ ID NOs: 849 and 937, respectively;
(dddd) SEQ ID NOs: 850 and 938, respectively;
(eeee) SEQ ID NOs: 851 and 939, respectively;
(ffff) SEQ ID NOs: 852 and 940, respectively;
(gggg) SEQ ID NOs: 853 and 941, respectively;
(hhhh) SEQ ID NOs: 854 and 942, respectively;

- (iii) SEQ ID NOs: 855 and 943, respectively; and,
- (jjj) SEQ ID NOs: 856 and 944, respectively.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand and an antisense strand comprising nucleotide sequences selected from:

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively; and,
- (d) SEQ ID NOs: 813 and 901, respectively.

In some embodiments, the sense strand comprises the sequence of SEQ ID NO: 786 and the antisense strand comprises the sequence of SEQ ID NO: 874.

In some embodiments, the sense strand comprises the sequence of SEQ ID NO: 787 and the antisense strand comprises the sequence of SEQ ID NO: 875.

In some embodiments, the sense strand comprises the sequence of SEQ ID NO: 1537 and the antisense strand comprises the sequence of SEQ ID NO: 929.

In some embodiments, the sense strand comprises the sequence of SEQ ID NO: 813 and the antisense strand comprises the sequence of SEQ ID NO: 901.

It should be appreciated that, in some embodiments, sequences presented in the Sequence Listing may be referred to in describing the structure of an oligonucleotide (*e.g.*, a dsRNAi oligonucleotide) or other nucleic acid. In such embodiments, the actual oligonucleotide or other nucleic acid may have one or more alternative nucleotides (*e.g.*, an 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.

In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) 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 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 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 oligonucleotide is longer than 25 nucleotides (*e.g.*, 26, 27, 28, 29, or 30 nucleotides). In some embodiments, the sense strand of the oligonucleotide comprises a nucleotide sequence selected from SEQ ID NOs: 769-856, 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 oligonucleotide comprises a nucleotide sequence selected from SEQ ID NOs: 1519-1552, 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 oligonucleotide comprises a nucleotide sequence selected from SEQ ID NOs: 769-856, wherein the nucleotide sequence is longer than 25 nucleotides (*e.g.*, 26, 27, 28, 29 or 30 nucleotides).

In some embodiments, oligonucleotides herein (*e.g.*, RNAi oligonucleotides) have one 5' end that is thermodynamically less stable when compared to the other 5' end. In some embodiments, an asymmetric oligonucleotide is provided that includes 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). In some embodiments, the oligonucleotide has an overhang comprising two (2) nucleotides on the 3' end of the antisense (guide) strand. However, other overhangs are possible. In some embodiments, an overhang is a 3'-overhang comprising a length of between 1 and 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 1 and 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 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: 1-384, and a 5'-overhang comprising a length of between 1 and 6 nucleotides. 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: 1125-1511, and a 5'-overhang

comprising a length of between 1 and 6 nucleotides. In some embodiments, the oligonucleotide comprises a sense strand comprising a nucleotide sequence selected from SEQ ID NOs: 769-856, wherein the oligonucleotide comprises a 5'-overhang comprising a length of between 1 and 6 nucleotides. In some embodiments, the oligonucleotide comprises a sense strand comprising a nucleotide sequence selected from SEQ ID NOs: 1519-1552, wherein the oligonucleotide comprises a 5'-overhang comprising a length of between 1 and 6 nucleotides. In some embodiments, the oligonucleotide comprises an antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 857-944, wherein the oligonucleotide comprises a 5'-overhang comprising a length of between 1 and 6 nucleotides. In some embodiments, the oligonucleotide comprises a sense strand comprising a nucleotide sequence selected from SEQ ID NOs: 769-856 and antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 857-944, wherein the oligonucleotide comprises a 5'-overhang comprising a length of between 1 and 6 nucleotides. In some embodiments, the oligonucleotide comprises a sense strand comprising a nucleotide sequence selected from SEQ ID NOs: 1519-1552 and antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 857-944, wherein the oligonucleotide comprises a 5'-overhang comprising a length of between 1 and 6 nucleotides.

In some embodiments, two (2) terminal nucleotides on the 3' end of an antisense strand are modified. In some embodiments, the two (2) terminal nucleotides on the 3' end of the antisense strand are complementary with the target mRNA (*e.g.*, *NR1H3* mRNA). In some embodiments, the two (2) terminal nucleotides on the 3' end of the antisense strand are not complementary with the target mRNA. In some embodiments, the two (2) terminal nucleotides on the 3' end of the antisense strand of an oligonucleotide herein are unpaired. In some embodiments, the two (2) terminal nucleotides on the 3' end of the antisense strand of an oligonucleotide herein comprise an unpaired GG. In some embodiments, the two (2) terminal nucleotides on the 3' end of an antisense strand of an oligonucleotide herein are not complementary to the target mRNA. In some embodiments, two (2) terminal nucleotides on each 3' end of an oligonucleotide are GG. In some embodiments, one or both of the two (2) terminal GG nucleotides on each 3' end of an oligonucleotide herein is not complementary with the target mRNA. 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: 1-384,

wherein the two (2) terminal nucleotides on the 3' end of the antisense strand of the oligonucleotide herein comprises an unpaired GG. 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: 1125-1511, wherein the two (2) terminal nucleotides on the 3' end of the antisense strand of the oligonucleotide herein comprises an unpaired GG. In some embodiments, the oligonucleotide comprises an antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 857-944, wherein the two (2) terminal nucleotides on the 3' end of the antisense strand of the oligonucleotide comprises an unpaired GG. In some embodiments, the oligonucleotide comprises a sense strand comprising a nucleotide sequence selected from SEQ ID NOs: 769-856 and antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 857-944, wherein the two (2) terminal nucleotides on the 3' end of the antisense strand of the oligonucleotide comprises an unpaired GG. In some embodiments, the oligonucleotide comprises a sense strand comprising a nucleotide sequence selected from SEQ ID NOs: 1519-1552 and antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 857-944, wherein the two (2) terminal nucleotides on the 3' end of the antisense strand of the oligonucleotide comprises an unpaired GG.

In some embodiments, there is one or more (*e.g.*, 1, 2, 3, 4, or 5) mismatch(s) between a sense and antisense strand comprising an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide). If there is more than one mismatch between a sense and antisense strand, 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 comprises one or more mismatches. In some embodiments, two (2) 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 an oligonucleotide herein improves or increases the potency of the oligonucleotide. In some embodiments, the sense and antisense strands of an oligonucleotide herein comprise nucleotides sequences selected from the group consisting of:

- (a) SEQ ID NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;

- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;

- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;
- (yy) SEQ ID NOs: 819 and 907, respectively;
- (zz) SEQ ID NOs: 820 and 908, respectively;
- (aaa) SEQ ID NOs: 821 and 909, respectively;
- (bbb) SEQ ID NOs: 822 and 910, respectively;
- (ccc) SEQ ID NOs: 823 and 911, respectively;
- (ddd) SEQ ID NOs: 824 and 912, respectively;
- (eee) SEQ ID NOs: 825 and 913, respectively;
- (fff) SEQ ID NOs: 826 and 914, respectively;
- (ggg) SEQ ID NOs: 827 and 915, respectively;
- (hhh) SEQ ID NOs: 828 and 916, respectively;
- (iii) SEQ ID NOs: 829 and 917, respectively;
- (jjj) SEQ ID NOs: 830 and 918, respectively;
- (kkk) SEQ ID NOs: 831 and 919, respectively;
- (lll) SEQ ID NOs: 832 and 920, respectively;

(mmm) SEQ ID NOs: 833 and 921, respectively;
 (nnn) SEQ ID NOs: 834 and 922, respectively;
 (ooo) SEQ ID NOs: 835 and 923, respectively;
 (ppp) SEQ ID NOs: 836 and 924, respectively;
 (qqq) SEQ ID NOs: 837 and 925, respectively;
 (rrr) SEQ ID NOs: 838 and 926, respectively;
 (sss) SEQ ID NOs: 839 and 927, respectively;
 (ttt) SEQ ID NOs: 840 and 928, respectively;
 (uuu) SEQ ID NOs: 1537 and 929, respectively;
 (vvv) SEQ ID NOs: 842 and 930, respectively;
 (www) SEQ ID NOs: 843 and 931, respectively;
 (xxx) SEQ ID NOs: 844 and 932, respectively;
 (yyy) SEQ ID NOs: 845 and 933, respectively;
 (zzz) SEQ ID NOs: 846 and 934, respectively;
 (aaaa) SEQ ID NOs: 847 and 935, respectively;
 (bbbb) SEQ ID NOs: 848 and 936, respectively;
 (cccc) SEQ ID NOs: 849 and 937, respectively;
 (dddd) SEQ ID NOs: 850 and 938, respectively;
 (eeee) SEQ ID NOs: 851 and 939, respectively;
 (ffff) SEQ ID NOs: 852 and 940, respectively;
 (gggg) SEQ ID NOs: 853 and 941, respectively;
 (hhhh) SEQ ID NOs: 854 and 942, respectively;
 (iiii) SEQ ID NOs: 855 and 943, respectively; and,
 (jjjj) SEQ ID NOs: 856 and 944, respectively,

wherein there is one or more (*e.g.*, 1, 2, 3, 4 or 5) mismatch(s) between the sense and antisense strands.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand and an antisense strand comprising nucleotide sequences selected from:

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;

(c) SEQ ID NOs: 1537 and 929, respectively; and,

(d) SEQ ID NOs: 813 and 901, respectively,

wherein there is one or more (*e.g.*, 1, 2, 3, 4, or 5) mismatch(s) between the sense and antisense strands.

Antisense Strands

In some embodiments, an antisense strand of an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) is referred to as a “guide strand”. For example, an antisense strand that engages with RNA-induced silencing complex (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, as the antisense strand is referred to as a guide strand. In some embodiments, a sense strand comprising a region of complementary to a guide strand is referred to herein as a “passenger strand.”

In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi 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, or up to 12 nucleotides in length). In some embodiments, an 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, an 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 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, an oligonucleotide comprises antisense strand of 15 to 30 nucleotides in length. In some embodiments, an antisense strand of any one of the oligonucleotides disclosed herein is 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, or 40 nucleotides in length. In some embodiments, an oligonucleotide comprises an antisense strand of 22 nucleotides in length.

In some embodiments, an oligonucleotide disclosed herein (*e.g.*, an RNAi oligonucleotide) for targeting *NR1H3* 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, an oligonucleotide herein 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, an oligonucleotide disclosed herein for targeting *NR1H3* comprises an antisense strand comprising or consisting of a sequence as set forth in any one of SEQ ID NOs: 857-944. In some embodiments, an oligonucleotide herein 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: 857-944. In some embodiments, an oligonucleotide disclosed herein for targeting *NR1H3* comprises an antisense strand comprising or consisting of a sequence as set forth in any one of SEQ ID NOs: 874, 875, 929, and 901. In some embodiments, an oligonucleotide herein 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: 874, 875, 929, and 901.

In some embodiments, an oligonucleotide herein comprises an antisense strand comprising a nucleotide sequence selected from SEQ ID NOs: 1512-1515.

Sense Strands

In some embodiments, an oligonucleotide disclosed herein (*e.g.*, an RNAi oligonucleotide) for targeting *NR1H3* mRNA and inhibiting *NR1H3* expression comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 1-384. In some embodiments, an oligonucleotide disclosed herein (*e.g.*, an RNAi oligonucleotide) for targeting *NR1H3* mRNA and inhibiting *NR1H3* expression comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 1125-1511. In some embodiments, an oligonucleotide herein has a sense strand comprised of 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, an oligonucleotide herein has a sense strand comprised of 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: 1125-1511. In some embodiments, an

oligonucleotide disclosed herein for targeting *NR1H3* mRNA and inhibiting *NR1H3* expression comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 769-856. In some embodiments, an oligonucleotide disclosed herein for targeting *NR1H3* mRNA and inhibiting *NR1H3* expression comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 1519-1552. In some embodiments, an oligonucleotide herein 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: 769-856. In some embodiments, an oligonucleotide herein 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: 1519-1552. In some embodiments, an oligonucleotide disclosed herein for targeting *NR1H3* mRNA and inhibiting *NR1H3* expression comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 786, 787, 1537, and 813. In some embodiments, an oligonucleotide herein 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: 786, 787, 1537, and 813. In some embodiments, an oligonucleotide disclosed herein for targeting *NR1H3* mRNA and inhibiting *NR1H3* expression comprises a sense strand sequence as set forth in any one of SEQ ID NOs: 1409, 1509, 1510 and 1511. In some embodiments, an oligonucleotide herein 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: 1409, 1509, 1510 and 1511.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand (or passenger 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, an oligonucleotide herein comprises 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, an oligonucleotide herein comprises 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, an oligonucleotide herein comprises a sense strand of 15 to 50 nucleotides in length. In some embodiments, an oligonucleotide herein comprises a sense strand of 18 to 36 nucleotides in length. In some embodiments, an oligonucleotide herein comprises 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, an oligonucleotide herein comprises a sense strand of 36 nucleotides in length.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi 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, a 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.

In some embodiments, a stem-loop provides the 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 both. For example, in some embodiments, the loop

of a stem-loop is comprised of nucleotides comprising one or more modifications that facilitate, improve, or increase targeting to a target mRNA (*e.g.*, a *NR1H3* mRNA), inhibition of target gene expression (*e.g.*, *NR1H3* expression), and/or delivery, uptake, and/or penetrance into a target cell, tissue, or organ (*e.g.*, the liver), or a combination thereof. In some embodiments, the stem-loop itself or modification(s) to the stem-loop do not affect or 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, uptake, and/or penetrance of the oligonucleotide to a target cell, tissue, or organ (*e.g.*, the liver). In certain embodiments, an oligonucleotide herein 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 single-stranded loop of linked nucleotides 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 loop (L) is 3 nucleotides in length. In some embodiments, the loop (L) is 4 nucleotides in length. In some embodiments, the loop (L) is 5 nucleotides in length. In some embodiments, the loop (L) is 6 nucleotides in length. In some embodiments, the loop (L) is 7 nucleotides in length. In some embodiments, the loop (L) is 8 nucleotides in length. In some embodiments, the loop (L) is 9 nucleotides in length. In some embodiments, the loop (L) is 10 nucleotides in length.

In some embodiments, the tetraloop comprises the sequence 5'-GAAA-3'. In some embodiments, the stem loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 1121).

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi 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: 1-384, 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 single-stranded 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, an oligonucleotide provided herein (*e.g.*, an RNAi 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: 1125-1511, 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 single-stranded 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: 1-384, 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 single-stranded loop between S1 and S2 of 4 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: 1-384, 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 single-stranded loop between S1 and S2 of 4 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: 1125-1511, 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 single-stranded loop between S1 and S2 of 4 nucleotides in length.

In some embodiments, a loop (L) of a stem-loop having the structure S1-L-S2 as described herein is a triloop. 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: 1-384 and a triloop. In some embodiments, the triloop comprises ribonucleotides, deoxyribonucleotides, modified nucleotides, ligands (*e.g.*, delivery ligands), and combinations thereof. In some embodiments, a loop (L) of a stem-loop having the structure S1-L-S2 as described herein is a triloop. 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: 1125-1511 and a triloop. In some embodiments, the triloop comprises ribonucleotides, deoxyribonucleotides, modified nucleotides, ligands (*e.g.*, delivery ligands), and combinations thereof.

In some embodiments, a loop (L) of a stem-loop having the structure S1-L-S2 as described above is a tetraloop. In some embodiments, an oligonucleotide herein 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: 1-384 and a tetraloop. In some embodiments, the tetraloop comprises ribonucleotides, deoxyribonucleotides, modified nucleotides, ligands (*e.g.*, delivery ligands), and combinations thereof. In some embodiments, a loop (L) of a stem-loop having the structure S1-L-S2 as described above is a tetraloop. In some embodiments, an oligonucleotide herein 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: 1125-1511 and a tetraloop. In some embodiments, the tetraloop comprises ribonucleotides, deoxyribonucleotides, modified nucleotides, ligands (*e.g.*, delivery ligands), and combinations thereof.

Duplex Length

In some embodiments, a duplex formed between a sense and antisense strand is at least 12 (*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, a duplex formed between a sense and antisense strand is in the range of 12-30 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, a duplex formed between a sense and antisense strand 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, a duplex formed between a sense and antisense strand is 12 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 13 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 14 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 15 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 16 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 17 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 18 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 19 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 20 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 21 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 22 nucleotides in length. In some embodiments, a duplex

formed between a sense and antisense strand is 23 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 24 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 25 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 26 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 27 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 28 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 29 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand is 30 nucleotides in length. In some embodiments, a duplex formed between a sense and antisense strand does not span the entire length of the sense strand and/or antisense strand. In some embodiments, a duplex between a sense and antisense strand spans the entire length of either the sense or antisense strands. In some embodiments, a duplex between a sense and antisense strand spans the entire length of both the sense strand and the antisense strand. 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 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;

- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;

(tt) SEQ ID NOs: 814 and 902, respectively;
(uu) SEQ ID NOs: 815 and 903, respectively;
(vv) SEQ ID NOs: 816 and 904, respectively;
(ww) SEQ ID NOs: 817 and 905, respectively;
(xx) SEQ ID NOs: 818 and 906, respectively;
(yy) SEQ ID NOs: 819 and 907, respectively;
(zz) SEQ ID NOs: 820 and 908, respectively;
(aaa) SEQ ID NOs: 821 and 909, respectively;
(bbb) SEQ ID NOs: 822 and 910, respectively;
(ccc) SEQ ID NOs: 823 and 911, respectively;
(ddd) SEQ ID NOs: 824 and 912, respectively;
(eee) SEQ ID NOs: 825 and 913, respectively;
(fff) SEQ ID NOs: 826 and 914, respectively;
(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm) SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;
(ooo) SEQ ID NOs: 835 and 923, respectively;
(ppp) SEQ ID NOs: 836 and 924, respectively;
(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;
(uuu) SEQ ID NOs: 1537 and 929, respectively;
(vvv) SEQ ID NOs: 842 and 930, respectively;
(www) SEQ ID NOs: 843 and 931, respectively;

- (xxx) SEQ ID NOs: 844 and 932, respectively;
- (yyy) SEQ ID NOs: 845 and 933, respectively;
- (zzz) SEQ ID NOs: 846 and 934, respectively;
- (aaaa) SEQ ID NOs: 847 and 935, respectively;
- (bbbb) SEQ ID NOs: 848 and 936, respectively;
- (cccc) SEQ ID NOs: 849 and 937, respectively;
- (dddd) SEQ ID NOs: 850 and 938, respectively;
- (eeee) SEQ ID NOs: 851 and 939, respectively;
- (ffff) SEQ ID NOs: 852 and 940, respectively;
- (gggg) SEQ ID NOs: 853 and 941, respectively;
- (hhhh) SEQ ID NOs: 854 and 942, respectively;
- (iiii) SEQ ID NOs: 855 and 943, respectively; and,
- (jjjj) SEQ ID NOs: 856 and 944, respectively,

wherein a duplex formed between a sense and antisense strand is in the range of 12-30 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, a duplex between a sense and antisense strand spans the entire length of both the sense strand and the antisense strand. In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively; and,
- (d) SEQ ID NOs: 813 and 901, respectively,

wherein a duplex formed between a sense and antisense strand is in the range of 12-30 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)

Oligonucleotide Termini

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

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

In some embodiments, the 3'-overhang is about one (1) to twenty (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). In some embodiments, the 3'-overhang is about one (1) to nineteen (19), one (1) to eighteen (18), one (1) to seventeen (17), one (1) to sixteen (16), one (1) to fifteen (15), one (1) to fourteen (14), one (1) to thirteen (13), one (1) to twelve (12), one (1) to eleven (11), one (1) to ten (10), one (1) to nine (9), one (1) to eight (8), one (1) to seven (7), one (1) to six (6), one (1) to five (5), one (1) to four (4), one (1) to three (3), or about one (1) to two (2) nucleotides in length. In some embodiments, the 3'-overhang is (1) nucleotide in length. In some embodiments, the 3'-overhang is two (2) nucleotides in length. In some embodiments, the 3'-overhang is three (3)

nucleotides in length. In some embodiments, the 3'-overhang is four (4) nucleotides in length. In some embodiments, the 3'-overhang is five (5) nucleotides in length. In some embodiments, the 3'-overhang is six (6) nucleotides in length. In some embodiments, the 3'-overhang is seven (7) nucleotides in length. In some embodiments, the 3'-overhang is eight (8) nucleotides in length. In some embodiments, the 3'-overhang is nine (9) nucleotides in length. In some embodiments, the 3'-overhang is ten (10) nucleotides in length. In some embodiments, the 3'-overhang is eleven (11) nucleotides in length. In some embodiments, the 3'-overhang is twelve (12) nucleotides in length. In some embodiments, the 3'-overhang is thirteen (13) nucleotides in length. In some embodiments, the 3'-overhang is fourteen (14) nucleotides in length. In some embodiments, the 3'-overhang is fifteen (15) nucleotides in length. In some embodiments, the 3'-overhang is sixteen (16) nucleotides in length. In some embodiments, the 3'-overhang is seventeen (17) nucleotides in length. In some embodiments, the 3'-overhang is eighteen (18) nucleotides in length. In some embodiments, the 3'-overhang is nineteen (19) nucleotides in length. In some embodiments, the 3'-overhang is twenty (20) nucleotides in length.

In some embodiments, an oligonucleotide disclosed herein (e.g., an RNAi 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 NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;

- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;

(qq) SEQ ID NOs: 811 and 899, respectively;
(rr) SEQ ID NOs: 812 and 900, respectively;
(ss) SEQ ID NOs: 813 and 901, respectively;
(tt) SEQ ID NOs: 814 and 902, respectively;
(uu) SEQ ID NOs: 815 and 903, respectively;
(vv) SEQ ID NOs: 816 and 904, respectively;
(ww) SEQ ID NOs: 817 and 905, respectively;
(xx) SEQ ID NOs: 818 and 906, respectively;
(yy) SEQ ID NOs: 819 and 907, respectively;
(zz) SEQ ID NOs: 820 and 908, respectively;
(aaa) SEQ ID NOs: 821 and 909, respectively;
(bbb) SEQ ID NOs: 822 and 910, respectively;
(ccc) SEQ ID NOs: 823 and 911, respectively;
(ddd) SEQ ID NOs: 824 and 912, respectively;
(eee) SEQ ID NOs: 825 and 913, respectively;
(fff) SEQ ID NOs: 826 and 914, respectively;
(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm) SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;
(ooo) SEQ ID NOs: 835 and 923, respectively;
(ppp) SEQ ID NOs: 836 and 924, respectively;
(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;

- (uuu) SEQ ID NOs: 1537 and 929, respectively;
- (vvv) SEQ ID NOs: 842 and 930, respectively;
- (www) SEQ ID NOs: 843 and 931, respectively;
- (xxx) SEQ ID NOs: 844 and 932, respectively;
- (yyy) SEQ ID NOs: 845 and 933, respectively;
- (zzz) SEQ ID NOs: 846 and 934, respectively;
- (aaaa) SEQ ID NOs: 847 and 935, respectively;
- (bbbb) SEQ ID NOs: 848 and 936, respectively;
- (cccc) SEQ ID NOs: 849 and 937, respectively;
- (dddd) SEQ ID NOs: 850 and 938, respectively;
- (eeee) SEQ ID NOs: 851 and 939, respectively;
- (ffff) SEQ ID NOs: 852 and 940, respectively;
- (gggg) SEQ ID NOs: 853 and 941, respectively;
- (hhhh) SEQ ID NOs: 854 and 942, respectively;
- (iiii) SEQ ID NOs: 855 and 943, respectively; and,
- (jjjj) SEQ ID NOs: 856 and 944, respectively,

and wherein the antisense strand comprises a 3'-overhang about one (1) to twenty (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 two (2) nucleotides in length.

In some embodiments, an oligonucleotide disclosed herein (*e.g.*, an RNAi 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 NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively; and,
- (d) SEQ ID NOs: 813 and 901, respectively,

and wherein the antisense strand comprises a 3'-overhang about one (1) to twenty (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 two (2) nucleotides in length.

In some embodiments, an oligonucleotide herein comprises a sense strand and an antisense strand, wherein the 5' terminus of either or both strands comprise a 5'-overhang comprising one or more nucleotides. In some embodiments, an oligonucleotide herein comprises a sense strand and an antisense strand, wherein the sense strand comprises a 5'-overhang comprising one or more nucleotides. In some embodiments, an oligonucleotide herein comprises a sense strand and an antisense strand, wherein the antisense strand comprises a 5'-overhang comprising one or more nucleotides. In some embodiments, an oligonucleotide herein comprises a sense strand and an antisense strand, wherein both the sense strand and the antisense strand comprises a 5'-overhang comprising one or more nucleotides.

In some embodiments, the 5'-overhang is about one (1) to twenty (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). In some embodiments, the 5'-overhang is about one (1) to nineteen (19), one (1) to eighteen (18), one (1) to seventeen (17), one (1) to sixteen (16), one (1) to fifteen (15), one (1) to fourteen (14), one (1) to thirteen (13), one (1) to twelve (12), one (1) to eleven (11), one (1) to ten (10), one (1) to nine (9), one (1) to eight (8), one (1) to seven (7), one (1) to six (6), one (1) to five (5), one (1) to four (4), one (1) to three (3), or about one (1) to two (2) nucleotides in length. In some embodiments, the 5'-overhang is (1) nucleotide in length. In some embodiments, the 5'-overhang is two (2) nucleotides in length. In some embodiments, the 5'-overhang is three (3) nucleotides in length. In some embodiments, the 5'-overhang is four (4) nucleotides in length. In some embodiments, the 5'-overhang is five (5) nucleotides in length. In some embodiments, the 5'-overhang is six (6) nucleotides in length. In some embodiments, the 5'-overhang is seven (7) nucleotides in length. In some embodiments, the 5'-overhang is eight (8) nucleotides in length. In some embodiments, the 5'-overhang is nine (9) nucleotides in length. In some embodiments, the 5'-overhang is ten (10) nucleotides in length. In some embodiments, the 5'-overhang is eleven (11) nucleotides in length. In some embodiments, the 5'-overhang is twelve (12) nucleotides in length. In some embodiments, the 5'-overhang is thirteen (13) nucleotides in length. In some embodiments, the 5'-overhang is fourteen (14) nucleotides in length. In some embodiments, the 5'-overhang is fifteen (15) nucleotides in length. In some embodiments, the 5'-overhang is sixteen (16) nucleotides in length. In some embodiments, the 5'-overhang is seventeen (17) nucleotides in length. In some embodiments, the 5'-overhang is eighteen (18) nucleotides in length. In some

embodiments, the 5'-overhang is nineteen (19) nucleotides in length. In some embodiments, the 5'-overhang is twenty (20) nucleotides in length.

In some embodiments, an oligonucleotide disclosed herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand and an antisense strand, wherein the antisense strand comprises a 5'-overhang, wherein the sense and antisense strands of the oligonucleotide comprise nucleotides sequences selected from the group consisting of:

- (a) SEQ ID NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;

- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;
- (yy) SEQ ID NOs: 819 and 907, respectively;
- (zz) SEQ ID NOs: 820 and 908, respectively;
- (aaa) SEQ ID NOs: 821 and 909, respectively;
- (bbb) SEQ ID NOs: 822 and 910, respectively;

(ccc) SEQ ID NOs: 823 and 911, respectively;
(ddd) SEQ ID NOs: 824 and 912, respectively;
(eee) SEQ ID NOs: 825 and 913, respectively;
(fff) SEQ ID NOs: 826 and 914, respectively;
(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm) SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;
(ooo) SEQ ID NOs: 835 and 923, respectively;
(ppp) SEQ ID NOs: 836 and 924, respectively;
(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;
(uuu) SEQ ID NOs: 1537 and 929, respectively;
(vvv) SEQ ID NOs: 842 and 930, respectively;
(www) SEQ ID NOs: 843 and 931, respectively;
(xxx) SEQ ID NOs: 844 and 932, respectively;
(yyy) SEQ ID NOs: 845 and 933, respectively;
(zzz) SEQ ID NOs: 846 and 934, respectively;
(aaaa) SEQ ID NOs: 847 and 935, respectively;
(bbbb) SEQ ID NOs: 848 and 936, respectively;
(cccc) SEQ ID NOs: 849 and 937, respectively;
(dddd) SEQ ID NOs: 850 and 938, respectively;
(eeee) SEQ ID NOs: 851 and 939, respectively;
(ffff) SEQ ID NOs: 852 and 940, respectively;

(gggg) SEQ ID NOs: 853 and 941, respectively;

(hhhh) SEQ ID NOs: 854 and 942, respectively;

(iiii) SEQ ID NOs: 855 and 943, respectively; and,

(jjjj) SEQ ID NOs: 856 and 944, respectively,

and wherein the antisense strand comprises a 3'-overhang about one (1) to twenty (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 two (2) nucleotides in length.

In some embodiments, an oligonucleotide disclosed herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand and an antisense strand, wherein the antisense strand comprises a 5'-overhang, wherein the sense and antisense strands of the oligonucleotide comprise nucleotide sequences selected from the group consisting of:

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively; and,
- (d) SEQ ID NOs: 813 and 901, respectively,

and wherein the antisense strand comprises a 5'-overhang about one (1) to twenty (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 5'-overhang is two (2) nucleotides in length.

In some embodiments, one or more (*e.g.*, 2, 3, 4, 5, or more) nucleotides comprising the 3' terminus or 5' terminus of a 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, *e.g.*, comprises 2' modification, *e.g.*, a 2'-O-methoxyethyl. In some embodiments, an oligonucleotide provided herein comprises a sense strand having the sugar moiety at positions 1-7, 12-27 and 31-36 modified with 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.

In some embodiments, an oligonucleotide disclosed herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand and an antisense strand, wherein the 3' terminus of the sense strand

comprises a stem-loop described herein (see FIG. 1A) and the 3' terminus of the antisense strand comprises a 3'-overhang described herein. In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand and an antisense strand that form a nicked tetraloop structure described herein (see FIG. 1A), wherein the 3' terminus of the sense strand comprises a stem-loop, wherein the loop is a tetraloop described herein, and wherein the 3' terminus of the antisense strand comprises a 3'-overhang described herein (see FIG. 1A). In some embodiments, the 3'-overhang is two (2) nucleotides in length. In some embodiments, the two (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.

Oligonucleotide Modifications

In some embodiments, an oligonucleotide described herein (*e.g.*, an RNAi oligonucleotide) comprises a modification. Oligonucleotides (*e.g.*, RNAi 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 or research use.

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 internucleotide linkage. In some embodiments, the modification is a modified base. In some embodiments, an oligonucleotide described herein can comprise any one of the modifications described herein or any combination thereof. For example, in some embodiments, an oligonucleotide described herein 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 an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

- (a) SEQ ID NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;

- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;

- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;
- (yy) SEQ ID NOs: 819 and 907, respectively;
- (zz) SEQ ID NOs: 820 and 908, respectively;
- (aaa) SEQ ID NOs: 821 and 909, respectively;
- (bbb) SEQ ID NOs: 822 and 910, respectively;
- (ccc) SEQ ID NOs: 823 and 911, respectively;
- (ddd) SEQ ID NOs: 824 and 912, respectively;
- (eee) SEQ ID NOs: 825 and 913, respectively;
- (fff) SEQ ID NOs: 826 and 914, respectively;
- (ggg) SEQ ID NOs: 827 and 915, respectively;
- (hhh) SEQ ID NOs: 828 and 916, respectively;
- (iii) SEQ ID NOs: 829 and 917, respectively;
- (jjj) SEQ ID NOs: 830 and 918, respectively;
- (kkk) SEQ ID NOs: 831 and 919, respectively;
- (lll) SEQ ID NOs: 832 and 920, respectively;

(mmm)SEQ ID NOs: 833 and 921, respectively;
 (nnn) SEQ ID NOs: 834 and 922, respectively;
 (ooo) SEQ ID NOs: 835 and 923, respectively;
 (ppp) SEQ ID NOs: 836 and 924, respectively;
 (qqq) SEQ ID NOs: 837 and 925, respectively;
 (rrr) SEQ ID NOs: 838 and 926, respectively;
 (sss) SEQ ID NOs: 839 and 927, respectively;
 (ttt) SEQ ID NOs: 840 and 928, respectively;
 (uuu) SEQ ID NOs: 1537 and 929, respectively;
 (vvv) SEQ ID NOs: 842 and 930, respectively;
 (www) SEQ ID NOs: 843 and 931, respectively;
 (xxx) SEQ ID NOs: 844 and 932, respectively;
 (yyy) SEQ ID NOs: 845 and 933, respectively;
 (zzz) SEQ ID NOs: 846 and 934, respectively;
 (aaaa) SEQ ID NOs: 847 and 935, respectively;
 (bbbb) SEQ ID NOs: 848 and 936, respectively;
 (cccc) SEQ ID NOs: 849 and 937, respectively;
 (dddd) SEQ ID NOs: 850 and 938, respectively;
 (eeee) SEQ ID NOs: 851 and 939, respectively;
 (ffff) SEQ ID NOs: 852 and 940, respectively;
 (gggg) SEQ ID NOs: 853 and 941, respectively;
 (hhhh) SEQ ID NOs: 854 and 942, respectively;
 (iiii) SEQ ID NOs: 855 and 943, respectively; and,
 (jjjj) SEQ ID NOs: 856 and 944, 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.

In some embodiments, an oligonucleotide described herein 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 an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively; and,
- (d) SEQ ID NOs: 813 and 901, 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.

The number of modifications on an oligonucleotide (*e.g.*, an RNAi 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 or 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 the nucleotides of an oligonucleotide 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).

Sugar Modifications

In some embodiments, an oligonucleotide described herein (*e.g.*, an RNAi oligonucleotide) comprises a modified sugar. In some embodiments, a 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, a 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.* TETRAHEDON (1998); 54: 3607-30), unlocked nucleic acids ("UNA"; *see, e.g.*, Snead *et al.* MOL. THER-NUCL. ACIDS (2013); 2: e103) and bridged nucleic acids ("BNA"; *see, e.g.*, Imanishi & Obika CHEM. COMMUN. (CAMB) (2002); 21: 1653-59).

In some embodiments, a nucleotide modification in a sugar comprises a 2'-modification. In some embodiments, a 2'-modification may be 2'-O-propargyl, 2'-O-propylamin, 2'-amino, 2'-ethyl, 2'-fluoro (2'-F), 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA) or 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA). In some embodiments, the modification is 2'-F, 2'-OMe or 2'-MOE. In some embodiments, a 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, a 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, a modified nucleotide has an acyclic sugar that lacks a 2'-carbon to 3'-carbon bond. In some embodiments, a modified nucleotide has a thiol group, *e.g.*, in the 4' position of the sugar.

In some embodiments, an oligonucleotide (*e.g.*, an RNAi 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 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).

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'-deoxy-2'-fluoro- β -d-arabinonucleic acid).

In some embodiments, the disclosure provides oligonucleotides having different modification patterns. In some embodiments, an oligonucleotide herein comprises a sense strand 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.

In some embodiments, an oligonucleotide disclosed herein (*e.g.*, an RNAi oligonucleotide) comprises an antisense strand having nucleotides that are modified with 2'-F. In some embodiments, an oligonucleotide herein comprises an antisense strand comprising nucleotides that are modified with 2'-F and 2'-OMe. In some embodiments, an oligonucleotide disclosed herein comprises a sense strand having nucleotides that are modified with 2'-F. In some embodiments, an oligonucleotide disclosed herein comprises a sense strand comprising nucleotides that are modified with 2'-F and 2'-OMe.

In some embodiments, an oligonucleotide described herein 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'-fluoro modification. In some embodiments, about 11% of the nucleotides of the sense strand comprise a 2'-fluoro modification. In some embodiments, an oligonucleotide described herein comprises an antisense strand with about 25-35%, 25%, 26%, 27%, 28%, 29%, 30%, 31%, 32%, 33%, 34%, or 35% of the nucleotides of the antisense strand comprising a 2'-fluoro modification. In some embodiments, about 32% of the nucleotides of the antisense strand comprise a 2'-fluoro modification. In some embodiments, the oligonucleotide has about 15-25%, 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, or 25% of its nucleotides comprising a 2'-fluoro modification. In some embodiments, about 19% of the nucleotides in the dsRNAi oligonucleotide comprise a 2'-fluoro modification.

In some embodiments, one or more of positions 8, 9, 10, or 11 of the sense strand is modified with a 2'-F group. In some embodiments, one or more of positions 3, 8, 9, 10, 12, 13, and 17 of the sense strand is modified with a 2'-F group. In some embodiments, one or more of positions 2, 3, 4, 5, 7, 10, and 14 of the antisense strand is modified with a 2'-F group. In some embodiments, one or more of positions 2, 3, 4, 5, 7, 8, 10, 14, 16, and 19 is modified with a 2'-F group. In some embodiments, the sugar moiety at each of nucleotides at positions 1-7 and 12-20 in the sense strand is modified with a 2'-OMe. In some embodiments, the sugar moiety at each of nucleotides at positions 1-7, 12-27, and 31-36 in the sense strand is modified with a 2'-OMe. In some embodiments, the sugar moiety at each of nucleotides at positions 6, 9, 11-13, 15, 17, 18, and 20-22 in the sense strand is modified with a 2'-OMe.

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 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;

- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;
- (yy) SEQ ID NOs: 819 and 907, respectively;
- (zz) SEQ ID NOs: 820 and 908, respectively;
- (aaa) SEQ ID NOs: 821 and 909, respectively;
- (bbb) SEQ ID NOs: 822 and 910, respectively;
- (ccc) SEQ ID NOs: 823 and 911, respectively;
- (ddd) SEQ ID NOs: 824 and 912, respectively;
- (eee) SEQ ID NOs: 825 and 913, respectively;
- (fff) SEQ ID NOs: 826 and 914, respectively;
- (ggg) SEQ ID NOs: 827 and 915, respectively;
- (hhh) SEQ ID NOs: 828 and 916, respectively;

(iii) SEQ ID NOs: 829 and 917, respectively;
 (jjj) SEQ ID NOs: 830 and 918, respectively;
 (kkk) SEQ ID NOs: 831 and 919, respectively;
 (lll) SEQ ID NOs: 832 and 920, respectively;
 (mmm) SEQ ID NOs: 833 and 921, respectively;
 (nnn) SEQ ID NOs: 834 and 922, respectively;
 (ooo) SEQ ID NOs: 835 and 923, respectively;
 (ppp) SEQ ID NOs: 836 and 924, respectively;
 (qqq) SEQ ID NOs: 837 and 925, respectively;
 (rrr) SEQ ID NOs: 838 and 926, respectively;
 (sss) SEQ ID NOs: 839 and 927, respectively;
 (ttt) SEQ ID NOs: 840 and 928, respectively;
 (uuu) SEQ ID NOs: 1537 and 929, respectively;
 (vvv) SEQ ID NOs: 842 and 930, respectively;
 (www) SEQ ID NOs: 843 and 931, respectively;
 (xxx) SEQ ID NOs: 844 and 932, respectively;
 (yyy) SEQ ID NOs: 845 and 933, respectively;
 (zzz) SEQ ID NOs: 846 and 934, respectively;
 (aaaa) SEQ ID NOs: 847 and 935, respectively;
 (bbbb) SEQ ID NOs: 848 and 936, respectively;
 (cccc) SEQ ID NOs: 849 and 937, respectively;
 (dddd) SEQ ID NOs: 850 and 938, respectively;
 (eeee) SEQ ID NOs: 851 and 939, respectively;
 (ffff) SEQ ID NOs: 852 and 940, respectively;
 (gggg) SEQ ID NOs: 853 and 941, respectively;
 (hhhh) SEQ ID NOs: 854 and 942, respectively;
 (iiii) SEQ ID NOs: 855 and 943, respectively; and,
 (jjjj) SEQ ID NOs: 856 and 944, respectively,
 wherein one or more of positions 8, 9, 10 or 11 of the sense strand is modified with a 2'-F group.

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

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively, and;
- (d) SEQ ID NOs: 813 and 901, respectively,

wherein one or more of positions 8, 9, 10, or 11 of the sense strand is modified with a 2'-F group.

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein comprises an antisense strand having the sugar moiety of each of the nucleotides at positions 2, 3, 4, 5, 7, 8, 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein 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.

In some embodiments, an oligonucleotide provided herein 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.

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -D-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein comprises a sense strand having the sugar moiety at positions 8-11 modified with 2'-F. In some embodiments, an oligonucleotide provided herein comprises a sense strand having the sugar moiety at positions 3, 8, 9, 10, 12, 13 and 17 modified with 2'-F. In some embodiments, an oligonucleotide provided herein comprises a sense strand having the sugar moiety at positions 1-7 and 12-17 or 12-20 modified with 2'OMe. In some embodiments, an oligonucleotide provided herein comprises a 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -D-arabinonucleic acid (2'-FANA). In some embodiments, an oligonucleotide provided herein comprises a sense strand having the sugar moiety at positions 1-2, 4-7, 11, 14-16, and 18-20 modified with 2'OMe. In some embodiments, an oligonucleotide provided herein comprises a sense strand having the sugar moiety of each of the nucleotides at positions 1-2, 4-7, 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -D-arabinonucleic acid (2'-FANA).

In some embodiments, an oligonucleotide provided herein 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.

In some embodiments, an oligonucleotide provided herein 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.

In some embodiments, an oligonucleotide provided herein 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, 2'-aminoethyl (EA), 2'-O-methyl (2'-OMe), 2'-O-methoxyethyl (2'-MOE), 2'-O-[2-(methylamino)-2-oxoethyl] (2'-O-NMA), and 2'-deoxy-2'-fluoro- β -d-arabinonucleic acid (2'-FANA).

5'-Terminal Phosphate

In some embodiments, an oligonucleotide described herein (*e.g.*, an RNAi 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 an RNAi 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 performance and/or bioavailability *in vivo*. In some embodiments, an oligonucleotide herein includes analogs of 5' phosphates that are resistant to such degradation. In some embodiments, the phosphate analog is oxymethylphosphonate, vinylphosphonate or malonylphosphonate, or a combination thereof. In certain embodiments, the 5' terminus of an oligonucleotide strand is attached to chemical moiety that mimics the electrostatic and steric properties of a natural 5'-phosphate group ("phosphate mimic"). 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 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;

- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;
- (yy) SEQ ID NOs: 819 and 907, respectively;
- (zz) SEQ ID NOs: 820 and 908, respectively;
- (aaa) SEQ ID NOs: 821 and 909, respectively;
- (bbb) SEQ ID NOs: 822 and 910, respectively;
- (ccc) SEQ ID NOs: 823 and 911, respectively;
- (ddd) SEQ ID NOs: 824 and 912, respectively;
- (eee) SEQ ID NOs: 825 and 913, respectively;
- (fff) SEQ ID NOs: 826 and 914, respectively;
- (ggg) SEQ ID NOs: 827 and 915, respectively;
- (hhh) SEQ ID NOs: 828 and 916, respectively;

- (iii) SEQ ID NOs: 829 and 917, respectively;
- (jjj) SEQ ID NOs: 830 and 918, respectively;
- (kkk) SEQ ID NOs: 831 and 919, respectively;
- (lll) SEQ ID NOs: 832 and 920, respectively;
- (mmm) SEQ ID NOs: 833 and 921, respectively;
- (nnn) SEQ ID NOs: 834 and 922, respectively;
- (ooo) SEQ ID NOs: 835 and 923, respectively;
- (ppp) SEQ ID NOs: 836 and 924, respectively;
- (qqq) SEQ ID NOs: 837 and 925, respectively;
- (rrr) SEQ ID NOs: 838 and 926, respectively;
- (sss) SEQ ID NOs: 839 and 927, respectively;
- (ttt) SEQ ID NOs: 840 and 928, respectively;
- (uuu) SEQ ID NOs: 1537 and 929, respectively;
- (vvv) SEQ ID NOs: 842 and 930, respectively;
- (www) SEQ ID NOs: 843 and 931, respectively;
- (xxx) SEQ ID NOs: 844 and 932, respectively;
- (yyy) SEQ ID NOs: 845 and 933, respectively;
- (zzz) SEQ ID NOs: 846 and 934, respectively;
- (aaaa) SEQ ID NOs: 847 and 935, respectively;
- (bbbb) SEQ ID NOs: 848 and 936, respectively;
- (cccc) SEQ ID NOs: 849 and 937, respectively;
- (dddd) SEQ ID NOs: 850 and 938, respectively;
- (eeee) SEQ ID NOs: 851 and 939, respectively;
- (ffff) SEQ ID NOs: 852 and 940, respectively;
- (gggg) SEQ ID NOs: 853 and 941, respectively;
- (hhhh) SEQ ID NOs: 854 and 942, respectively;
- (iiii) SEQ ID NOs: 855 and 943, respectively; and,
- (jjjj) SEQ ID NOs: 856 and 944, respectively,

wherein the oligonucleotide comprises a 5'-terminal phosphate, optionally a 5'-terminal phosphate analog.

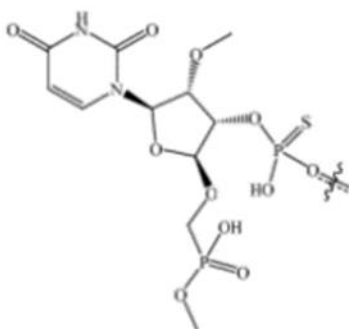
In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively; and,
- (d) SEQ ID NOs: 813 and 901, respectively,

wherein the oligonucleotide comprises a 5'-terminal phosphate, optionally a 5'-terminal phosphate analog.

In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi 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, an oligonucleotide herein comprises a 4'-phosphate analog at a 5'-terminal nucleotide. In some embodiments, a phosphate analog is an 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. In other embodiments, a 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, a 4'-phosphate analog is an oxymethylphosphonate. In some embodiments, an oxymethylphosphonate is represented by the formula $-O-CH_2-PO(OH)_2$, $-O-CH_2-PO(OR)_2$, or $-O-CH_2-PO(OH)(R)$, in which R is independently selected from -H, -CH₃, an alkyl group, -CH₂CH₂CN, -CH₂OCOC(CH₃)₃, -CH₂OCH₂CH₂Si(CH₃)₃ or a protecting group. In certain embodiments, the alkyl group is -CH₂CH₃. More typically, R is independently selected from H, -CH₃ or -CH₂CH₃. In some embodiment, R is -CH₃. In some embodiments, the 4'-phosphate analog is 5'-methoxyphosphonate-4'-oxy.

In some embodiments, an oligonucleotide provided herein comprises an antisense strand comprising a 4'-phosphate analog at the 5'-terminal nucleotide, wherein 5'-terminal nucleotide comprises the following structure (Chem. formula 1):



5'-methoxyphosphonate-4'-oxy-2'-O-methyluridine phosphorothioate [MePhosphonate-4O-mUs]

Modified Internucleotide Linkage

In some embodiments, an oligonucleotide provided 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, any one of the oligonucleotides disclosed herein 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, any one of the oligonucleotides disclosed herein comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 modified internucleotide linkages.

A modified internucleotide linkage may be a phosphorodithioate linkage, a phosphorothioate linkage, a phosphotriester linkage, a thionoalkylphosphonate linkage, a thionoalkylphosphotriester linkage, a phosphoramidite linkage, a phosphonate linkage or a boranophosphate linkage. In some embodiments, at least one modified internucleotide linkage of any one of the oligonucleotides as disclosed herein is a phosphorothioate linkage.

In some embodiments, an oligonucleotide provided herein (*e.g.*, a RNAi 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 sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

- (a) SEQ ID NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;

- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;
- (yy) SEQ ID NOs: 819 and 907, respectively;
- (zz) SEQ ID NOs: 820 and 908, respectively;
- (aaa) SEQ ID NOs: 821 and 909, respectively;
- (bbb) SEQ ID NOs: 822 and 910, respectively;
- (ccc) SEQ ID NOs: 823 and 911, respectively;
- (ddd) SEQ ID NOs: 824 and 912, respectively;

(eee) SEQ ID NOs: 825 and 913, respectively;
(fff) SEQ ID NOs: 826 and 914, respectively;
(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm)SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;
(ooo) SEQ ID NOs: 835 and 923, respectively;
(ppp) SEQ ID NOs: 836 and 924, respectively;
(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;
(uuu) SEQ ID NOs: 1537 and 929, respectively;
(vvv) SEQ ID NOs: 842 and 930, respectively;
(www) SEQ ID NOs: 843 and 931, respectively;
(xxx) SEQ ID NOs: 844 and 932, respectively;
(yyy) SEQ ID NOs: 845 and 933, respectively;
(zzz) SEQ ID NOs: 846 and 934, respectively;
(aaaa) SEQ ID NOs: 847 and 935, respectively;
(bbbb) SEQ ID NOs: 848 and 936, respectively;
(cccc) SEQ ID NOs: 849 and 937, respectively;
(dddd) SEQ ID NOs: 850 and 938, respectively;
(eeee) SEQ ID NOs: 851 and 939, respectively;
(ffff) SEQ ID NOs: 852 and 940, respectively;
(gggg) SEQ ID NOs: 853 and 941, respectively;
(hhhh) SEQ ID NOs: 854 and 942, respectively;

- (iii) SEQ ID NOs: 855 and 943, respectively; and,
 - (jjjj) SEQ ID NOs: 856 and 944, respectively,
- wherein the oligonucleotide comprises a modified internucleotide linkage.

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

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively, and;
- (d) SEQ ID NOs: 813 and 901, respectively,

wherein the oligonucleotide comprises a modified internucleotide linkage.

Base Modifications

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotides) comprises 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 some 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). 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 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;

- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;

(kk) SEQ ID NOs: 805 and 893, respectively;
(ll) SEQ ID NOs: 806 and 894, respectively;
(mm) SEQ ID NOs: 807 and 895, respectively;
(nn) SEQ ID NOs: 808 and 896, respectively;
(oo) SEQ ID NOs: 809 and 897, respectively;
(pp) SEQ ID NOs: 810 and 898, respectively;
(qq) SEQ ID NOs: 811 and 899, respectively;
(rr) SEQ ID NOs: 812 and 900, respectively;
(ss) SEQ ID NOs: 813 and 901, respectively;
(tt) SEQ ID NOs: 814 and 902, respectively;
(uu) SEQ ID NOs: 815 and 903, respectively;
(vv) SEQ ID NOs: 816 and 904, respectively;
(ww) SEQ ID NOs: 817 and 905, respectively;
(xx) SEQ ID NOs: 818 and 906, respectively;
(yy) SEQ ID NOs: 819 and 907, respectively;
(zz) SEQ ID NOs: 820 and 908, respectively;
(aaa) SEQ ID NOs: 821 and 909, respectively;
(bbb) SEQ ID NOs: 822 and 910, respectively;
(ccc) SEQ ID NOs: 823 and 911, respectively;
(ddd) SEQ ID NOs: 824 and 912, respectively;
(eee) SEQ ID NOs: 825 and 913, respectively;
(fff) SEQ ID NOs: 826 and 914, respectively;
(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm)SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;

- (ooo) SEQ ID NOs: 835 and 923, respectively;
- (ppp) SEQ ID NOs: 836 and 924, respectively;
- (qqq) SEQ ID NOs: 837 and 925, respectively;
- (rrr) SEQ ID NOs: 838 and 926, respectively;
- (sss) SEQ ID NOs: 839 and 927, respectively;
- (ttt) SEQ ID NOs: 840 and 928, respectively;
- (uuu) SEQ ID NOs: 1537 and 929, respectively;
- (vvv) SEQ ID NOs: 842 and 930, respectively;
- (www) SEQ ID NOs: 843 and 931, respectively;
- (xxx) SEQ ID NOs: 844 and 932, respectively;
- (yyy) SEQ ID NOs: 845 and 933, respectively;
- (zzz) SEQ ID NOs: 846 and 934, respectively;
- (aaaa) SEQ ID NOs: 847 and 935, respectively;
- (bbbb) SEQ ID NOs: 848 and 936, respectively;
- (cccc) SEQ ID NOs: 849 and 937, respectively;
- (dddd) SEQ ID NOs: 850 and 938, respectively;
- (eeee) SEQ ID NOs: 851 and 939, respectively;
- (ffff) SEQ ID NOs: 852 and 940, respectively;
- (gggg) SEQ ID NOs: 853 and 941, respectively;
- (hhhh) SEQ ID NOs: 854 and 942, respectively;
- (iiii) SEQ ID NOs: 855 and 943, respectively; and,
- (jjjj) SEQ ID NOs: 856 and 944, respectively,

wherein the oligonucleotide comprises one or more modified nucleobases.

In some embodiments, a modified nucleotide comprises a universal base. In some embodiments, a modified nucleotide does not contain a nucleobase (abasic). In some embodiments, the sense and antisense strands of an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively; and,

(d) SEQ ID NOs: 813 and 901, respectively, wherein the oligonucleotide comprises one or more modified nucleobases.

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 single-stranded nucleic acid (*e.g.*, oligonucleotide) that is fully complementary to a target nucleic acid (*e.g.*, a *NR1H3* mRNA), a single-stranded 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 single-stranded nucleic acid in which the universal base has been replaced with a base to generate a single mismatch, the single-stranded 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.

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.* NUCLEIC ACIDS RES. (1995); 23: 4363-4370; Loakes *et al.* NUCLEIC ACIDS RES. (1995); 23: 2361-66; and Loakes & Brown NUCLEIC ACIDS RES. (1994); 22: 4039-43).

Targeting Ligands

In some embodiments, it is desirable to target an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide) to one or more cells or cell type, tissues, organs, or anatomical regions or compartments. Such a strategy may help to avoid undesirable effects and/or to avoid undue loss of the oligonucleotide to cells, tissues, organs, or anatomical regions or compartments that would not benefit from the oligonucleotide or its effects (*e.g.*, inhibition or reduction of *NR1H3* expression). Accordingly, in some embodiments, oligonucleotides disclosed herein (*e.g.*, RNAi oligonucleotides) are modified to facilitate targeting and/or delivery to particular cells or cell types, tissues, organs, or anatomical regions or compartments (*e.g.*, to facilitate delivery of the oligonucleotide to the liver). In some embodiments, an 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 an oligonucleotide comprise nucleotide sequences selected from the group consisting of:

- (a) SEQ ID NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;

- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;
- (yy) SEQ ID NOs: 819 and 907, respectively;
- (zz) SEQ ID NOs: 820 and 908, respectively;
- (aaa) SEQ ID NOs: 821 and 909, respectively;
- (bbb) SEQ ID NOs: 822 and 910, respectively;
- (ccc) SEQ ID NOs: 823 and 911, respectively;
- (ddd) SEQ ID NOs: 824 and 912, respectively;
- (eee) SEQ ID NOs: 825 and 913, respectively;

(fff) SEQ ID NOs: 826 and 914, respectively;
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(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
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(ooo) SEQ ID NOs: 835 and 923, respectively;
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(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;
(uuu) SEQ ID NOs: 1537 and 929, respectively;
(vvv) SEQ ID NOs: 842 and 930, respectively;
(www) SEQ ID NOs: 843 and 931, respectively;
(xxx) SEQ ID NOs: 844 and 932, respectively;
(yyy) SEQ ID NOs: 845 and 933, respectively;
(zzz) SEQ ID NOs: 846 and 934, respectively;
(aaaa) SEQ ID NOs: 847 and 935, respectively;
(bbbb) SEQ ID NOs: 848 and 936, respectively;
(cccc) SEQ ID NOs: 849 and 937, respectively;
(dddd) SEQ ID NOs: 850 and 938, respectively;
(eeee) SEQ ID NOs: 851 and 939, respectively;
(ffff) SEQ ID NOs: 852 and 940, respectively;
(gggg) SEQ ID NOs: 853 and 941, respectively;
(hhhh) SEQ ID NOs: 854 and 942, respectively;
(iiii) SEQ ID NOs: 855 and 943, respectively; and,

(jjjj) SEQ ID NOs: 856 and 944, respectively,

wherein the oligonucleotide comprises a targeting ligand conjugated to at least one nucleotide.

In some embodiments, an 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 an oligonucleotide comprise nucleotides sequences selected from the group consisting of:

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively, and;
- (d) SEQ ID NOs: 813 and 901, respectively,

wherein the oligonucleotide comprises a targeting ligand conjugated to at least one nucleotide.

In some embodiments, the targeting ligand comprises a carbohydrate, amino sugar, cholesterol, peptide, polypeptide, protein, or part of a protein (*e.g.*, an antibody or antibody fragment), or lipid. In certain embodiments, the targeting ligand is a carbohydrate comprising at least one GalNAc moiety.

In some embodiments, 1 or more (*e.g.*, 1, 2, 3, 4, 5, or 6) nucleotides of an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide) are each conjugated to a separate targeting ligand (*e.g.*, a GalNAc moiety). In some embodiments, 2 to 4 nucleotides of an 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' terminus of the sense or antisense strand) such that the targeting ligands resemble bristles of a toothbrush and the oligonucleotide resembles a toothbrush. For example, an oligonucleotide may comprise a stem-loop at either the 5' or 3' terminus 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, an oligonucleotide provided by the disclosure (*e.g.*, a RNAi oligonucleotide) comprises a stem-loop at the 3' terminus of the sense strand, wherein the loop of the stem-loop comprises a triloop or a tetraloop, and wherein the 3 or 4 nucleotides comprising the triloop or tetraloop, respectively, are individually conjugated to a targeting ligand. In some embodiments, an oligonucleotide provided by the disclosure (*e.g.*, a RNAi oligonucleotide) comprises a stem-loop at the 3' terminus of the

sense strand, wherein the loop of the stem-loop comprises a tetraloop, and wherein 3 nucleotides of the tetraloop are individually conjugated to a targeting ligand.

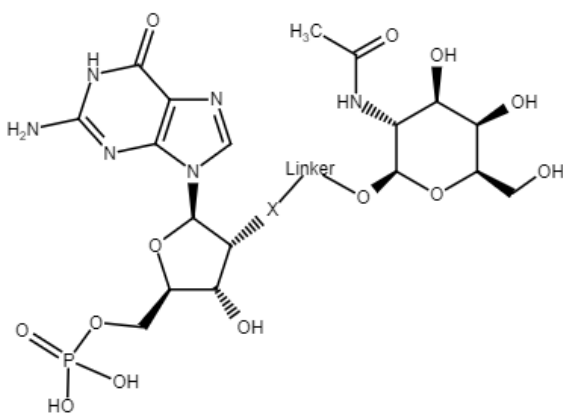
GalNAc is a high affinity carbohydrate ligand for the asialoglycoprotein receptor (ASGPR), which is primarily expressed on the surface of hepatocyte cells and has a major role in binding, internalizing and subsequent clearing circulating glycoproteins that contain terminal galactose or GalNAc residues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

In some embodiments, an oligonucleotide of the instant disclosure (*e.g.*, an RNAi oligonucleotide) is conjugated directly or indirectly to a monovalent GalNAc moiety. 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, an oligonucleotide is conjugated to one or more bivalent GalNAc, trivalent GalNAc or tetravalent GalNAc moieties. . In some embodiments, a bivalent, trivalent or tetravalent GalNAc moiety is conjugated to an oligonucleotide via a branched linker. In some embodiments, a monovalent GalNAc moiety is conjugated to a first nucleotide and a bivalent, trivalent, or tetravalent GalNAc moiety is conjugated to a second nucleotide via a branched linker.

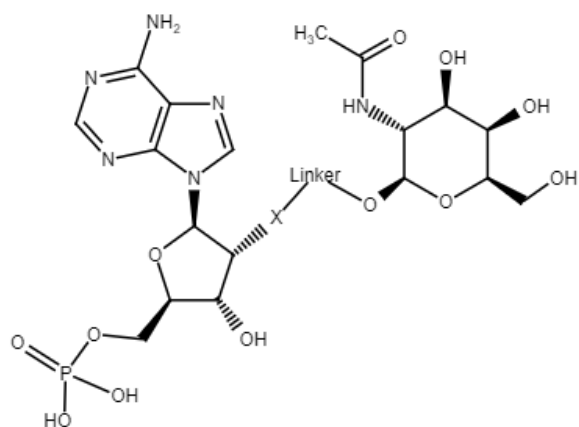
In some embodiments, one (1) or more (*e.g.*, 1, 2, 3, 4, 5, or 6) nucleotides of an oligonucleotide described herein (*e.g.*, an RNAi oligonucleotide) are each conjugated to a GalNAc moiety. In some embodiments, two (2) to four (4) nucleotides of a tetraloop are each conjugated to a separate GalNAc moiety. In some embodiments, one (1) to three (3) nucleotides of a triloop are each conjugated to a separate GalNAc moiety. In some embodiments, targeting ligands are conjugated to two (2) to four (4) nucleotides at either ends of the sense or antisense strand (*e.g.*, ligands are conjugated to a two (2) to four (4) nucleotide overhang or extension on the 5' or 3' terminus 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, three (3) or four (4) GalNAc moieties can be conjugated to nucleotides in the tetraloop of the sense strand where each GalNAc moiety is conjugated to one (1) nucleotide.

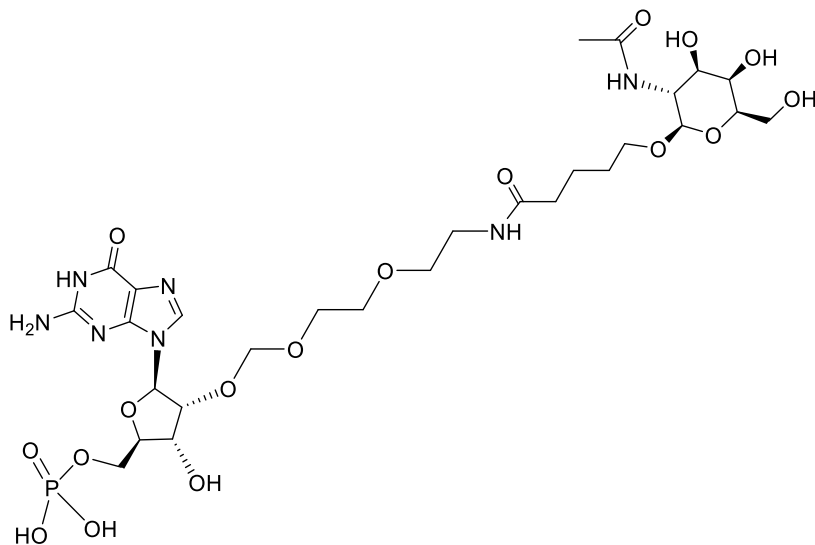
In some embodiments, an oligonucleotide described herein (*e.g.*, an RNAi oligonucleotide) comprises a tetraloop, wherein the tetraloop (L) is any combination of adenine (A) and guanine (G) nucleotides. In some embodiments, the tetraloop (L) comprises a monovalent GalNAc moiety attached to any one or more guanine (G) nucleotides of the tetraloop *via* any linker described herein, as depicted below (X = heteroatom) in **Chem. formula 2**:



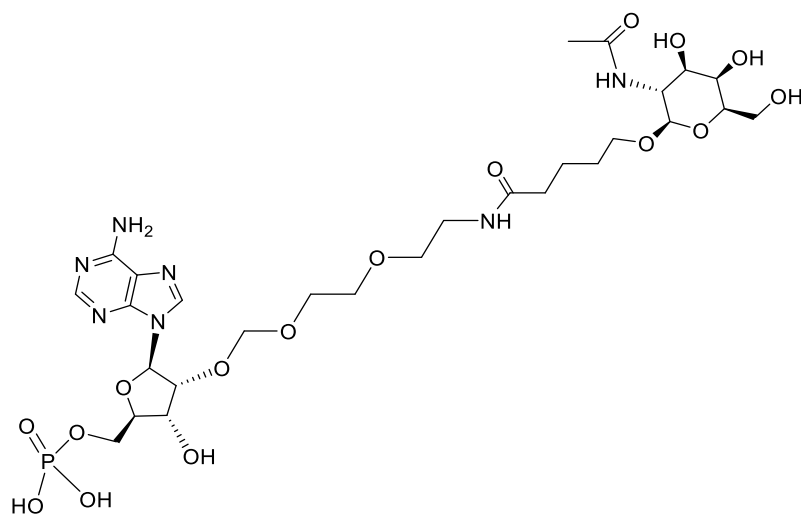
In some embodiments, the tetraloop (L) has a monovalent GalNAc attached to any one or more adenine nucleotides of the tetraloop *via* any linker described herein, as depicted below (X = heteroatom) in **Chem. formula 3**:



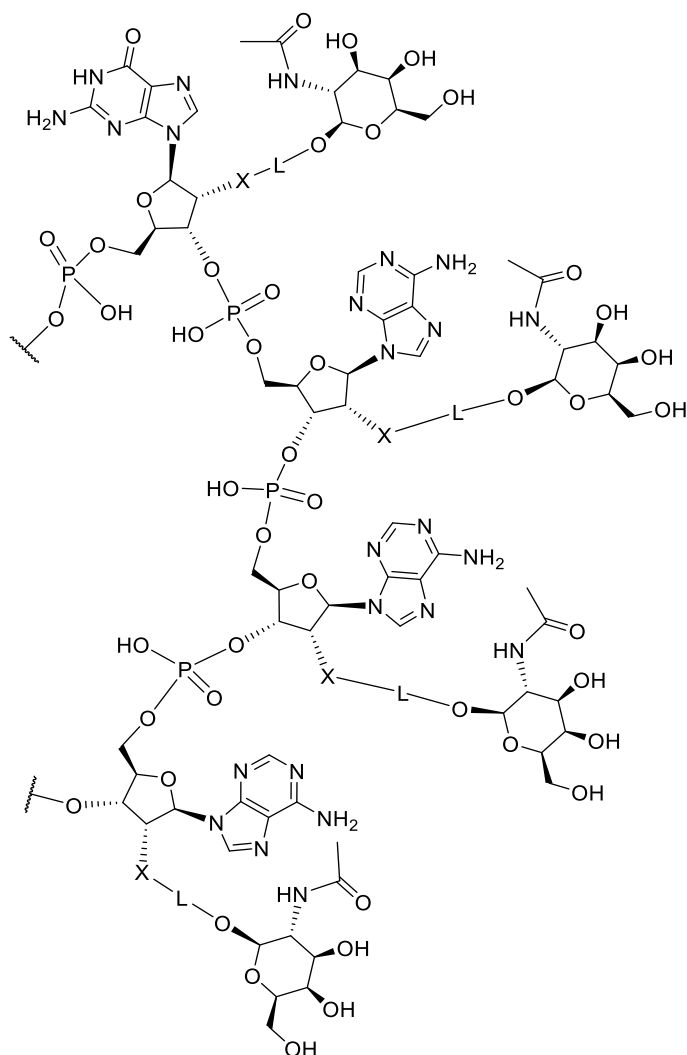
In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) comprises a monovalent GalNAc moiety attached to a guanine (G) nucleotide referred to as [ademG-GalNAc] or 2'-aminodiethoxymethanol-Guanine-GalNAc, as depicted below in **Chem. formula 4:**



In some embodiments, an oligonucleotide herein comprises a monovalent GalNAc moiety attached to an adenine nucleotide, referred to as [ademaA-GalNAc] or 2'-aminodiethoxymethanol-Adenine-GalNAc, as depicted below **Chem. formula 5:**

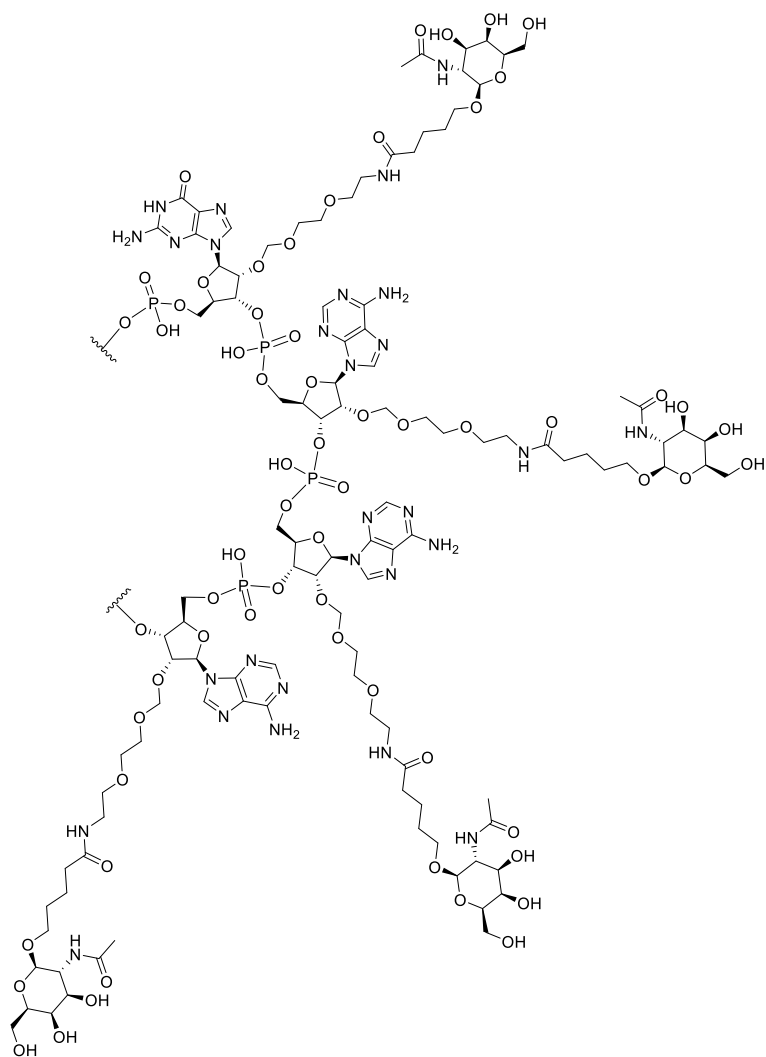


An example of such conjugation is shown below for a loop comprising from 5' to 3' the nucleotide sequence GAAA (L = linker, X = heteroatom). Such a loop may be present, for example, at positions 27-30 of a sense strand provided herein. In the **Chem. formula 6** is used to describe an attachment point to the oligonucleotide strand.

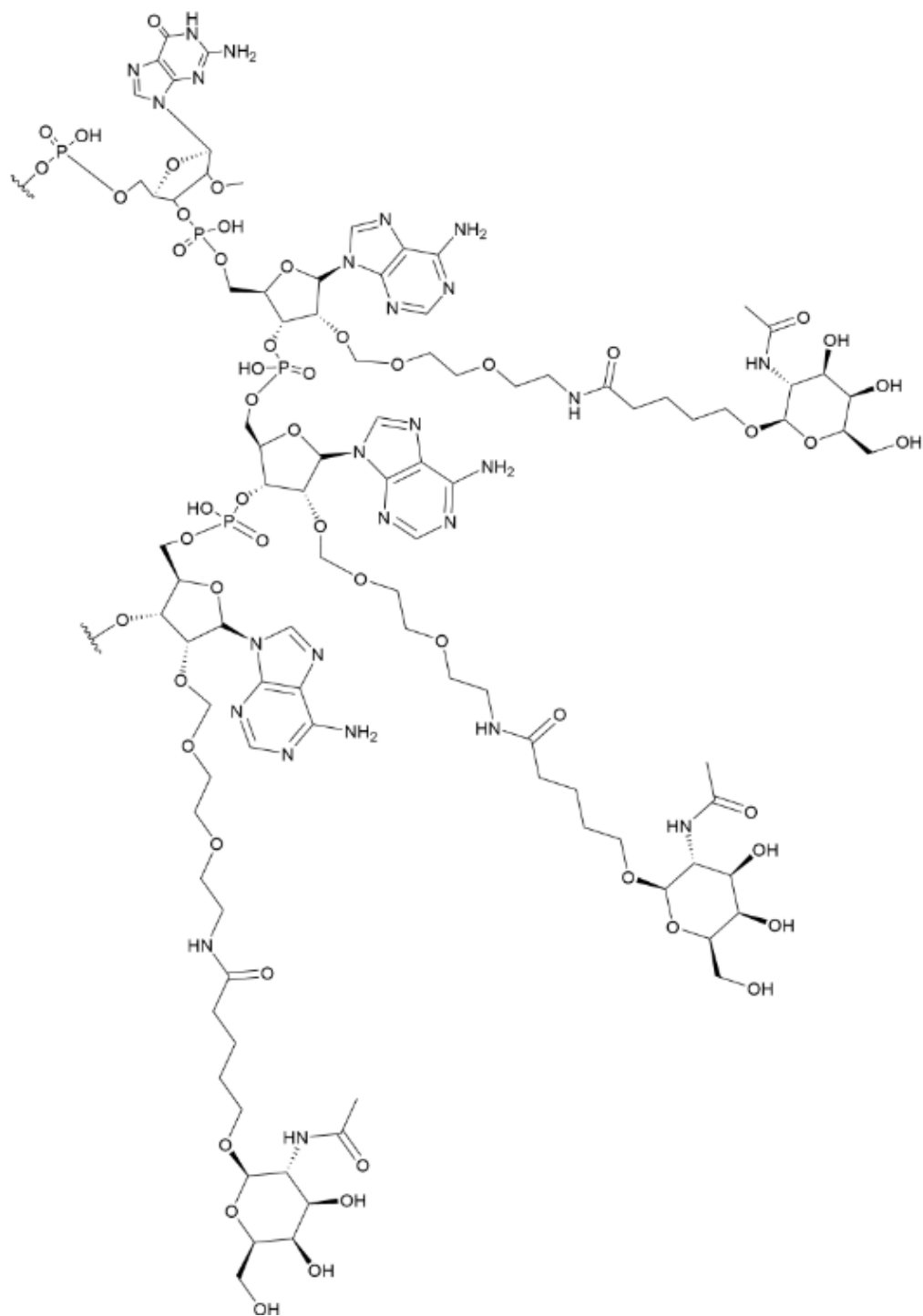


Appropriate methods or chemistry (*e.g.*, click chemistry) can be used to link a targeting ligand to a nucleotide. In some embodiments, a targeting ligand is conjugated to a nucleotide comprising an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide) using a click linker. In some embodiments, an 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. WO2016/100401. In some embodiments, the linker is a labile linker. However, in other embodiments, the linker is stable. An example is shown below for a loop comprising from 5' to 3' the nucleotides GAAA, in which GalNAc moieties are attached to 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. In the **Chem. formula 7** is an attachment point to the oligonucleotide strand.



or



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.

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 the oligonucleotide. In some embodiments, the oligonucleotides herein (*e.g.*, RNAi oligonucleotides) do not have a GalNAc conjugated thereto.

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 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;

- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;

(yy) SEQ ID NOs: 819 and 907, respectively;
(zz) SEQ ID NOs: 820 and 908, respectively;
(aaa) SEQ ID NOs: 821 and 909, respectively;
(bbb) SEQ ID NOs: 822 and 910, respectively;
(ccc) SEQ ID NOs: 823 and 911, respectively;
(ddd) SEQ ID NOs: 824 and 912, respectively;
(eee) SEQ ID NOs: 825 and 913, respectively;
(fff) SEQ ID NOs: 826 and 914, respectively;
(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm) SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;
(ooo) SEQ ID NOs: 835 and 923, respectively;
(ppp) SEQ ID NOs: 836 and 924, respectively;
(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;
(uuu) SEQ ID NOs: 1537 and 929, respectively;
(vvv) SEQ ID NOs: 842 and 930, respectively;
(www) SEQ ID NOs: 843 and 931, respectively;
(xxx) SEQ ID NOs: 844 and 932, respectively;
(yyy) SEQ ID NOs: 845 and 933, respectively;
(zzz) SEQ ID NOs: 846 and 934, respectively;
(aaaa) SEQ ID NOs: 847 and 935, respectively;
(bbbb) SEQ ID NOs: 848 and 936, respectively;

- (cccc) SEQ ID NOs: 849 and 937, respectively;
- (dddd) SEQ ID NOs: 850 and 938, respectively;
- (eeee) SEQ ID NOs: 851 and 939, respectively;
- (ffff) SEQ ID NOs: 852 and 940, respectively;
- (gggg) SEQ ID NOs: 853 and 941, respectively;
- (hhhh) SEQ ID NOs: 854 and 942, respectively;
- (iiii) SEQ ID NOs: 855 and 943, respectively; and,
- (jjjj) SEQ ID NOs: 856 and 944, respectively,

wherein the oligonucleotide comprises at least one GalNAc moiety conjugated to a nucleotide.

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

- (a) SEQ ID NOs: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively; and,
- (d) SEQ ID NOs: 813 and 901, respectively,

wherein the oligonucleotide comprises at least one GalNAc moiety conjugated to a nucleotide.

Exemplary Oligonucleotides for Reducing NR1H3 Expression

In some embodiments, the *NR1H3*-targeting dsRNAi oligonucleotide for reducing *NR1H3* expression provided by the disclosure comprise a sense strand and an antisense strand, wherein all nucleotides comprising the sense strand and antisense strand are modified, wherein the antisense strand comprises a region of complementarity to a *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, 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 5'-methoxyphosphonate-4'-oxy-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'-fluoro (2'-F) and 2'-O-methyl (2'-OMe) modified nucleotides and at least one phosphorothioate linkage. In some embodiments, the antisense strand comprises four (4) phosphorothioate linkages and the sense strand comprises one (1) phosphorothioate linkage.

In some embodiments, the antisense strand comprises five (5) phosphorothioate linkages and the sense strand comprises one (1) phosphorothioate linkage.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an 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 selected from SEQ ID NOs: 385-768.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand having a sequence of any one of SEQ ID NOs: 769-856 and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 857-944.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand having a sequence of any one of SEQ ID NOs: 1519-1552 and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 857-944.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide) comprises a sense strand having a sequence of any one of SEQ ID NOs: 945- 1032 and an antisense strand comprising a complementary sequence selected from SEQ ID NOs: 1033-1120.

In some embodiments, an oligonucleotide provided herein (*e.g.*, and RNAi oligonucleotide) for reducing *NR1H3* expression comprises:

a sense strand comprising a 2'-F modified nucleotide at positions 8-11, a 2'-OMe modified nucleotide at positions 1-7, 12-27, and 31-36, a GalNAc-conjugated nucleotide at position 28, 29 and 30; and a phosphorothioate linkage between positions 1 and 2;

an antisense strand comprising a 2'-F modified nucleotide at positions 2, 3, 4, 5, 7, 10 and 14, a 2'-OMe at positions 1, 6, 8, 9, 11-13, and 15-22, a phosphorothioate linkage between positions 1 and 2, positions 2 and 3, positions 3 and 4, 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 5'-methoxyphosphonate-4'-oxy-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: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;

- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;
- (yy) SEQ ID NOs: 819 and 907, respectively;
- (zz) SEQ ID NOs: 820 and 908, respectively;
- (aaa) SEQ ID NOs: 821 and 909, respectively;
- (bbb) SEQ ID NOs: 822 and 910, respectively;
- (ccc) SEQ ID NOs: 823 and 911, respectively;
- (ddd) SEQ ID NOs: 824 and 912, respectively;
- (eee) SEQ ID NOs: 825 and 913, respectively;
- (fff) SEQ ID NOs: 826 and 914, respectively;
- (ggg) SEQ ID NOs: 827 and 915, respectively;
- (hhh) SEQ ID NOs: 828 and 916, respectively;

- (iii) SEQ ID NOs: 829 and 917, respectively;
- (jjj) SEQ ID NOs: 830 and 918, respectively;
- (kkk) SEQ ID NOs: 831 and 919, respectively;
- (lll) SEQ ID NOs: 832 and 920, respectively;
- (mmm) SEQ ID NOs: 833 and 921, respectively;
- (nnn) SEQ ID NOs: 834 and 922, respectively;
- (ooo) SEQ ID NOs: 835 and 923, respectively;
- (ppp) SEQ ID NOs: 836 and 924, respectively;
- (qqq) SEQ ID NOs: 837 and 925, respectively;
- (rrr) SEQ ID NOs: 838 and 926, respectively;
- (sss) SEQ ID NOs: 839 and 927, respectively;
- (ttt) SEQ ID NOs: 840 and 928, respectively;
- (uuu) SEQ ID NOs: 1537 and 929, respectively;
- (vvv) SEQ ID NOs: 842 and 930, respectively;
- (www) SEQ ID NOs: 843 and 931, respectively;
- (xxx) SEQ ID NOs: 844 and 932, respectively;
- (yyy) SEQ ID NOs: 845 and 933, respectively;
- (zzz) SEQ ID NOs: 846 and 934, respectively;
- (aaaa) SEQ ID NOs: 847 and 935, respectively;
- (bbbb) SEQ ID NOs: 848 and 936, respectively;
- (cccc) SEQ ID NOs: 849 and 937, respectively;
- (dddd) SEQ ID NOs: 850 and 938, respectively;
- (eeee) SEQ ID NOs: 851 and 939, respectively;
- (ffff) SEQ ID NOs: 852 and 940, respectively;
- (gggg) SEQ ID NOs: 853 and 941, respectively;
- (hhhh) SEQ ID NOs: 854 and 942, respectively;
- (iiii) SEQ ID NOs: 855 and 943, respectively; and,
- (jjjj) SEQ ID NOs: 856 and 944, respectively,

In some embodiments, the *NR1H3*-targeting dsRNAi oligonucleotides for reducing *NR1H3* expression comprise:

a sense strand comprising a 2'-F modified nucleotide at positions 8-11, a 2'-OMe modified nucleotide at positions 1-7, 12-27, and 31-36, a GalNAc-conjugated nucleotide at position 28, 29 and 30; and a phosphorothioate linkage between positions 1 and 2;

an antisense strand comprising a 2'-F modified nucleotide at positions 2, 3, 4, 5, 7, 10 and 14, a 2'-OMe at positions 1, 6, 8, 9, 11-13, and 15-22, a phosphorothioate linkage between positions 1 and 2, positions 2 and 3, positions 3 and 4, 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 5'-methoxyphosphonate-4'-oxy-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: 786 and 874, respectively;
- (b) SEQ ID NOs: 787 and 875, respectively;
- (c) SEQ ID NOs: 1537 and 929, respectively; and,
- (d) SEQ ID NOs: 813 and 901, respectively.

In some embodiments, a *NR1H3*-targeting oligonucleotide for reducing *NR1H3* expression provided by the disclosure comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 786 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 874. In some embodiments, a *NR1H3*-targeting oligonucleotide for reducing *NR1H3* expression provided by the disclosure comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 787 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 875. In some embodiments, a *NR1H3*-targeting oligonucleotide for reducing *NR1H3* expression provided by the disclosure comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 1537 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 929. In some embodiments, a *NR1H3*-targeting oligonucleotide for reducing *NR1H3* expression provided by the disclosure

comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 813 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 901.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1512; 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1513; 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1515;

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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1512; 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1513; 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1515; 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1512; 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: 1509, wherein the antisense and sense strands are separate strands which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1513; 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: 1510, wherein the antisense and sense strands are separate strands

which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 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: 1409, wherein the antisense and sense strands are separate strands which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1515; 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: 1511, wherein the antisense and sense strands are separate strands which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1512; 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: 1509, 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1513; 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: 1510, 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 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: 1409, 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, a NR1H3-targeting dsRNAi oligonucleotide for reducing NR1H3 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 NR1H3 mRNA target sequence, wherein the region of complementarity is set forth in SEQ ID NO: 1515; 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: 1511, 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 which form an asymmetric duplex region having an overhang of 1-4 nucleotides at the 3' terminus of the antisense strand.

In some embodiments, the disclosure provides an oligonucleotide (*e.g.*, an RNAi oligonucleotide) for reducing *NR1H3* expression, wherein the oligonucleotide 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-[ademA-GalNAc]-[ademA-GalNAc]-[ademA-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-mX-mX-mX-mX-mX-mX-S-mX-S-mX-3';

wherein mX = 2'-O-methyl modified nucleotide, fX = 2'- fluoro modified nucleotide, -S- = phosphorothioate linkage, - = phosphodiester linkage, [MePhosphonate-4O-mX] = 5'-methoxyphosphonate-4-oxy modified nucleotide, and ademA-GalNAc = GalNAc attached to an adenine nucleotide.

In some embodiments, the disclosure provides an oligonucleotide (*e.g.*, an RNAi oligonucleotide) for reducing *NR1H3* expression, wherein the oligonucleotide 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-[ademA-GalNAc]-[ademA-GalNAc]-[ademA-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-mX-S-mX-S-mX-3';

wherein mX = 2'-O-methyl modified nucleotide, fX = 2'- fluoro modified nucleotide, -S- = phosphorothioate linkage, - = phosphodiester linkage, [MePhosphonate-4O-mX] = 5'-

methoxyphosphonate-4-oxy modified nucleotide, and ademA-GalNAc = GalNAc attached to an adenine nucleotide.

In some embodiments, the disclosure provides an oligonucleotide (*e.g.*, an RNAi oligonucleotide) for reducing *NR1H3* 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: 945 and 1033, respectively;
- (b) SEQ ID NOs: 946 and 1034, respectively;
- (c) SEQ ID NOs: 947 and 1035, respectively;
- (d) SEQ ID NOs: 948 and 1036, respectively;
- (e) SEQ ID NOs: 949 and 1037, respectively;
- (f) SEQ ID NOs: 950 and 1038, respectively;
- (g) SEQ ID NOs: 951 and 1039, respectively;
- (h) SEQ ID NOs: 952 and 1040, respectively;
- (i) SEQ ID NOs: 953 and 1041, respectively;
- (j) SEQ ID NOs: 954 and 1042, respectively;
- (k) SEQ ID NOs: 955 and 1043, respectively;
- (l) SEQ ID NOs: 956 and 1044 respectively;
- (m) SEQ ID NOs: 957 and 1045, respectively;
- (n) SEQ ID NOs: 958 and 1046, respectively;
- (o) SEQ ID NOs: 959 and 1047, respectively;
- (p) SEQ ID NOs: 960 and 1048, respectively;
- (q) SEQ ID NOs: 961 and 1049, respectively;
- (r) SEQ ID NOs: 962 and 1050, respectively;
- (s) SEQ ID NOs: 963 and 1051, respectively;
- (t) SEQ ID NOs: 964 and 1052, respectively;
- (u) SEQ ID NOs: 965 and 1053, respectively;
- (v) SEQ ID NOs: 966 and 1054, respectively;
- (w) SEQ ID NOs: 967 and 1055, respectively;
- (x) SEQ ID NOs: 968 and 1056, respectively;

- (y) SEQ ID NOs: 969 and 1057, respectively;
- (z) SEQ ID NOs: 970 and 1058, respectively;
- (aa) SEQ ID NOs: 971 and 1059, respectively;
- (bb) SEQ ID NOs: 972 and 1060, respectively;
- (cc) SEQ ID NOs: 973 and 1061, respectively;
- (dd) SEQ ID NOs: 974 and 1062, respectively;
- (ee) SEQ ID NOs: 975 and 1063, respectively;
- (ff) SEQ ID NOs: 976 and 1064, respectively;
- (gg) SEQ ID NOs: 977 and 1065, respectively;
- (hh) SEQ ID NOs: 978 and 1066, respectively;
- (ii) SEQ ID NOs: 979 and 1067, respectively;
- (jj) SEQ ID NOs: 980 and 1068, respectively;
- (kk) SEQ ID NOs: 981 and 1069, respectively;
- (ll) SEQ ID NOs: 982 and 1070, respectively;
- (mm) SEQ ID NOs: 983 and 1071, respectively;
- (nn) SEQ ID NOs: 984 and 1072, respectively;
- (oo) SEQ ID NOs: 985 and 1073, respectively;
- (pp) SEQ ID NOs: 986 and 1074, respectively;
- (qq) SEQ ID NOs: 987 and 1075, respectively;
- (rr) SEQ ID NOs: 988 and 1076, respectively;
- (ss) SEQ ID NOs: 989 and 1077, respectively;
- (tt) SEQ ID NOs: 990 and 1078, respectively;
- (uu) SEQ ID NOs: 991 and 1079, respectively;
- (vv) SEQ ID NOs: 992 and 1080, respectively;
- (ww) SEQ ID NOs: 993 and 1081, respectively;
- (xx) SEQ ID NOs: 994 and 1082, respectively;
- (yy) SEQ ID NOs: 995 and 1083, respectively;
- (zz) SEQ ID NOs: 996 and 1084, respectively;
- (aaa) SEQ ID NOs: 997 and 1085, respectively;
- (bbb) SEQ ID NOs: 998 and 1086, respectively;

(ccc) SEQ ID NOs: 999 and 1087, respectively;
(ddd) SEQ ID NOs: 1000 and 1088, respectively;
(eee) SEQ ID NOs: 1001 and 1089, respectively;
(fff) SEQ ID NOs: 1002 and 1090, respectively;
(ggg) SEQ ID NOs: 1003 and 1091, respectively;
(hhh) SEQ ID NOs: 1004 and 1092 respectively;
(iii) SEQ ID NOs: 1005 and 1093 respectively;
(jjj) SEQ ID NOs: 1006 and 1094, respectively;
(kkk) SEQ ID NOs: 1007 and 1095, respectively;
(lll) SEQ ID NOs: 1008 and 1096, respectively;
(mmm)SEQ ID NOs: 1009 and 1097, respectively;
(nnn) SEQ ID NOs: 1010 and 1098, respectively;
(ooo) SEQ ID NOs: 1011 and 1099, respectively;
(ppp) SEQ ID NOs: 1012 and 1100, respectively;
(qqq) SEQ ID NOs: 1013 and 1101, respectively;
(rrr) SEQ ID NOs: 1014 and 1102 respectively;
(sss) SEQ ID NOs: 1015 and 1103, respectively;
(ttt) SEQ ID NOs: 1016 and 1104, respectively;
(uuu) SEQ ID NOs: 1017 and 1105, respectively;
(vvv) SEQ ID NOs: 1018 and 1106, respectively;
(www) SEQ ID NOs: 1019 and 1107, respectively;
(xxx) SEQ ID NOs: 1020 and 1108, respectively;
(yyy) SEQ ID NOs: 1021 and 1109, respectively;
(zzz) SEQ ID NOs: 1022 and 1110, respectively;
(aaaa) SEQ ID NOs: 1023 and 1111, respectively;
(bbbb) SEQ ID NOs: 1024 and 1112, respectively;
(cccc) SEQ ID NOs: 1025 and 1113, respectively;
(dddd) SEQ ID NOs: 1026 and 1114, respectively;
(eeee) SEQ ID NOs: 1027 and 1115, respectively;
(ffff) SEQ ID NOs: 1028 and 1116, respectively;

- (gggg) SEQ ID NOs: 1029 and 1117, respectively;
- (hhhh) SEQ ID NOs: 1030 and 1118, respectively;
- (iiii) SEQ ID NOs: 1031 and 1119, respectively; and,
- (jjjj) SEQ ID NOs: 1032 and 1120, respectively.

In some embodiments, a *NR1H3*-targeting oligonucleotide for reducing *NR1H3* expression provided by the disclosure comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 963 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 1051. In some embodiments, a *NR1H3*-targeting oligonucleotide for reducing *NR1H3* expression provided by the disclosure comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 964 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 1052. In some embodiments, a *NR1H3*-targeting oligonucleotide for reducing *NR1H3* expression provided by the disclosure comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 1006 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 1094. In some embodiments, a *NR1H3*-targeting oligonucleotide for reducing *NR1H3* expression provided by the disclosure comprises a sense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 1018 and an antisense strand comprising the nucleotide sequence as set forth in SEQ ID NO: 1106.

Formulations

Various formulations (*e.g.*, pharmaceutical formulations) have been developed for 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 (*e.g.*, RNAi oligonucleotides) reduce the expression of *NR1H3*. 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 *NR1H3* expression. Any variety of suitable oligonucleotide formulations can be used to deliver oligonucleotides for the reduction of *NR1H3* as disclosed herein. In some embodiments, an oligonucleotide is formulated in buffer solutions such as phosphate buffered saline solutions,

liposomes, micellar structures, and capsids. Any of the oligonucleotides described herein may be provided not only as nucleic acids, but also in the form of a pharmaceutically acceptable salt.

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.

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).

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).

In some embodiments, a pharmaceutical composition is formulated to be compatible with its intended route of administration. The route of administration may be any route which effectively transports a compound of this invention to the desired or appropriate place in the body. 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.

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 dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.) 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, and 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, 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.

In some embodiments, a composition may contain at least about 0.1% of the therapeutic agent (*e.g.*, a RNAi oligonucleotide for reducing *NR1H3* 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.

Methods of Use

Reducing NR1H3 Expression

In some embodiments, the disclosure provides methods for contacting or delivering to a cell or population of cells an effective amount of oligonucleotides provided herein (*e.g.*, RNAi oligonucleotides) to reduce *NR1H3* expression. In some embodiments, a reduction of *NR1H3* expression is determined by measuring a reduction in the amount or level of *NR1H3* mRNA, *NR1H3* protein, or *NR1H3* activity in a cell. The methods include those described herein and known to one of ordinary skill in the art.

Methods provided herein are useful in any appropriate cell type. In some embodiments, a cell is any cell that expresses *NR1H3* mRNA (*e.g.*, hepatocytes). 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 its 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).

In some embodiments, the oligonucleotides herein (*e.g.*, RNAi oligonucleotides) 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 containing the oligonucleotides, bombardment by particles covered by the oligonucleotides, exposing the cell or population of cells to a solution containing the oligonucleotides, or electroporation of cell membranes in the presence of the oligonucleotides. 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.

In some embodiments, reduction of *NR1H3* 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 *NR1H3* expression, or by an assay or technique that evaluates molecules that are directly indicative of *NR1H3* expression in a cell or population of cells (*e.g.*, *NR1H3* mRNA or *NR1H3* protein). In some embodiments, the extent to which an oligonucleotide provided herein reduces *NR1H3* expression is evaluated by comparing *NR1H3* expression in a cell or population of cells contacted with the oligonucleotide to an appropriate control (*e.g.*, an appropriate 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 *NR1H3* 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.

In some embodiments, contacting or delivering an oligonucleotide described herein (*e.g.*, an RNAi oligonucleotide) to a cell or a population of cells results in a reduction in *NR1H3* expression in a cell or population of cells not contacted with the oligonucleotide or contacted with a control oligonucleotide. In some embodiments, the reduction in *NR1H3* 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 *NR1H3* expression. In some embodiments, the control amount or level of *NR1H3* expression is an amount or level of *NR1H3* mRNA and/or *NR1H3* 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 herein 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, *NR1H3* 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, or about 84 days or more after contacting or delivering the oligonucleotide to the cell or population of cells. In some embodiments, *NR1H3* 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, or about 6 months or more after contacting or delivering the oligonucleotide to the cell or population of cells.

In some embodiments, an oligonucleotide provided herein (*e.g.*, an RNAi 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, an oligonucleotide herein 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.

Treatment Methods

The disclosure provides oligonucleotides (*e.g.*, RNAi oligonucleotides) for use as a medicament, in particular for use in a method for the treatment of diseases, disorders, and conditions associated with expression of *NR1H3*. The disclosure also provides oligonucleotides

for use, or adaptable for use, to treat a subject (*e.g.*, a human having a disease, disorder or condition associated with *NR1H3* expression) that would benefit from reducing *NR1H3* expression. In some respects, the disclosure provides oligonucleotides for use, or adapted for use, to treat a subject having a disease, disorder or condition associated with expression of *NR1H3*. 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 *NR1H3* expression. In some embodiments, the oligonucleotides for use, or adaptable for use, target *NR1H3* mRNA and reduce *NR1H3* expression (*e.g.*, *via* the RNAi pathway). In some embodiments, the oligonucleotides for use, or adaptable for use, target *NR1H3* mRNA and reduce the amount or level of *NR1H3* mRNA, *NR1H3* protein and/or *NR1H3* activity.

In addition, in some embodiments of the methods herein, a subject having a disease, disorder, or condition associated with *NR1H3* expression or is predisposed to the same is selected for treatment with an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide). In some embodiments, the method comprises selecting an individual having a marker (*e.g.*, a biomarker) for a disease, disorder, or condition associated with *NR1H3* expression or predisposed to the same, such as, but not limited to, *NR1H3* mRNA, *NR1H3* 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 *NR1H3* expression (*e.g.*, *NR1H3* mRNA), 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.

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 a *NR1H3* expression with an oligonucleotide provided herein. In some respects, the current disclosure provides methods of treating or attenuating the onset or progression of a disease, disorder or condition associated with *NR1H3* expression using the oligonucleotides 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 *NR1H3* 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 *NR1H3* expression. In some embodiments, the subject is treated therapeutically. In some embodiments, the subject is treated prophylactically.

In some embodiments of the methods herein, one or more oligonucleotides herein (*e.g.*, RNAi oligonucleotides), or a pharmaceutical composition comprising one or more oligonucleotides, is administered to a subject having a disease, disorder or condition associated with *NR1H3* expression such that *NR1H3* expression is reduced in the subject, thereby treating the subject. In some embodiments, an amount or level of *NR1H3* mRNA is reduced in the subject. In some embodiments, an amount or level of *NR1H3* protein is reduced in the subject. In some embodiments, an amount or level of *NR1H3* activity is reduced in the subject.

In some embodiments of the methods herein, an oligonucleotide provided herein (*e.g.*, an RNAi oligonucleotide), or a pharmaceutical composition comprising the oligonucleotide, is administered to a subject having a disease, disorder or condition associated with *NR1H3* such that *NR1H3* 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 *NR1H3* expression prior to administration of one or more oligonucleotides or pharmaceutical composition. In some embodiments, *NR1H3* 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 *NR1H3* expression in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or oligonucleotides or pharmaceutical composition or receiving a control oligonucleotide or oligonucleotides, pharmaceutical composition or treatment.

In some embodiments of the methods herein, an oligonucleotide or oligonucleotides herein (*e.g.*, RNAi oligonucleotides), or a pharmaceutical composition comprising the oligonucleotide or oligonucleotides, is administered to a subject having a disease, disorder or condition associated with *NR1H3* expression such that an amount or level of *NR1H3* 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 *NR1H3* mRNA prior to administration of the oligonucleotide or pharmaceutical composition. In some embodiments, an amount or level

of *NR1H3* 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 *NR1H3* mRNA in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or oligonucleotides or pharmaceutical composition or receiving a control oligonucleotide or oligonucleotides, pharmaceutical composition or treatment.

In some embodiments of the methods herein, an oligonucleotide or oligonucleotides herein, or a pharmaceutical composition comprising the oligonucleotide or oligonucleotides, is administered to a subject having a disease, disorder or condition associated with *NR1H3* expression such that an amount or level of *NR1H3* 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 *NR1H3* protein prior to administration of the oligonucleotide or pharmaceutical composition. In some embodiments, an amount or level of *NR1H3* 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 *NR1H3* protein in a subject (*e.g.*, a reference or control subject) not receiving the oligonucleotide or oligonucleotides or pharmaceutical composition or receiving a control oligonucleotide, oligonucleotides or pharmaceutical composition or treatment.

In some embodiments of the methods herein, an oligonucleotide or oligonucleotides (*e.g.*, RNAi oligonucleotides) herein, or a pharmaceutical composition comprising the oligonucleotide or oligonucleotides, is administered to a subject having a disease, disorder or condition associated with *NR1H3* such that an amount or level of *NR1H3* gene activity/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 the amount or level of *NR1H3* activity prior to administration of the oligonucleotide or pharmaceutical composition. In some embodiments, an amount or level of *NR1H3* 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 *NR1H3* 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.

Suitable methods for determining *NR1H3* expression, the amount or level of *NR1H3* mRNA, *NR1H3* protein, *NR1H3* activity, or a biomarker related to or affected by modulation of *NR1H3* expression (*e.g.*, a plasma biomarker), in the subject, or in a sample from the subject, are known in the art. Further, the Examples set forth herein illustrate methods for determining *NR1H3* expression.

In some embodiments, *NR1H3* expression, the amount or level of *NR1H3* mRNA, *NR1H3* protein, *NR1H3* activity, or a biomarker related to or affected by modulation of *NR1H3* expression, or any combination thereof, is reduced in a cell (*e.g.*, a hepatocyte), a population or a group of cells (*e.g.*, an organoid), an organ (*e.g.*, liver), blood or a fraction thereof (*e.g.*, plasma), a tissue (*e.g.*, liver tissue), a sample (*e.g.*, a liver biopsy sample), or any other appropriate biological material obtained or isolated from the subject. In some embodiments, *NR1H3* expression, the amount or level of *NR1H3* mRNA, *NR1H3* protein, *NR1H3* activity, or a biomarker related to or affected by modulation of *NR1H3* expression, or any combination thereof, is reduced in more than one type of cell (*e.g.*, a hepatocyte and one or more other type(s) of cell), more than one groups of cells, more than one organ (*e.g.*, liver 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.*, liver tissue and one or more other type(s) of tissue), or more than one type of sample (*e.g.*, a liver biopsy sample and one or more other type(s) of biopsy sample).

Because of their high specificity, the oligonucleotides provided herein (*e.g.*, dsRNAi oligonucleotides) specifically target mRNA of target genes (*e.g.*, *NR1H3* mRNA) of cells and tissue(s), or organs(s) (*e.g.*, liver). In preventing disease, the target gene may be one which is required for initiation or maintenance of the disease or which 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.*, liver) exhibiting or responsible for mediating the disease. For example, an oligonucleotide (*e.g.*, an RNAi 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 *NR1H3* expression may be brought into contact with or introduced into a cell or tissue type of interest such as a hepatocyte or other liver cell.

In some embodiments, the target gene may be a target gene from any mammal, such as a human target. Any target gene may be silenced according to the method described herein.

Methods described herein typically involve administering to a subject an effective amount of an oligonucleotide herein (*e.g.*, a RNAi oligonucleotide), that is, an amount that produces or generates a desirable therapeutic result. A therapeutically acceptable amount may be an amount that therapeutically treats 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 composition to be administered, the active ingredient(s) in the composition, time and route of administration, general health, and other drugs being administered concurrently.

In some embodiments, a subject is administered any one of the compositions herein (*e.g.*, a composition comprising an RNAi oligonucleotide described 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, 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 liver of a subject). Typically, oligonucleotides herein are administered intravenously or subcutaneously.

In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide), or a pharmaceutical composition comprising the oligonucleotide, is administered alone or in combination. In some embodiments, the oligonucleotides herein are administered in combination concurrently, sequentially (in any order), or intermittently. For example, two oligonucleotides may be co-administered concurrently. Alternatively, one oligonucleotide may be administered and followed any amount of time later (*e.g.*, one hour, one day, one week or one month) by the administration of a second oligonucleotide.

In some embodiments, an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide), or a pharmaceutical composition comprising the oligonucleotide, is administered in combination with one or more additional pharmacologically active substances. In some embodiments the additional

pharmacologically active substances are selected from *e.g.*, anti-diabetic agents, anti-obesity agents, appetite regulating agents, antihypertensive agents, agents.

In some embodiments, the subject to be treated is a human or non-human primate 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.

Kits

In some embodiments, the disclosure provides a kit comprising an oligonucleotide herein (*e.g.*, an RNAi oligonucleotide), and instructions for use. In some embodiments, the kit comprises an oligonucleotide herein, 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, an oligonucleotide herein, 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.

In some embodiments, a kit comprises an oligonucleotide herein (*e.g.*, an RNAi 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 *NR1H3* expression in a subject in need thereof.

Definitions

As used herein, the term “antisense oligonucleotide” encompasses a nucleic acid-based molecule which has a sequence complementary to all or part of the target mRNA, in particular seed sequence thereby capable of forming a duplex with a mRNA. Thus, the term “antisense

oligonucleotide”, as used herein, may be referred to as “complementary nucleic acid-based inhibitor”.

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).

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 disease, disorder, or condition in the subject).

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 non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), or systemic lupus erythematosus 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 non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), or systemic lupus erythematosus, no detectable progression (worsening) of one or more aspects fatty liver disease, or systemic lupus erythematosus, or no detectable aspects of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), or systemic lupus erythematosus in a subject when they might otherwise be expected.

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.

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.

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 double-stranded 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 double-stranded 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 double-stranded 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 double-stranded oligonucleotide comprises two covalently separate nucleic acid strands that are fully duplexed with one another. However, in some embodiments, a double-stranded 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 double-stranded 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.

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.

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.

As used herein, “hepatocyte” or “hepatocytes” refers to cells of the parenchymal tissues of the liver. These cells make up about 70-85% of the liver's mass and manufacture serum albumin, FBN and the prothrombin group of clotting factors (except for Factors 3 and 4). Markers for

hepatocyte lineage cells include, but are not limited to, transthyretin (Ttr), glutamine synthetase (Glul), hepatocyte nuclear factor 1a (Hnf1a) and hepatocyte nuclear factor 4a (Hnf4a). Markers for mature hepatocytes may include, but are not limited to, cytochrome P450 (Cyp3a11), fumarylacetoacetate hydrolase (Fah), glucose 6-phosphate (G6p), albumin (Alb) and OC2-2F8. *See, e.g., Huch et al. NATURE (2013); 494: 247-50.*

As used herein, a “hepatotoxic agent” refers to a chemical compound, virus or other substance that is itself toxic to the liver or can be processed to form a metabolite that is toxic to the liver. Hepatotoxic agents may include, but are not limited to, carbon tetrachloride (CCl₄), acetaminophen (paracetamol), vinyl chloride, arsenic, chloroform, nonsteroidal anti-inflammatory drugs (such as aspirin and phenylbutazone).

As used herein, the term “*NR1H3*” refers to the gene which encodes to the protein Liver X receptor alpha, or LXR-alpha. LXR-alpha is a nuclear receptor protein that is encoded by *NR1H3* (nuclear receptor subfamily 1, group H, member 3). The term “*NR1H3*” is intended to refer to all isoforms unless stated otherwise.

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 readily cleaved.

As used herein, “liver inflammation” or “hepatitis” refers to a physical condition in which the liver becomes swollen, dysfunctional and/or painful, especially as a result of injury or infection, as may be caused by exposure to a hepatotoxic agent. Symptoms may include jaundice (yellowing of the skin or eyes), fatigue, weakness, nausea, vomiting, appetite reduction and weight loss. Liver inflammation, if left untreated, may progress to fibrosis, cirrhosis, liver failure or liver cancer.

As used herein, “liver fibrosis” “Liver Fibrosis” or “fibrosis of the liver” refers to an excessive accumulation in the liver of extracellular matrix proteins, which could include collagens (I, III, and IV), FBN, undulin, elastin, laminin, hyaluronan and proteoglycans resulting from inflammation and liver cell death. Liver fibrosis, if left untreated, may progress to cirrhosis, liver failure or liver cancer.

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 cell), the two antiparallel regions, which flank the unpaired region, hybridize to form a duplex (referred to as a “stem”).

As used herein, “Metabolic syndrome’ or “metabolic liver disease” refers to a disorder characterized by a cluster of associated medical conditions and associated pathologies including, but not limited to the following medical conditions: abdominal obesity, elevated blood pressure, elevated fasting plasma glucose, high serum triglycerides, liver fibrosis, and low levels of high-density lipoprotein (HDL) levels. As used herein, the term metabolic syndrome or metabolic liver disease may encompass a wide array of direct and indirect manifestations, diseases and pathologies associated with metabolic syndrome and metabolic liver disease, with an expanded list of conditions used throughout the document.

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 internucleotide linkage may improve thermal stability, resistance to degradation, nuclease resistance, solubility, bioavailability, bioactivity, reduced immunogenicity, *etc.*

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.*

As used herein, “nicked tetraloop structure” refers to a structure of a 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 tetraloop configured to stabilize an adjacent stem region formed within the at least one strand.

As used herein, “oligonucleotide” refers to a short nucleic acid (*e.g.*, less than about 100 nucleotides in length). An oligonucleotide may be single-stranded (ss) or double-stranded (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 double-stranded (dsRNA) is an RNAi oligonucleotide.

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 an oligonucleotide. In certain embodiments, the overhang is a 3'- or 5'-overhang on the antisense strand or sense strand of an oligonucleotide.

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' methylene phosphonate (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 No. WO 2011/133871; US Patent No. 8,927,513; and Prakash *et al.* NUCLEIC ACIDS RES. (2015); 43: 2993-3011).

As used herein, “reduced expression” of a gene (*e.g.*, *NR1H3*) refers to a decrease in the amount or level of RNA transcript (*e.g.*, *NR1H3* 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 *NR1H3* mRNA) may result in a decrease in the amount or level of *NR1H3* mRNA, protein and/or activity (*e.g.*, *via* degradation of *NR1H3* mRNA by the RNAi pathway) when compared to a cell that is not treated with the oligonucleotide. Similarly, and as used herein, “reducing expression” refers to an act that results in reduced expression of a gene (*e.g.*, *NR1H3*).

As used herein, “reduction of *NR1H3* expression” refers to a decrease in the amount or level of *NR1H3* mRNA, *NR1H3* protein and/or *NR1H3* 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).

As used herein, “region of complementarity” refers to a sequence of nucleotides of a nucleic acid (*e.g.*, an 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.

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.

As used herein, “RNAi oligonucleotide” refers to either (a) a double-stranded 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., *NR1H3* mRNA) or (b) a single-stranded 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., *NR1H3* mRNA).

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).

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.”

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.

As used herein, “targeting ligand” refers to a molecule (e.g., a carbohydrate, amino sugar, cholesterol, polypeptide, or lipid) 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. In some embodiments, the targeting ligand comprises at least one GalNAc moiety and targets the liver and human liver cells (e.g., human hepatocytes).

As used herein, “tetraloop” 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 tetraloop 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 Na_2HPO_4 to a hairpin comprising a duplex of at least 2 base pairs (bp) in length. In some embodiments, a tetraloop 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 NaH_2PO_4 to a hairpin comprising a duplex of at least 2 base pairs (bp) in length. In some embodiments, a tetraloop may stabilize a bp in an adjacent stem duplex by stacking interactions. In addition, interactions among the nucleotides in a tetraloop include, but are not limited to, non-Watson-Crick base pairing, stacking interactions, hydrogen bonding and contact interactions (Cheong *et al.* NATURE (1990); 346: 680-82; and Heus & Pardi SCIENCE (1991); 253: 191-94). In some embodiments, a tetraloop comprises or consists of 3 to 6 nucleotides and is typically 4 to 5 nucleotides. In certain embodiments, a tetraloop 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 one embodiment, a tetraloop 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 NUCLEIC ACIDS RES. (1985); 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), or T (thymine) may be in that position. Examples of tetraloops include the UNCG family of tetraloops (*e.g.*, UUCG), the GNRA family of tetraloops (*e.g.*, GAAA), and the CUUG tetraloop (Woese *et al.* PROC. NATL. ACAD. SCI. USA (1990); 87: 8467-71; Antao *et al.* NUCLEIC ACIDS RES. (1991); 19: 5901-05). Examples of DNA tetraloops include the d(GNNA) family of tetraloops (*e.g.*, d(GTTA), the d(GNRA)) family of tetraloops, the d(GNAB) family of tetraloops, the d(CNNG) family of tetraloops, and the d(TNCG) family of tetraloops (*e.g.*, d(TTCG)). *See, e.g.*, Nakano *et al.* BIOCHEM. (2002); 41: 14281-92; Shinji *et al.* NIPPON KAGAKKAI KOEN YOKOSHU (2000); 78: 731. In some embodiments, the tetraloop is contained within a nicked tetraloop structure.

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, disorder) experienced by a subject.

EXAMPLES

While the disclosure has been described with reference to the specific embodiments set forth in the following Examples, it should be understood by those skilled in the art that various changes may be made, and equivalents may be substituted without departing from the true spirit and scope of the disclosure. Further, the following Examples are offered by way of illustration and are not intended to limit the scope of the disclosure in any manner. In addition, modifications may be made to adapt to a situation, material, composition of matter, process, process step or steps, to the objective, spirit, and scope of the disclosure. All such modifications are intended to be within the scope of the disclosure. Standard techniques well known in the art or the techniques specifically described below were utilized.

Example 1: Preparation of RNAi Oligonucleotides

Oligonucleotide Synthesis and Purification

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.* NUCLEIC ACIDS RES. (1990); 18: 5433-41 and Usman *et al.* J. AM. CHEM. SOC. (1987); 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 and Ellington, COLD SPRING HARB. PERSPECT. BIOL. (2017); 9(1): a023812; Beaucage S.L., Caruthers M.H. *Studies on Nucleotide Chemistry V: Deoxynucleoside Phosphoramidites—A New Class of Key Intermediates for Deoxypolynucleotide Synthesis*, TETRAHEDRON LETT. (1981); 22: 1859–62. doi:10.1016/S0040-4039(01)90461-7). dsRNAi oligonucleotides having 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 NR1H3 mRNA.

Individual RNA strands were synthesized and HPLC purified according to standard methods (Integrated DNA Technologies; Coralville, IA). For example, RNA oligonucleotides were synthesized using solid phase phosphoramidite chemistry, deprotected and desalted on NAP-5 columns (Amersham Pharmacia Biotech; Piscataway, NJ) using standard techniques (Damha & Olgivie, *METHODS MOL. BIOL.* (1993); 20: 81-114; Wincott *et al.* *NUCLEIC ACIDS RES.* (1995); 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.

The purity of each oligomer was determined by capillary electrophoresis (CE) on a Beckman PACE 5000 (Beckman Coulter, Inc.; Fullerton, CA). The CE capillaries have a 100 μ m 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 DETM Biospectrometry Work Station (Applied Biosystems; Foster City, CA) following the manufacturer's recommended protocol. Relative molecular masses of all oligomers were obtained, often within 0.2% of expected molecular mass.

Preparation of Duplexes

Single strand RNA oligomers were resuspended (e.g., at 100 μ M 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 μ M duplex. Samples were heated to 100 °C for 5' in RNA buffer (IDT) and were allowed to

cool to room temperature before use. The RNAi oligonucleotides were stored at -20°C . Single strand RNA oligomers were stored lyophilized or in nuclease-free water at -80°C .

Example 2: Generation of NR1H3-Targeting Double Stranded RNAi Oligonucleotides

Identification of NR1H3 mRNA Target Sequences

Nuclear Receptor Subfamily 1 Group H Member 3 (NR1H3) is a protein that regulates macrophage function, lipid homeostasis, and inflammation. To generate RNAi oligonucleotide inhibitors of *NR1H3* expression, a computer-based algorithm was used to computationally identify *NR1H3* mRNA target sequences suitable for assaying inhibition of *NR1H3* expression by the RNAi pathway. The algorithm provided RNAi oligonucleotide guide (antisense) strand sequences each having a region of complementarity to a suitable *NR1H3* target sequence of human *NR1H3* mRNA. Some of the guide strand sequences identified by the algorithm were also complementary to the corresponding *NR1H3* target sequence of monkey and/or mouse *NR1H3* mRNA. *NR1H3* RNAi oligonucleotides comprising a region of complementarity to homologous *NR1H3* mRNA target sequences with nucleotide sequence similarity are predicted to have the ability to target homologous *NR1H3* mRNAs.

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 *NR1H3* target sequence identified by the algorithm. Modifications for the sense and anti-sense DsiRNA included the following (X- any nucleotide; m- 2'-O-methyl modified nucleotide; r- ribosyl modified nucleotide):

Sense Strand:

rXmXrXmXrXrXrXrXrXrXrXrXmXrXmXrXrXrXrXrXrXXX

Anti-sense Strand:

mXmXmXmXrXrXrXrXrXrXmXrXmXrXrXrXrXrXrXmXrXmXmXmX

In Vitro Cell-Based Assays

The ability of each of the modified DsiRNA in **Table 1** to reduce *NR1H3* mRNA was measured using *in vitro* cell-based assays. Briefly, human Huh-7 cells expressing endogenous

human *NR1H3* gene were transfected with each of the DsiRNAs listed in **Table 1** 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 *NR1H3* mRNA from the transfected cells was determined using an RT-qPCR assay. The assay used the following primers and probe normalized to the geometric mean of two reference genes HPRT1 and SFRS9: Forward-1198 GTTATAACCGGGAAGACTTTGC (SEQ ID NO:1122); Reverse-1326: TGATAGCAATGAGCAAGGCA (SEQ ID NO:1123); Probe-1253: ATGGCCCTGGAGAACTCGAAGATG (SEQ ID NO:1124). The primer pair was assayed for % remaining RNA as shown in **Table 1**. DsiRNAs resulting in less than or equal to 10% *NR1H3* mRNA remaining in DsiRNA-transfected cells when compared to mock-transfected cells were considered DsiRNA “hits”. The HuH-7 cell-based assay evaluating the ability of the DsiRNAs listed in **Table 1** to inhibit *NR1H3* expression identified several candidate DsiRNAs.

Taken together, these results show that DsiRNAs designed to target human *NR1H3* mRNA inhibit *NR1H3* expression in cells, as determined by a reduced amount of *NR1H3* 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 *NR1H3* expression. Further, these results demonstrate that multiple *NR1H3* mRNA target sequences are suitable for the RNAi-mediated inhibition of *NR1H3* expression.

Table 1. *In Vitro* Screening Results

			NR1H3-F1198	
SED ID NO (Sense Strand)	SED ID NO (Anti-sense Strand)	DsiRNA name	% remaining	SEM
1	385	NR1H3-764-784-861	8.9	4.43
2	386	NR1H3-766-786-863	16.25	3.11
3	387	NR1H3-789-809-886	15.08	1.03
4	388	NR1H3-790-810-887	18.74	3.03
5	389	NR1H3-791-811-888	40.34	2.62
6	390	NR1H3-792-812-889	32.44	4.47
7	391	NR1H3-793-813-890	33.77	2.89
8	392	NR1H3-795-815-892	10.87	4.86
9	393	NR1H3-796-816-893	14.94	1.85
10	394	NR1H3-797-817-894	45.07	9.79
11	395	NR1H3-798-818-895	17.91	4.71
12	396	NR1H3-799-819-896	17.87	2.13
13	397	NR1H3-802-822-899	8.47	3.71
14	398	NR1H3-803-823-900	26.43	3.01
15	399	NR1H3-804-824-901	13.60	2.34
16	400	NR1H3-806-826-903	47.05	7.86
17	401	NR1H3-808-828-905	14.07	1.86
18	402	NR1H3-809-829-906	37.06	10.23
19	403	NR1H3-810-830-907	27.90	12.22
20	404	NR1H3-811-831-908	41.69	8.58
21	405	NR1H3-813-833-910	29.81	2.83
22	406	NR1H3-844	22.31	3.43
23	407	NR1H3-895-915-992	13.4	2.84
24	408	NR1H3-898-918-995	21.63	3.63
25	409	NR1H3-915-935	23.64	3.59

26	410	NR1H3-917-937	13.58	3.29
27	411	NR1H3-922-942	21.35	3.75
28	412	NR1H3-924-944	32.89	16.44
29	413	NR1H3-925-945	15.74	4.69
30	414	NR1H3-927-947	26.60	5.18
31	415	NR1H3-928-948	14.55	3.21
32	416	NR1H3-929-949	9.89	1.40
33	417	NR1H3-930-950	26.20	3.86
34	418	NR1H3-931-951	27.44	1.62
35	419	NR1H3-932-952	12.31	6.33
36	420	NR1H3-933-953	13.29	1.84
37	421	NR1H3-941-961	10.08	2.10
38	422	NR1H3-944-964	13.78	1.05
39	423	NR1H3-945-965	27.16	2.75
40	424	NR1H3-946-966	15.99	1.88
41	425	NR1H3-947-967	8.63	3.01
42	426	NR1H3-949-969	17.43	1.64
43	427	NR1H3-951-971	9.66	1.70
44	428	NR1H3-952-972	9.92	1.39
45	429	NR1H3-953-973	21.75	4.12
46	430	NR1H3-1151-1171	18.83	2.78
47	431	NR1H3-1153-1173	78.76	9.71
48	432	NR1H3-1154-1174	45.38	5.78
49	433	NR1H3-1155-1175	23.72	2.37
50	434	NR1H3-1156-1176	23.75	2.37
51	435	NR1H3-1157-1177	67.42	6.83
52	436	NR1H3-1158-1178	17.98	2.57
53	437	NR1H3-1159-1179	17.47	2.49

54	438	NR1H3-1160-1180	9.14	1.61
55	439	NR1H3-1161-1181	22.52	2.41
56	440	NR1H3-1162-1182	10.89	1.66
57	441	NR1H3-1163-1183	38.50	7.62
58	442	NR1H3-1164-1184	23.52	9.14
59	443	NR1H3-1165-1185	22.81	3.68
60	444	NR1H3-1166-1186	23.01	4.64
61	445	NR1H3-1167-1187	50.54	10.76
62	446	NR1H3-1169-1189	15.60	2.02
63	447	NR1H3-1170-1190	22.78	5.79
64	448	NR1H3-1171-1191	80.98	9.76
65	449	NR1H3-1173-1193	16.14	4.16
66	450	NR1H3-1175-1195	45.81	7.47
67	451	NR1H3-1176-1196	18.32	4.59
68	452	NR1H3-1177-1197	26.85	5.22
69	453	NR1H3-1178-1198	63.10	17.52
70	454	NR1H3-1179-1199	12.86	1.65
71	455	NR1H3-1180-1200	20.97	4.62
72	456	NR1H3-1181-1201	16.21	4.23
73	457	NR1H3-1182-1202	30.61	5.64
74	458	NR1H3-1183-1203	30.96	6.72
75	459	NR1H3-1184-1204	23.71	6.05
76	460	NR1H3-1185-1205	14.77	1.30
77	461	NR1H3-1186-1206	19.94	6.28
78	462	NR1H3-1187-1207	14.48	1.77
79	463	NR1H3-1188-1208	37.28	3.76
80	464	NR1H3-1190-1210	38.58	4.63
81	465	NR1H3-1191-1211	15.02	2.19

82	466	NR1H3-1192-1212	51.23	7.43
83	467	NR1H3-1193-1213	17.05	3.23
84	468	NR1H3-1194-1214	31.91	6.24
85	469	NR1H3-1196-1216	32.00	9.03
86	470	NR1H3-1197-1217	8.36	2.55
87	471	NR1H3-1198-1218	29.10	4.48
88	472	NR1H3-1199-1219	13.22	2.89
89	473	NR1H3-1200-1220	8.59	2.38
90	474	NR1H3-1203-1223	15.92	3.29
91	475	NR1H3-1204-1224	5.07	0.83
92	476	NR1H3-1207-1227	3.54	2.18
93	477	NR1H3-1211-1231	1.88	1.19
94	478	NR1H3-1212-1232	17.48	7.55
95	479	NR1H3-1213-1233	8.32	4.17
96	480	NR1H3-1214-1234	16.53	1.70
97	481	NR1H3-1215-1235	11.84	1.93
98	482	NR1H3-1216-1236	9.48	1.67
99	483	NR1H3-1217-1237	11.9	2.34
100	484	NR1H3-1218-1238	8.45	1.98
101	485	NR1H3-1219-1239	6.80	1.35
102	486	NR1H3-1220-1240	3.60	1.88
103	487	NR1H3-1222-1242	8.53	1.67
104	488	NR1H3-1223-1243	12.69	1.63
105	489	NR1H3-1224-1244	6.15	2.42
106	490	NR1H3-1225-1245	9.72	3.87
107	491	NR1H3-1226-1246	47.24	5.54
108	492	NR1H3-1227-1247	13.80	2.63
109	493	NR1H3-1228-1248	6.76	1.78

110	494	NR1H3-1229-1249	8.75	2.71
111	495	NR1H3-1232-1252	36.21	3.20
112	496	NR1H3-1233-1253	20.37	2.75
113	497	NR1H3-1234-1254	18.42	1.50
114	498	NR1H3-1235-1255	16.37	1.48
115	499	NR1H3-1236-1256	58.83	6.78
116	500	NR1H3-1237-1257	16.03	2.29
117	501	NR1H3-1238-1258	19.29	5.59
118	502	NR1H3-1241-1261	12.44	2.25
119	503	NR1H3-1242-1262	29.53	10.05
120	504	NR1H3-1243-1263	6.22	5.33
121	505	NR1H3-1244-1264	5.51	0.94
122	506	NR1H3-1245-1265	15.00	2.82
123	507	NR1H3-1246-1266	10.14	2.84
124	508	NR1H3-1247-1267	13.70	3.55
125	509	NR1H3-1248-1268	37.81	4.12
126	510	NR1H3-1250-1270	10.08	2.10
127	511	NR1H3-1251-1271	6.50	0.47
128	512	NR1H3-1252-1272	3.35	0.65
129	513	NR1H3-1253-1273	14.22	1.35
130	514	NR1H3-1256-1276	8.26	1.63
131	515	NR1H3-1258-1278	7.38	1.26
132	516	NR1H3-1259-1279	4.72	1.13
133	517	NR1H3-1261-1281	4.39	1.31
134	518	NR1H3-1262-1282	27.66	5.46
135	519	NR1H3-1265-1285	3.35	1.10
136	520	NR1H3-1266-1286	4.91	0.83
137	521	NR1H3-1267-1287	21.91	4.48

138	522	NR1H3-1268-1288	21.59	3.96
139	523	NR1H3-1269-1289	11.31	1.44
140	524	NR1H3-1270-1290	9.87	5.24
141	525	NR1H3-1271-1291	6.95	1.9
142	526	NR1H3-1272-1292	7.07	0.99
143	527	NR1H3-1273-1293	11.01	3.72
144	528	NR1H3-1275-1295	18.49	2.31
145	529	NR1H3-1276-1296	17.77	3.25
146	530	NR1H3-1277-1297	18.20	1.62
147	531	NR1H3-1278-1298	9.35	1.70
148	532	NR1H3-1279-1299	8.96	1.60
149	533	NR1H3-1280-1300	19.16	3.95
150	534	NR1H3-1281-1301	12.33	1.94
151	535	NR1H3-1282-1302	40.52	7.51
152	536	NR1H3-1283-1303	15.26	7.23
153	537	NR1H3-1284-1304	37.09	9.79
154	538	NR1H3-1285-1305	29.28	4.88
155	539	NR1H3-1286-1306	41.56	4.92
156	540	NR1H3-1288-1308	68.84	4.13
157	541	NR1H3-1289-1309	34.44	10.86
158	542	NR1H3-1290-1310	17.67	3.83
159	543	NR1H3-1291-1311	21.47	2.26
160	544	NR1H3-1292-1312	41.99	7.72
161	545	NR1H3-1293-1313	13.77	1.40
162	546	NR1H3-1294-1314	20.97	3.76
163	547	NR1H3-1295-1315	14.39	3.21
164	548	NR1H3-1296-1316	28.04	10.25
165	549	NR1H3-1297-1317	12.70	2.20

166	550	NR1H3-1338-1358	22.20	4.81
167	551	NR1H3-1339-1359	7.86	1.5
168	552	NR1H3-1340-1360	4.72	1.10
169	553	NR1H3-1341-1361	11.49	4.26
170	554	NR1H3-1342-1362	4.84	1.18
171	555	NR1H3-1343-1363	17.05	4.21
172	556	NR1H3-1344-1364	13.83	6.27
173	557	NR1H3-1345-1365	9.55	1.22
174	558	NR1H3-1346-1366	4.54	1.14
175	559	NR1H3-1347-1367	6.47	1.87
176	560	NR1H3-1377-1443	46.13	5.08
177	561	NR1H3-1379-1445	28.21	2.69
178	562	NR1H3-1383-1449	27.33	3.23
179	563	NR1H3-1384-1450	27.81	4.58
180	564	NR1H3-1385-1451	44.36	4.37
181	565	NR1H3-1387-1453	15.50	2.5
182	566	NR1H3-1388-1454	46.03	6.42
183	567	NR1H3-1391-1457	20.33	2.82
184	568	NR1H3-1393-1459	27.25	2.95
185	569	NR1H3-1394-1460	11.31	2.71
186	570	NR1H3-1395-1461	30.82	3.24
187	571	NR1H3-1396-1462	34.98	4.45
188	572	NR1H3-1397-1463	41.12	4.28
189	573	NR1H3-1398-1464	14.14	2.79
190	574	NR1H3-1399-1465	14.46	2.61
191	575	NR1H3-1400-1466	49.48	5.89
192	576	NR1H3-1401-1467	21.19	3.39
193	577	NR1H3-1402-1468	14.17	2.73

194	578	NR1H3-1403-1469	18.25	1.29
195	579	NR1H3-1404-1470	34.21	2.29
196	580	NR1H3-1406-1472	46.79	7.22
197	581	NR1H3-1407-1473	13.59	2.47
198	582	NR1H3-1408-1474	44.63	5.37
199	583	NR1H3-1410-1476	43.93	9.37
200	584	NR1H3-1411-1477	28.12	4.11
201	585	NR1H3-1412-1478	50.22	11.35
202	586	NR1H3-1413-1479	45.56	6.23
203	587	NR1H3-1414-1480	56.42	9.61
204	588	NR1H3-1415-1481	32.43	10.32
205	589	NR1H3-1416-1482	16.66	2.27
206	590	NR1H3-1417-1483	31.84	4.71
207	591	NR1H3-1418-1484	7.07	0.80
208	592	NR1H3-1419-1485	69.83	8.81
209	593	NR1H3-1420-1486	16.01	5.34
210	594	NR1H3-1421-1487	38.29	6.31
211	595	NR1H3-1422-1488	80.48	13.59
212	596	NR1H3-1423-1489	9.79	1.47
213	597	NR1H3-1424-1490	9.36	1.84
214	598	NR1H3-1425-1491	22.14	3.77
215	599	NR1H3-1426-1492	9.86	2.14
216	600	NR1H3-1427-1493	18.88	6.80
217	601	NR1H3-1428-1494	17.55	5.52
218	602	NR1H3-1429-1495	2.77	1.08
219	603	NR1H3-1430-1496	19.29	3.14
220	604	NR1H3-1431-1497	8.66	3.71
221	605	NR1H3-1432-1498	19.76	3.07

222	606	NR1H3-1433-1499	3.37	2.29
223	607	NR1H3-1434-1500	77.93	11.83
224	608	NR1H3-1435-1501	14.53	5.77
225	609	NR1H3-1436-1502	11.42	2.45
226	610	NR1H3-1437-1503	4.97	1.57
227	611	NR1H3-1438-1504	7.40	1.89
228	612	NR1H3-1439-1505	3.26	0.97
229	613	NR1H3-1440-1506	40.21	5.31
230	614	NR1H3-1442-1508	50.09	3.47
231	615	NR1H3-1443-1509	11.50	5.54
232	616	NR1H3-1444-1510	29.36	15.66
233	617	NR1H3-1445-1511	47.59	6.76
234	618	NR1H3-1446-1512	2.37	0.65
235	619	NR1H3-1447-1513	10.29	4.95
236	620	NR1H3-1448-1514	45.74	4.52
237	621	NR1H3-1449-1515	35.27	4.39
238	622	NR1H3-1450-1516	39.10	5.63
239	623	NR1H3-1451-1517	9.58	2.83
240	624	NR1H3-1452-1518	64.45	15.14
241	625	NR1H3-1453-1519	14.78	2.76
242	626	NR1H3-1454-1520	5.01	2.14
243	627	NR1H3-1455-1521	21.75	3.59
244	628	NR1H3-1456-1522	9.11	2.01
245	629	NR1H3-1457-1523	7.52	3.29
246	630	NR1H3-1459-1525	7.81	1.75
247	631	NR1H3-1460-1526	4.57	1.07
248	632	NR1H3-1461-1527	30.77	4.42
249	633	NR1H3-1462-1528	6.29	1.92

250	634	NR1H3-1463-1529	2.58	0.85
251	635	NR1H3-1465-1531	4.17	1.14
252	636	NR1H3-1466-1532	15.04	1.90
253	637	NR1H3-1468-1534	14.47	1.37
254	638	NR1H3-1469-1535	14.04	2.26
255	639	NR1H3-1471-1537	14.94	1.55
256	640	NR1H3-1472-1538	45.97	3.01
257	641	NR1H3-1473-1539	19.37	8.93
258	642	NR1H3-1474-1540	9.53	2.70
259	643	NR1H3-1475-1541	3.21	1.94
260	644	NR1H3-1476-1542	11.27	4.12
261	645	NR1H3-1477-1543	14.30	2.78
262	646	NR1H3-1478-1544	13.06	3.66
263	647	NR1H3-1479-1545	3.97	0.86
264	648	NR1H3-1480-1546	4.82	1.41
265	649	NR1H3-1481-1547	2.81	0.57
266	650	NR1H3-1483-1549	5.56	1.60
267	651	NR1H3-1484-1550	20.18	2.39
268	652	NR1H3-1485-1551	3.52	2.10
269	653	NR1H3-1486-1552	13.41	1.81
270	654	NR1H3-1487-1553	25.35	3.42
271	655	NR1H3-1488-1554	28.45	6.63
272	656	NR1H3-1489-1555	15.31	5.00
273	657	NR1H3-1491-1557	6.33	1.03
274	658	NR1H3-1492-1558	20.75	4.42
275	659	NR1H3-1494-1560	24.97	4.76
276	660	NR1H3-1505-1571	38.74	5.88
277	661	NR1H3-1507-1573	9.42	2.29

278	662	NR1H3-1508-1574	36.57	6.54
279	663	NR1H3-1509-1575	29.82	5.45
280	664	NR1H3-1510-1576	19.45	3.79
281	665	NR1H3-1511-1577	23.73	3.3
282	666	NR1H3-1512-1578	42.41	7.68
283	667	NR1H3-1513-1579	33.80	5.58
284	668	NR1H3-1514-1580	26.85	4.79
285	669	NR1H3-1515-1581	3.95	0.84
286	670	NR1H3-1516-1582	16.48	3.36
287	671	NR1H3-1517-1583	4.38	1.57
288	672	NR1H3-1518-1584	3.43	1.32
289	673	NR1H3-1519-1585	5.73	1.72
290	674	NR1H3-1520-1586	14.37	1.95
291	675	NR1H3-1521-1587	15.60	9.44
292	676	NR1H3-1522-1588	14.40	3.9
293	677	NR1H3-1523-1589	9.60	2.11
294	678	NR1H3-1525-1591	13.51	4.15
295	679	NR1H3-1526-1592	50.59	16.74
296	680	NR1H3-1527-1593	8.47	4.27
297	681	NR1H3-1528-1594	25.44	3.59
298	682	NR1H3-1529-1595	12.55	2.77
299	683	NR1H3-1530-1596	11.6	3.15
300	684	NR1H3-1531-1597	6.14	2.83
301	685	NR1H3-1532-1598	15.35	4.55
302	686	NR1H3-1533-1599	3.13	3
303	687	NR1H3-1534-1600	8.51	3.07
304	688	NR1H3-1535-1601	1.48	0.67
305	689	NR1H3-1536-1602	30.02	10.69

306	690	NR1H3-1537-1603	17.55	6.31
307	691	NR1H3-1538-1604	21.90	1.81
308	692	NR1H3-1539-1605	28.62	6.45
309	693	NR1H3-1540-1606	19.29	5.08
310	694	NR1H3-1541-1607	10.51	2.94
311	695	NR1H3-1542-1608	8.39	6.98
312	696	NR1H3-1543-1609	5.68	3.86
313	697	NR1H3-1544-1610	23.78	4.02
314	698	NR1H3-1545-1611	3.93	1.19
315	699	NR1H3-1546-1612	11.55	1.89
316	700	NR1H3-1547-1613	16.77	3.13
317	701	NR1H3-1548-1614	10.86	7.45
318	702	NR1H3-1549-1615	33.40	8.27
319	703	NR1H3-1550-1616	13.98	3.23
320	704	NR1H3-1551-1617	32.11	9.43
321	705	NR1H3-1553-1619	43.83	11.06
322	706	NR1H3-1554-1620	5.16	1.29
323	707	NR1H3-1555-1621	89.05	22.10
324	708	NR1H3-1556-1622	33.15	4.79
325	709	NR1H3-1558-1624	15.27	4.11
326	710	NR1H3-1559-1625	15.15	3.47
327	711	NR1H3-1560-1626	34.65	4.83
328	712	NR1H3-1561-1627	63.67	7.04
329	713	NR1H3-1562-1628	16.78	10.54
330	714	NR1H3-1563-1629	26.54	9.20
331	715	NR1H3-1564-1630	34.34	14.27
332	716	NR1H3-1565-1631	89.42	16.51
333	717	NR1H3-1567-1633	66.56	5.80

334	718	NR1H3-1569-1635	39.41	11.96
335	719	NR1H3-1570-1636	25.11	4.45
336	720	NR1H3-1572-1638	24.43	4.3
337	721	NR1H3-1573-1639	13.36	2.16
338	722	NR1H3-1574-1640	82.95	11.20
339	723	NR1H3-1577-1643	35.42	6.60
340	724	NR1H3-1579-1645	18.88	2.81
341	725	NR1H3-1580-1646	21.56	5.67
342	726	NR1H3-1581-1647	4.90	1.52
343	727	NR1H3-1582-1648	10.89	3.83
344	728	NR1H3-1583-1649	13.79	6.45
345	729	NR1H3-1584-1650	16.62	7.10
346	730	NR1H3-1585-1651	5.99	2.91
347	731	NR1H3-1586-1652	3.86	0.94
348	732	NR1H3-1587-1653	4.72	0.90
349	733	NR1H3-1588-1654	2.35	0.39
350	734	NR1H3-1589-1655	47.09	6.4
351	735	NR1H3-1590-1656	12.18	2.49
352	736	NR1H3-1591-1657	7.90	3.08
353	737	NR1H3-1592-1658	13.57	3.13
354	738	NR1H3-1593-1659	31.19	18.86
355	739	NR1H3-1656-1720	31.57	13.68
356	740	NR1H3-1657-1721	21.24	4.73
357	741	NR1H3-1658-1722	15.81	4.89
358	742	NR1H3-1659-1723	12.33	4.79
359	743	NR1H3-1660-1724	22.98	7.43
360	744	NR1H3-1661-1725	9.37	3.58
361	745	NR1H3-1662-1726	8.29	2.01

362	746	NR1H3-1663-1727	4.60	1.56
363	747	NR1H3-1664-1728	16.48	1.97
364	748	NR1H3-1665-1729	17.41	2.6
365	749	NR1H3-1666-1730	23.86	4.49
366	750	NR1H3-1667-1731	23.67	5.80
367	751	NR1H3-1668-1732	27.34	4.76
368	752	NR1H3-1669-1733	9.25	2.46
369	753	NR1H3-1671-1735	5.99	1.88
370	754	NR1H3-1677-1741	28.16	4.53
371	755	NR1H3-1679-1743	10.30	2.96
372	756	NR1H3-1680-1744	13.50	3.80
373	757	NR1H3-1681-1745	12.10	2.74
374	758	NR1H3-1682-1746	17.59	5.47
375	759	NR1H3-1683-1747	17.57	14.50
376	760	NR1H3-1684-1748	3.97	0.47
377	761	NR1H3-1685-1749	7.55	2.88
378	762	NR1H3-1686-1750	8.97	4.18
379	763	NR1H3-1687-1751	16.24	8.75
380	764	NR1H3-1728-1792	6.44	1.49
381	765	NR1H3-1729-1793	8.96	3.52
382	766	NR1H3-1730-1794	15.41	8.06
383	767	NR1H3-1731-1795	5.40	2.04
384	768	NR1H3-1732-1796	3.85	0.85

Example 3: GalNAc-Conjugated *NR1H3* RNAi Oligonucleotides Inhibit Human *NR1H3* *in vitro*

The *in vitro* screening assay in **Example 2** validated the ability of NR1H3-targeting DsiRNA to knockdown *NR1H3* mRNA. To further evaluate the ability of *NR1H3* RNAi

oligonucleotides to inhibit *NR1H3* mRNA expression, GalNAc-conjugated *NR1H3* oligonucleotides were generated using sequences identified by the algorithm in **Example 2**.

Specifically, a subset of the DsiRNAs identified by the algorithm were used to generate corresponding double-stranded RNAi oligonucleotides comprising a nicked tetraloop GalNAc-conjugated structure (referred to herein as “GalNAc-conjugated *NR1H3* oligonucleotides” or “GalNAc-*NR1H3* constructs”) having a 36-mer passenger strand and a 22-mer guide strand (**Table 3**). Further, two nucleotide sequences comprising the passenger strand and guide strand have a distinct pattern of modified nucleotides and phosphorothioate linkages (sense strand SEQ ID Nos: 945-1032; antisense SEQ ID Nos: 1037 and 1086). Three of the nucleotides comprising the tetraloop were each conjugated to a GalNAc moiety (CAS#14131-60-3). The modification pattern of each strand is illustrated below:

Sense Strand: 5'-mX-S-mX-mX-mX-mX-mX-fX-fX-fX-fX[-mX-]₁₆-[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-fX-mX-mX-mX-mX-mX-mX-S-mX-S-mX-3'.

(Modification key: **Table 2** and [ademX-GalNAc] = GalNAc-conjugated nucleotide)

Or, represented as:

Sense Strand: [mXs][mX][mX][mX][mX][mX][fX][fX][fX][fX][mX][mX][mX]
[mX][mX][mX][mX][mX][mX][mX][mX][mX][mX][mX][mX][ademA-GalNAc][ademA-
GalNAc][ademA-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]

The remainder of the nucleotide sequences comprising the passenger strand and guide strand have a second distinct pattern of modified nucleotides and phosphorothioate linkages (sense strand SEQ ID Nos: 945-1032; antisense SEQ ID NOs: 1033-1036, 1038-1085 and 1087-1120). Three of the nucleotides comprising the tetraloop were each conjugated to a GalNAc moiety (CAS#14131-60-3). The modification pattern of each strand is illustrated below:

Sense Strand: 5'-mX-S-mX-mX-mX-mX-mX-mX-fX-fX-fX-fX[-mX-]₁₆-[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 2** and [ademX-GalNAc] = GalNAc-conjugated nucleotide)

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][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mX][mX][mX][mX][mX][mX]

Hybridized to:

Antisense Strand: [MePhosphonate-4O-mXs][fXs][fXs][fX][fX][mX][fX][mX][mX][fX][mX][mX][mX][mX][mX][mX][mXs][mXs][mX]

(Modification key: **Table 2**).

Symbol	Modification/linkage
Key 1	
mX	2'-O-methyl modified nucleotide
fX	2'-fluoro modified nucleotide
-S-	phosphorothioate linkage
-	phosphodiester linkage

[MePhosphonate-4O-mX]	5'-methoxyphosphonate-4'-oxy modified nucleotide
ademA-GalNAc	GalNAc attached to an adenine nucleotide
Key 2	
[mXs]	2'-O-methyl modified nucleotide with a phosphorothioate linkage to the neighboring nucleotide
[fXs]	2'-fluoro modified nucleotide with a phosphorothioate linkage to the neighboring nucleotide
[mX]	2'-O-methyl modified nucleotide with phosphodiester linkages to neighboring nucleotides
[fX]	2'-fluoro modified nucleotide with phosphodiester linkages to neighboring nucleotides

GalNAc-NR1H3 constructs were used to evaluate inhibition efficacy in cells expressing human *NR1H3*. Specifically, Huh-7 cells were transfected with the GalNAc-NR1H3 constructs using methods described in **Example 2**. Results are provided in **Table 3**, which demonstrate successful knock-down of human *NR1H3* mRNA with several constructs.

Table 3. GalNAc-Conjugated Human *NR1H3* RNAi Oligonucleotides

SED ID NO (modified Sense Strand)	SED ID NO (modified Anti-sense Strand)	DsiRNA name	% remaining	SEM
945	1033	NR1H3-763-783-860	109.29	17.94
946	1034	NR1H3-765-785-862	57.30	15.34
947	1035	NR1H3-767-787-864	31.55	7.72
948	1036	NR1H3-768-788-865	89.93	18.03
949	1037	NR1H3-769-789-866	18.84	4.39
950	1038	NR1H3-794-814-891	40.26	12.66
951	1039	NR1H3-1152-1172-1249	74.17	12.97
952	1040	NR1H3-1189-1209-1286	47.09	11.14
953	1041	NR1H3-1195-1215-1292	41.72	9.81
954	1042	NR1H3-1200-1220-1297	102.50	25.27
955	1043	NR1H3-1201-1221-1298	28.78	4.63
956	1044	NR1H3-1202-1222-1299	16.81	5.40
957	1045	NR1H3-1203-1223-1300	11.40	3.12
958	1046	NR1H3-1204-1224-1301	10.27	9.33
959	1047	NR1H3-1205-1225-1302	15.93	5.10
960	1048	NR1H3-1206-1226-1303	59.82	14.86

962	1050	NR1H3-1208-1228-1305	10.94	1.83
963	1051	NR1H3-1209-1229-1306	101.62	23.09
964	1052	NR1H3-1210-1230-1307	25.85	6.52
965	1053	NR1H3-1211-1231-1308	29.68	4.19
966	1054	NR1H3-1212-1232-1309	39.90	13.07
967	1055	NR1H3-1213-1233-1310	15.16	4.91
968	1056	NR1H3-1214-1234-1311	25.26	16.03
970	1058	NR1H3-1221-1241-1318	23.77	6.65
973	1061	NR1H3-1249-1269-1346	45.75	8.54
975	1063	NR1H3-1254-1274-1351	36.79	10.59
976	1064	NR1H3-1255-1275-1352	16.79	4.54
977	1065	NR1H3-1256-1276-1353	55.93	16.15
978	1066	NR1H3-1257-1277-1354	90.17	15.01
980	1068	NR1H3-1260-1280-1357	17.80	2.89
981	1069	NR1H3-1261-1281-1358	81.65	24.27
982	1070	NR1H3-1263-1283-1360	15.12	5.37
983	1071	NR1H3-1264-1284-1361	25.69	6.43
986	1074	NR1H3-1405-1471-1502	40.51	10.03
987	1075	NR1H3-1409-1475-1506	43.45	7.797
993	1081	NR1H3-1458-1524-1555	6.54	1.345
995	1083	NR1H3-1464-1530-1561	53.64	10.29
996	1084	NR1H3-1465-1531-1562	33.78	10.83
997	1085	NR1H3-1467-1533-1564	33.29	19.93
998	1086	NR1H3-1469-1535-1566	20.17	7.60
999	1087	NR1H3-1470-1536-1567	34.02	6.95
1002	1088	NR1H3-1480-1546-1577	31.73	6.53
1004	1092	NR1H3-1482-1548-1579	12.18	3.56
1009	1097	NR1H3-1524-1590-1621	28.36	10.49
1018	1106	NR1H3-1594-1660-1691	30.67	13.85
1019	1107	NR1H3-1595-1661-1692	50.80	8.90
1020	1108	NR1H3-1596-1662	56.02	19.49
1022	1110	NR1H3-1670-1734	10.71	5.09
1024	1112	NR1H3-1672-1736	25.94	11.33
1025	1113	NR1H3-1673-1737	53.70	17.23
1026	1114	NR1H3-1674-1738	14.48	2.82
1027	1115	NR1H3-1675-1739-1766	55.04	10.59
1028	1116	NR1H3-1676-1740-1767	33.47	12.90
1029	1117	NR1H3-1678-1742-1769	364.22	31.30

Example 4: RNAi Oligonucleotide Inhibition of *NR1H3* Expression in Mice *In Vivo*

The *in vitro* screening assays in **Examples 2** and **3** validated the ability of *NR1H3*-targeting oligonucleotides to knock-down target mRNA. To confirm the ability of the RNAi oligonucleotides to knockdown *NR1H3* *in vivo*, an HDI mouse model was used. Two sets of GalNAc-conjugated *NR1H3* oligonucleotides were evaluated. Specifically, a set of GalNAc-conjugated *NR1H3* oligonucleotides were generated from DsiRNA screened in **Example 2** (as shown in **Table 4**) and the GalNAc-conjugated *NR1H3* oligonucleotides from **Example 3** (as shown in **Table 5**). Both sets of constructs were evaluated in mice engineered to transiently express human *NR1H3* 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 *NR1H3* oligonucleotides at a dose of 2mg/kg formulated in PBS. A control group of mice (n = 5) were administered only PBS. Three days later (72 hours), the mice were hydrodynamically injected (HDI) with a DNA plasmid encoding the full human *NR1H3* gene (25µg) 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 *NR1H3* mRNA levels as described in **Example 2**. mRNA levels were measured for both human and mouse mRNA. The values were normalized for transfection efficiency using the NeoR gene included on the DNA plasmid.

Table 4. GalNAc-Conjugated Human *NR1H3* RNAi Oligonucleotides for HDI screen

	Unmodified Sense Strand (SED ID NO)	Unmodified Antisense strand (SED ID NO)	Modified Sense Strand (SED ID NO)	Modified Antisense strand (SED ID NO)
NR1H3-1207-1227	823	911	961	1049
NR1H3-1220-1240	824	912	969	1057
NR1H3-1224-1244	825	913	971	1059
NR1H3-1244-1264	826	914	972	1060
NR1H3-1252-1272	827	915	974	1062
NR1H3-1259-1279	828	916	979	1067

NR1H3-1265-1285	829	917	984	1072
NR1H3-1266-1286	830	918	985	1073
NR1H3-1429-1495	831	919	988	1076
NR1H3-1433-1499	832	920	989	1077
NR1H3-1437-1503	833	921	990	1078
NR1H3-1439-1505	834	922	991	1079
NR1H3-1446-1512	835	923	992	1080
NR1H3-1463-1529	836	924	994	1082
NR1H3-1475-1541	837	925	1000	1088
NR1H3-1479-1545	838	926	1001	1089
NR1H3-1481-1547	839	927	1003	1091
NR1H3-1485-1551	840	928	1005	1093
NR1H3-1515-1581	1537	929	1006	1094
NR1H3-1517-1583	842	930	1007	1095
NR1H3-1518-1584	843	931	1008	1096
NR1H3-1533-1599	844	932	1010	1098
NR1H3-1535-1601	845	933	1011	1099
NR1H3-1545-1611	846	934	1012	1100
NR1H3-1554-1620	847	935	1013	1101
NR1H3-1581-1647	848	936	1014	1102
NR1H3-1586-1652	849	937	1015	1103
NR1H3-1587-1653	850	938	1016	1104

NR1H3-1588-1654	851	939	1017	1105
NR1H3-1663-1727	852	940	1021	1109
NR1H3-1671-1735	853	941	1023	1111
NR1H3-1684-1748	854	942	1030	1118
NR1H3-1731-1795	855	943	1031	1119
NR1H3-1732-1796	856	944	1032	1120

Table 5. GalNAc-Conjugated Human *NR1H3* RNAi Oligonucleotides for HDI screen

	Unmodified Sense Strand (SED ID NO)	Unmodified Antisense strand (SED ID NO)	Modified Sense Strand (SED ID NO)	Modified Antisense strand (SED ID NO)
NR1H3-763-783-860	769	857	945	1033
NR1H3-765-785-862	770	858	946	1034
NR1H3-767-787-864	771	859	947	1035
NR1H3-768-788-865	772	860	948	1036
NR1H3-769-789-866	773	861	949	1037
NR1H3-794-814-891	774	862	950	1038
NR1H3-1152-1172-1249	775	863	951	1039
NR1H3-1189-1209-1286	776	864	952	1040
NR1H3-1195-1215-1292	777	865	953	1041
NR1H3-1200-1220-1297	778	866	954	1042
NR1H3-1201-1221-1298	779	867	955	1043
NR1H3-1202-1222-1299	780	868	956	1044
NR1H3-1203-1223-1300	781	869	957	1045

NR1H3-1204-1224-1301	782	870	958	1046
NR1H3-1205-1225-1302	783	871	959	1047
NR1H3-1206-1226-1303	784	872	960	1048
NR1H3-1208-1228-1305	785	873	962	1050
NR1H3-1209-1229-1306	786	874	963	1051
NR1H3-1210-1230-1307	787	875	964	1052
NR1H3-1211-1231-1308	788	876	965	1053
NR1H3-1212-1232-1309	789	877	966	1054
NR1H3-1213-1233-1310	790	878	967	1055
NR1H3-1214-1234-1311	791	879	968	1056
NR1H3-1221-1241-1318	792	880	970	1058
NR1H3-1249-1269-1346	793	881	973	1061
NR1H3-1254-1274-1351	794	882	975	1063
NR1H3-1255-1275-1352	795	883	976	1064
NR1H3-1256-1276-1353	796	884	977	1065
NR1H3-1257-1277-1354	797	885	978	1066
NR1H3-1260-1280-1357	798	886	980	1068
NR1H3-1261-1281-1358	799	887	981	1069
NR1H3-1263-1283-1360	800	888	982	1070
NR1H3-1264-1284-1361	801	889	983	1071
NR1H3-1405-1471-1502	802	890	986	1074

NR1H3-1409-1475-1506	803	891	987	1075
NR1H3-1458-1524-1555	804	892	993	1081
NR1H3-1464-1530-1561	805	893	995	1083
NR1H3-1465-1531-1562	806	894	996	1084
NR1H3-1467-1533-1564	807	895	997	1085
NR1H3-1469-1535-1566	808	896	998	1086
NR1H3-1470-1536-1567	809	897	999	1087
NR1H3-1480-1546-1577	810	898	1002	1090
NR1H3-1482-1548-1579	811	899	1004	1092
NR1H3-1524-1590-1621	812	900	1009	1097
NR1H3-1594-1660-1691	813	901	1018	1106
NR1H3-1595-1661-1692	814	902	1019	1107
NR1H3-1596-1662	815	903	1020	1108
NR1H3-1670-1734	816	904	1022	1110
NR1H3-1672-1736	817	905	1024	1112
NR1H3-1673-1737	818	906	1025	1113
NR1H3-1674-1738	819	907	1026	1114
NR1H3-1675-1739-1766	820	908	1027	1115
NR1H3-1676-1740-1767	821	909	1028	1116
NR1H3-1678-1742-1769	822	910	1029	1117

The results in **FIG. 1B** and **FIG. 2** demonstrate that GalNAc-conjugated *NR1H3* oligonucleotides designed to target human *NR1H3* mRNA successfully inhibited human *NR1H3*

mRNA expression in HDI mice, as determined by a reduction in the amount of human *NR1H3* mRNA expression in liver samples from HDI mice treated with GalNAc-conjugated *NR1H3* oligonucleotides relative to control HDI mice treated with only PBS. Benchmark controls (*NR1H3*-769 and *NR1H3*-1469), which were selected from a prior sequence screening, were used to confirm successful knock-down.

The GalNAc-conjugated *NR1H3* oligonucleotides tested in **FIGs. 1B and FIG. 2** were further validated in repeat assays as shown in **FIGs. 3 and 4** using constructs from **Table 4** and **Table 5**. The assays verified knock-down efficiency of each GalNAc-conjugated *NR1H3* oligonucleotide, and four constructs were selected for further analysis in non-human primates (NHP).

Example 5: RNAi Oligonucleotide Inhibition of *NR1H3* Expression in Non-human Primates *In Vivo*

Effective GalNAc-*NR1H3* constructs identified in the HDI mouse studies were assayed for targeting efficiency in non-human primates. Specifically, GalNAc-conjugated *NR1H3* oligonucleotides listed in **Table 6** were evaluated in non-naïve cynomolgus monkeys (*Macaca fascicularis*).

Table 6. GalNAc Constructs evaluated in non-human primate

	Modified Sense strand (SED ID NO)	Modified Antisense strand (SED ID NO)
NR1H3-1209-1229-1306	963	1051
NR1H3-1210-1230-1307	964	1052
NR1H3-1515-1581	1006	1094
NR1H3-1594-1660-1691	1018	1106

In this study, the monkeys were grouped so that their mean body weights (about 5.4 kg) were comparable between the control and experimental groups. Each cohort contained at least two female and at least two male subjects. The GalNAc-conjugated *NR1H3* oligonucleotides were administered subcutaneously at a dose of 1 or 4 mg/kg on Study Day 0, 28, 56, and 112 as

outlined in **FIG. 5**. Blood samples and liver biopsies were collected as outlined in **Table 7** and **FIG. 5**.

Table 7. Treatment plan for NHP study

Group	Dose (mg/kg)	Dosing	GalXC	DP Number	Blood Collection	Liver Biopsy	N
A	N/A	sc	PBS	N/A	-8, 0, 14, 28, 56, 112	-8, 28, 56, 112	5
B	1	sc	NR1H3-1209-1229-1306	DP18987P: DP18986G	-8, 0, 14, 28, 56, 112	28, 56, 112	5
C	4	sc	NR1H3-1209-1229-1306	DP18987P: DP18986G	-8, 0, 14, 28, 56, 112	-8, 28, 56, 112	5
D	1	sc	NR1H3-1210-1230-1307	DP18989P: DP18988G	-8, 0, 14, 28, 56, 112	28, 56, 112	5
E	4	sc	NR1H3-1210-1230-1307	DP18989P: DP18988G	-8, 0, 14, 28, 56, 112	-8, 28, 56, 112	5
F	1	sc	NR1H3-1515-1581	DP20645P: DP20644G	-8, 0, 14, 28, 56, 112	28, 56, 112	5
G	4	sc	NR1H3-1515-1581	DP20645P: DP20644G	-8, 0, 14, 28, 56, 112	-8, 28, 56, 112	5
H	1	sc	NR1H3-1594-1660-1691	DP19040P: DP19039G	-8, 0, 14, 28, 56, 112	28, 56, 112	4
I	4	sc	NR1H3-1594-1660-1691	DP19040P: DP19039G	-8, 0, 14, 28, 56, 112	-8, 28, 56, 112	5

At each time point, total RNA derived from the liver biopsy samples was subjected to qRT-PCR analysis to measure *NR1H3* mRNA in oligonucleotide-treated monkeys relative to those treated with a comparable volume of PBS. To normalize the data, the measurements were made relative to the reference gene, PPIB (Rh02802984_m1(Taqman)). The following SYBR assays purchased from Integrated DNA Technologies were used to evaluate gene expressions: Forward-942: GTCTCTGTGCAGGAGATAGTTG (SEQ ID NO: 1517), Reverse-1399: GGAGGCTCACCAGTTTCATTA (SEQ ID NO: 1518). As shown in **Table 8** (Day 28), treating NHPs with the GalNAc-conjugated *NR1H3* oligonucleotides listed in **Table 6** inhibited *NR1H3* expression in the liver, as determined by a reduced amount of *NR1H3* mRNA in liver samples from oligonucleotide-treated NHPs relative to NHPs treated with PBS. Days 56 and 112 were also measured (**Table 8**). These results demonstrate that treating NHPs with the GalNAc-

conjugated *NR1H3* oligonucleotides reduces the amount of *NR1H3* mRNA in the liver in a dose dependent manner.

Table 8. *NR1H3* mRNA remaining after treatment with the indicated NR1H3-GalNAc in the liver from the oligonucleotide-treated NHP

		NR1H3 Gene Expression (% Time-Matched PBS)							
Day 28									
	PBS	-1209		-1210		-1515		-1594	
		1mg/kg	4mg/kg	1mg/kg	4mg/kg	1mg/kg	4mg/kg	1mg/kg	4mg/kg
Animal 1	107.3	58.6	35.6	60.1	45.1	95.8	55.4	111.6	80.4
Animal 2	116.6	62.4	27.8	48.5	34.7	101.3	NS	108.3	103.6
Animal 3	122.1	79.4	44.5	73.8	35.7	111.8	74.1	145.5	45.9
Animal 4	77.4	78.5	50.5	65.1	27.5	70.0	45.1	195.4	73.2
Animal 5	76.6	89.2	37.4	77.5	45.2	78.9	34.9	NS	68.5
Average	100.0	73.6	39.2	65.0	37.6	91.6	52.4	140.2	74.3
SEM	9.7	5.7	3.9	5.1	3.4	7.6	8.4	20.2	9.3
Day 56									
	PBS	-1209		-1210		-1515		-1594	
		1mg/kg	4mg/kg	1mg/kg	4mg/kg	1mg/kg	4mg/kg	1mg/kg	4mg/kg
Animal 1	96.7	72.9	29.0	43.7	39.0	59.7	30.0	67.7	78.2
Animal 2	115.0	60.1	29.7	75.9	32.1	68.7	NS	85.1	103.4
Animal 3	87.1	52.7	32.6	36.8	40.4	48.1	45.0	104.3	70.0
Animal 4	103.4	34.9	45.0	51.9	26.9	43.6	37.3	76.2	72.1
Animal 5	97.8	45.9	32.3	55.9	36.0	47.1	31.1	NS	72.4
Average	100.0	53.3	33.7	52.8	34.9	53.4	35.9	83.3	79.2
SEM	4.6	6.4	2.9	6.6	2.5	4.7	3.4	7.8	6.2
Day 112									
	PBS	-1209		-1210		-1515		-1594	
		1mg/kg	4mg/kg	1mg/kg	4mg/kg	1mg/kg	4mg/kg	1mg/kg	4mg/kg
Animal 1	113.2	44.2	27.3	34.4	33.1	52.8	46.8	56.6	34.8
Animal 2	106.6	56.2	21.7	42.8	33.0	36.2	NS	57.9	31.2
Animal 3	100.2	59.6	22.1	33.4	29.6	46.2	45.7	48.5	44.2
Animal 4	103.1	47.8	45.0	44.9	33.1	44.1	44.9	65.7	32.1
Animal 5	77.0	55.9	34.4	45.3	32.1	52.6	37.6	NS	33.6
Average	100.0	52.7	30.1	40.2	32.2	46.4	43.8	57.2	35.2
SEM	6.2	2.9	4.4	2.6	0.7	3.1	2.1	3.5	2.3

NS = no sample

To confirm if the GalNAc conjugated *NR1H3* were specific targeting *NR1H3*, both *NR1H3* and *NR1H2* expression was evaluated in liver samples. Non-human primates treated with 4mg/kg of GalNAc- conjugated *NR1H3* were assayed for expression at days 0, 28, 56, and 112 in the liver for knock-down (KD) of *NR1H3* mRNA in (**Table 9**), and *NR1H2* (**Table 10**). The results demonstrate that the constructs are specific to *NR1H3* and do not have significant off target effects for *NR1H2*.

Table 9. NR1H3 mRNA remaining after treatment with the indicated NR1H3-GalNAc in NHP

		NR1H3 Gene Expression (% Time Matched PBS)				
		Day -6				
		4mg/kg				
		PBS	-1209	-1210	-1515	-1594
Animal 1		65.8	136.6	204.3	103.8	NS
Animal 2		102.4	78.1	113.3	49.3	80.3
Animal 3		86.1	101.0	150.2	94.0	104.3
Animal 4		137.3	89.9	155.0	82.8	109.7
Animal 5		108.4	90.8	92.5	83.1	124.2
Average		100.0	99.3	143.1	82.6	104.6
SEM		11.9	10.0	19.2	9.2	9.1
		Day 28				
		4mg/kg				
		PBS	-1209	-1210	-1515	-1594
		PBS	-1209	-1210	-1515	-1594
Animal 1		107.3	35.6	45.1	55.4	80.4
Animal 2		116.6	27.8	34.7	NS	103.6
Animal 3		122.1	44.5	35.7	74.1	45.9
Animal 4		77.4	50.5	27.5	45.1	73.2
Animal 5		76.6	37.4	45.2	34.9	68.5
Average		100.0	39.2	37.6	52.4	74.3
SEM		9.7	3.9	3.4	8.4	9.3
		Day 56				
		4mg/kg				
		PBS	-1209	-1210	-1515	-1594
		PBS	-1209	-1210	-1515	-1594
Animal 1		96.7	29.0	39.0	30.0	78.2
Animal 2		115.0	29.7	32.1	NS	103.4
Animal 3		87.1	32.6	40.4	45.0	70.0
Animal 4		103.4	45.0	26.9	37.3	72.1
Animal 5		97.8	32.3	36.0	31.1	72.4

Average	100.0	33.7	34.9	35.9	79.2
SEM	4.6	2.9	2.5	3.4	6.2
Day 112					
4mg/kg					
	PBS	-1209	-1210	-1515	-1594
Animal 1	113.2	27.3	33.1	46.8	34.8
Animal 2	106.6	21.7	33.0	NS	31.2
Animal 3	100.2	22.1	29.6	45.7	44.2
Animal 4	103.1	45.0	33.1	44.9	32.1
Animal 5	77.0	34.4	32.1	37.6	33.6
Average	100.0	30.1	32.2	43.8	35.2
SEM	6.2	4.4	0.7	2.1	2.3
NS = no sample					

Table 10. NR1H2 mRNA remaining after treatment with the indicated NR1H3-GalNAc in NHP

NR1H2 Gene Expression (% Time Matched PBS)					
Day -6					
	4mg/kg				
	PBS	-1209	-1210	-1515	-1594
Animal 1	119.7	84	324.9	79.8	NS
Animal 2	96.3	107.5	116.1	89.3	175.9
Animal 3	105.7	86.2	106.6	103	151.1
Animal 4	82.1	105.7	672	127.9	113.2
Animal 5	96.3	134.9	126.7	101.6	113.9
Average	100.0	103.7	269.3	100.3	138.5
SEM	6.2	9.2	108.5	8.1	15,3
Day 28					
	4mg/kg				
	PBS	-1209	-1210	-1515	-1594
Animal 1	101	80.2	122.2	102.7	117.5
Animal 2	123.3	80.9	103.7	NS	130
Animal 3	111.8	78.1	107.3	87.8	61.2
Animal 4	88.5	120.4	113.7	98.3	80.2
Animal 5	75.3	129.4	102.7	97.1	75.4
Average	100.0	97.8	109.9	96.5	92.9
SEM	8.4	11.2	3.6	3.1	13.1
Day 56					
	4mg/kg				
	PBS	-1209	-1210	-1515	-1594

Animal 1	118.5	127.9	119.2	90.9	88.5
Animal 2	118.4	98.6	99.6	NS	112
Animal 3	90.9	91	131.8	76.3	103
Animal 4	88.5	115.4	117.8	100.7	121.1
Animal 5	83.8	107.6	87.1	85.5	119.4
Average	100.0	108.1	111.1	88.4	108.8
SEM	7.6	6.4	7.9	5.1	6.0
Day 112					
4mg/kg					
	PBS	-1209	-1210	-1515	-1594
Animal 1	105.6	114.2	107.9	95.6	89.6
Animal 2	108.5	81.5	106.8	NS	80.8
Animal 3	119.1	76.7	118.4	90.5	96.8
Animal 4	100.4	121.1	97.2	95.4	98.6
Animal 5	66.4	99.1	104.8	111.9	98.1
Average	100.0	98.5	107.0	98.4	92.8
SEM	8.9	8.7	3.4	4.7	3.4

Taken together, these results show that GalNAc-conjugated *NR1H3* oligonucleotides designed to target human *NR1H3* mRNA inhibit total *NR1H3* expression *in vivo* (as determined by the reduction of the amount of *NR1H3* mRNA).

Example 6

In order to determine the effect of hepatic NR1H3 knockdown on liver and plasma triglycerides and total plasma cholesterol, C57Bl mice fed a high fat, high fructose, high cholesterol (HFFC - NASH) diet were administrated a NR1H3 GalNAc siRNA probe specifically designed to reduce NR1H3 expression in mice. The compound was administrated by subcutaneous injection 3 mg/kg once a week for 4 weeks. The respective vehicle treated groups (chow and HFFC - NASH diet) were treated with PBS.

As seen in **Table 11**, hepatocyte specific knockdown (KD) of murine NR1H3-specific GalNAc siRNA led to a significant decrease in murine NR1H3 transcript expression in the liver of treated animals as compared to vehicle. Treatment leading to such hepatic NR1H3 mRNA reduction in turn induced reductions in liver triglycerides, plasma triglyceride and plasma total cholesterol. Furthermore, genes involved in hepatic de novo lipogenesis (fatty acid synthase (Fasn)

and Acetyl-CoA carboxylase 2 (Acc2)) were decreased by treatment with the murine NR1H3-specific GalNac siRNA. In conclusion, hepatocyte-specific knockdown of NR1H3 mRNA in a mouse model for NAFLD led to significant improvement in NASH related dyslipidemia.

Table 11.

	CHOW diet AVG ±ST.DEV.	NASH AVG ±ST.DEV.	NASH diet/NR1H3 KD AVG ±ST.DEV.	p-value NASH/NASH NR1H3 KD
Liver triglycerides mg/g liver	9.39 ± 2.88	47.00 ± 12.56	19.39 ± 11.07	<0.0001
Plasma triglycerides mM	1.31 ± 0.31	0.86 ± 0.21	0.46 ± 0.11	0.0036
Plasma total cholesterol mM	2.06 ± 0.21	4.19 ± 0.54	3.37 ± 0.67	0.0145
NR1H3 mRNA expression	100 ± 5.27	106.19 ± 8.75	43.88 ± 6.27	<0.0001
Fasn mRNA expression	100 ± 44.53	56.60 ± 27.23	17.58 ± 6.06	0.0327
Acc2 mRNA expression	100 ± 20.30	43.34 ± 21.89	12.21 ± 4.31	0.0034

Example 7: GalNac-conjugated siRNA targeting *NR1H3* for knock down in obese rhesus monkeys fed a high cholesterol diet

A GalNac-conjugated *NR1H3* oligonucleotide (sense strand SEQ ID NO: 964 antisense strand SEQ ID NO: 1052) was administered to obese rhesus monkeys fed a high cholesterol diet (0.06% cholesterol). Eight obese rhesus monkeys fed a high cholesterol diet (0.06% cholesterol) for more than 4 years, and with a body weight ranging from 8–25 kg, were dosed with 4 mg/kg lead at weeks 0, 4 and 8 and study was terminated at week 12. A liver biopsy (week -3) and an ultrasound scan of the liver (week -1) were performed prior to dosing of the animals. Liver enzymes and plasma lipids were determined prior to dosing and every 2 weeks posttreatment to assess potential adverse effects. At the end of the study, liver and plasma samples were collected to measure the effect of NR1H3 α knock down on lipid and cholesterol metabolism, hepatic genes involved in these pathways, as well as liver histology.

At the end of the study NR1H3 α mRNA in the liver was decreased 50%. mRNA is calculated as Δ/Δ Ct levels relative to 18s gene expression in each sample. As NR1H3 α is

expressed in other liver cells, e.g. the Kupffer cells, a full knockdown of NR1H3a was not expected from a liver homogenate.

The plasma levels of liver enzymes and plasma levels of lipids are presented in **Table 12**. During the treatment period, there was no change in the plasma level of alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT) or total bilirubin (TB), while a small increase was observed in aspartate aminotransferase (AST) after 8 and 10 weeks of treatment. During the treatment period, there was no change in the plasma level total cholesterol (TC) or low-density lipoprotein cholesterol (LDL C), while a significant increase in high-density lipoprotein cholesterol (HDL C) was observed already after 2 weeks of treatment. After 12 weeks of treatment a significant decrease in plasma triglycerides (TG) was observed. In Table 12, data represent mean $\pm$ standard error of the mean. Baseline is the average of measures from week -4 to week 0 (pre-dose). Statistics are done relative to baseline: One-Way ANOVA. $P^* < 0.05$ $P^{**} < 0.01$, $P^{***} < 0.001$.

Table 12. Liver enzymes and plasma lipids in response to NR1H3a KD in obese rhesus monkeys.

	AST (IU/L)	ALT (IU/L)	GGT (IU/L)	TBili (mg/dL)	Plasma TG (mg/dL)	Plasma Total Cholesterol (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)
Baseline	31.9 $\pm$ 1.5	55.6 $\pm$ 7.1	55.1 $\pm$ 4.2	0.21 $\pm$ 0.01	110 $\pm$ 19	206 $\pm$ 21.9	80 $\pm$ 4.6	107 $\pm$ 17.3
Week 2	32.9 $\pm$ 2.9	58.4 $\pm$ 6.2	55.6 $\pm$ 5.2	0.17 $\pm$ 0.03	84.9 $\pm$ 10.3	209 $\pm$ 20	98 $\pm$ 6.0**	98 $\pm$ 14.5
Week 4	36.6 $\pm$ 4.1	68.9 $\pm$ 9.3	58.0 $\pm$ 3.8	0.18 $\pm$ 0.02	103 $\pm$ 20.2	210 $\pm$ 15	107 $\pm$ 4.3***	101 $\pm$ 10.8
Week 6	38.5 $\pm$ 3.2	66.3 $\pm$ 6.0	49.9 $\pm$ 3.2	0.23 $\pm$ 0.02	74.1 $\pm$ 6.7	208 $\pm$ 16	102 $\pm$ 6.4**	98 $\pm$ 9.8
Week 8	42.5 $\pm$ 2.5***	70.4 $\pm$ 9.0	54.1 $\pm$ 4.5	0.15 $\pm$ 0.02*	93.3 $\pm$ 18.0	211 $\pm$ 14	105 $\pm$ 6.2**	104 $\pm$ 9.4
Week 10	39.5 $\pm$ 2.8**	58.5 $\pm$ 3.7	60.0 $\pm$ 3.3	0.17 $\pm$ 0.02	91.6 $\pm$ 12.4	219 $\pm$ 15	107 $\pm$ 4.9**	105 $\pm$ 10.4

Week 12	36.1 ± 2.1	59.3 ± 7.0	62.8 ± 3.5	0.16 ± 0.02*	84.9 ± 17.2*	214 ± 14	108 ± 4.3**	116 ± 11.1
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The effect of NR1H3 α knock down on liver triglycerides and liver cholesterol is presented in **Table 13**. No significant change in liver triglycerides or cholesterol was observed. However, a tendency ($p=0.055$, paired t-test) towards a decrease in liver stiffness as measured by FibroScan™ was observed in response to hepatic NR1H3 α knock down. In Table 13 data represent mean $\pm$ standard error of the mean analyzed by a paired t-test. One monkey was excluded from the FibroScan™ analysis as it was not fully sedated during the second scan.

Table 13. TG and cholesterol levels and FibroScan™ liver stiffness in obese rhesus monkeys

	Baseline	Week 13–14
Liver triglycerides (mg/dL)	40.9 $\pm$ 6.6	40.0 $\pm$ 5.5
Liver cholesterol (mg/dL)	42.6 $\pm$ 3.9	41.4 $\pm$ 3.0
Liver stiffness kPa	5.7 $\pm$ 0.5	4.3 $\pm$ 0.2

From the study, it can be concluded that knockdown of NR1H3a in hepatocytes does not cause hepatic cholesterol accumulation in obese monkeys fed a high cholesterol diet. An increased in plasma HDL C was observed 2 weeks after dosing, while a lowering of plasma TG was observed at week 12. No effect on liver TG was observed but none of the monkeys had steatosis at the start of the study. However, a tendency toward a decrease in liver stiffness was observed in response to hepatic NR1H3a knockdown.

List of Embodiments:

Embodiment 1. An RNAi oligonucleotide for reducing *NR1H3* 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 *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

Embodiment 2. The RNAi oligonucleotide of embodiment 1, wherein the sense strand is 15 to 50 nucleotides in length.

Embodiment 3. The RNAi oligonucleotide of embodiments 1 or 2, wherein the sense strand is 18 to 36 nucleotides in length.

Embodiment 4. The RNAi oligonucleotide of any one of embodiments 1 to 3, wherein the antisense strand is 15 to 30 nucleotides in length.

Embodiment 5. The RNAi oligonucleotide of any one of embodiments 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.

Embodiment 6. The RNAi oligonucleotide of any one of embodiments 1 to 5, wherein the region of complementarity is at least 19 contiguous nucleotides in length, optionally at least 20 nucleotides in length.

Embodiment 7. The RNAi oligonucleotide of any one of embodiments 1 to 6, 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.

Embodiment 8. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand of 15 to 50 nucleotides in length 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 *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

Embodiment 9. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand of 15 to 50 nucleotides in length and an antisense strand

of 15 to 30 nucleotides in length, wherein the sense strand and the antisense strand form a duplex region, wherein the antisense strand comprises a region of complementarity to a *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

Embodiment 10. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand of 15 to 50 nucleotides in length 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 *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

Embodiment 11. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand of 18 to 36 nucleotides in length 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 *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

Embodiment 12. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand of 18 to 36 nucleotides in length and an antisense strand of 22 nucleotides in length, wherein the sense strand and the antisense strand form a duplex region, wherein the antisense strand comprises a region of complementarity to a *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

Embodiment 13. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand of 18 to 36 nucleotides in length and an antisense strand of 22 nucleotides in length, wherein the sense strand and the antisense strand form a duplex region, 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, wherein the antisense strand comprises a region of complementarity to a *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

Embodiment 14. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand of 36 nucleotides in length and an antisense strand of 22 nucleotides in length, wherein the sense strand and the antisense strand form a duplex region, 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, wherein the antisense strand comprises a region of complementarity to a *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

Embodiment 15. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand of 36 nucleotides in length and an antisense strand of 22 nucleotides in length, wherein the sense strand and the antisense strand form a duplex region of at least 19 nucleotides in length, optionally 20 nucleotides in length, 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, wherein the antisense strand comprises a region of complementarity to a *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is 19 contiguous nucleotides in length, optionally 20 nucleotides in length.

Embodiment 16. The RNAi oligonucleotide of any one of embodiments 7 and 13-15, wherein L is a triloop or a tetraloop.

Embodiment 17. The RNAi oligonucleotide of embodiment 16, wherein L is a tetraloop.

Embodiment 18. The RNAi oligonucleotide of embodiment 17, wherein the tetraloop comprises the sequence 5'-GAAA-3'.

Embodiment 19. The RNAi oligonucleotide of any one of embodiments 16-18, wherein the S1 and S2 are 1-10 nucleotides in length and have the same length.

Embodiment 20. The RNAi oligonucleotide of embodiment 19, 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.

Embodiment 21. The RNAi oligonucleotide of embodiment 20, wherein S1 and S2 are 6 nucleotides in length.

Embodiment 22. The RNAi oligonucleotide of any one of embodiments 16 to 21, wherein the stem-loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 1121).

Embodiment 23. The RNAi oligonucleotide of any one of embodiments 1 to 22, wherein the antisense strand comprises a 3'-overhang sequence of one or more nucleotides in length.

Embodiment 24. The RNAi oligonucleotide of embodiment 23, wherein the 3'-overhang sequence is 2 nucleotides in length, optionally wherein the 3'-overhang sequence is GG.

Embodiment 25. The RNAi oligonucleotide of any one of the preceding embodiments, wherein the oligonucleotide comprises at least one modified nucleotide.

Embodiment 26. The RNAi oligonucleotide of embodiment 25, wherein the modified nucleotide comprises a 2'-modification.

Embodiment 27. The RNAi oligonucleotide of embodiment 26, 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.

Embodiment 28. The RNAi oligonucleotide of any one of embodiments 25 to 27, wherein all nucleotides comprising the oligonucleotide are modified, optionally wherein the modification is a 2'-modification selected from 2'-fluoro and 2'-O-methyl.

Embodiment 29. The RNAi oligonucleotide of any one of embodiments 25-28, wherein about 10-15%, 10%, 11%, 12%, 13%, 14%, or 15% of the nucleotides of the sense strand comprise a 2'-fluoro modification.

Embodiment 30. The RNAi oligonucleotide of any one of embodiments 25-29, 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.

Embodiment 31. The RNAi oligonucleotide of any one of embodiments 25-30, 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

Embodiment 32. The RNAi oligonucleotide of any one of embodiments 25-31, wherein the sense strand comprises 36 nucleotides with positions 1-36 from 5' to 3', wherein positions 8-11 comprise a 2'-fluoro modification.

Embodiment 33. The RNAi oligonucleotide of any one of embodiments 25-32, wherein the antisense strand comprises 22 nucleotides with positions 1-22 from 5' to 3', and wherein positions 2, 3, 4, 5, 7, 10, and 14 comprise a 2'-fluoro modification.

Embodiment 34. The RNAi oligonucleotide of any one of embodiments 25-33, wherein the remaining nucleotides comprise a 2'-O-methyl modification.

Embodiment 35. The RNAi oligonucleotide of any one of the preceding embodiments, wherein the oligonucleotide comprises at least one modified internucleotide linkage.

Embodiment 36. The RNAi oligonucleotide of embodiment 35, wherein the at least one modified internucleotide linkage is a phosphorothioate linkage.

Embodiment 37. The RNAi oligonucleotide of any one of the preceding embodiments, wherein the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog.

Embodiment 38. The RNAi oligonucleotide of embodiment 37, wherein the phosphate analog is oxymethylphosphonate, vinylphosphonate or malonylphosphonate, optionally wherein the phosphate analog is a 4'-phosphate analog comprising 5'-methoxyphosphonate-4'-oxy.

Embodiment 39. The RNAi oligonucleotide of any one of the preceding embodiments, wherein at least one nucleotide of the oligonucleotide is conjugated to one or more targeting ligands.

Embodiment 40. The RNAi oligonucleotide of embodiment 39, wherein each targeting ligand comprises a carbohydrate, amino sugar, cholesterol, polypeptide or lipid.

Embodiment 41. The RNAi oligonucleotide of embodiment 39, wherein each targeting ligand comprises a N-acetylgalactosamine (GalNAc) moiety.

Embodiment 42. The RNAi oligonucleotide of embodiment 35, wherein the GalNAc moiety is a monovalent GalNAc moiety, a bivalent GalNAc moiety, a trivalent GalNAc moiety or a tetravalent GalNAc moiety.

Embodiment 43. The RNAi oligonucleotide of any one of embodiments 16 to 38, wherein up to 4 nucleotides of L of the stem-loop are each conjugated to a monovalent GalNAc moiety.

Embodiment 44. The RNAi oligonucleotide of any one of embodiments 1 to 43, wherein the sense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 769-856 or 1519-1552.

Embodiment 45. The RNAi oligonucleotide of any one of embodiments 1 to 44, wherein the antisense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 857-944.

Embodiment 46. The RNAi oligonucleotide of any one of embodiments 1 to 45, wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

- (a) SEQ ID NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;

- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;

(ww) SEQ ID NOs: 817 and 905, respectively;
(xx) SEQ ID NOs: 818 and 906, respectively;
(yy) SEQ ID NOs: 819 and 907, respectively;
(zz) SEQ ID NOs: 820 and 908, respectively;
(aaa) SEQ ID NOs: 821 and 909, respectively;
(bbb) SEQ ID NOs: 822 and 910, respectively;
(ccc) SEQ ID NOs: 823 and 911, respectively;
(ddd) SEQ ID NOs: 824 and 912, respectively;
(eee) SEQ ID NOs: 825 and 913, respectively;
(fff) SEQ ID NOs: 826 and 914, respectively;
(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm)SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;
(ooo) SEQ ID NOs: 835 and 923, respectively;
(ppp) SEQ ID NOs: 836 and 924, respectively;
(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;
(uuu) SEQ ID NOs: 1537 and 929, respectively;
(vvv) SEQ ID NOs: 842 and 930, respectively;
(www) SEQ ID NOs: 843 and 931, respectively;
(xxx) SEQ ID NOs: 844 and 932, respectively;
(yyy) SEQ ID NOs: 845 and 933, respectively;
(zzz) SEQ ID NOs: 846 and 934, respectively;

- (aaaa) SEQ ID NOs: 847 and 935, respectively;
- (bbbb) SEQ ID NOs: 848 and 936, respectively;
- (cccc) SEQ ID NOs: 849 and 937, respectively;
- (dddd) SEQ ID NOs: 850 and 938, respectively;
- (eeee) SEQ ID NOs: 851 and 939, respectively;
- (ffff) SEQ ID NOs: 852 and 940, respectively;
- (gggg) SEQ ID NOs: 853 and 941, respectively;
- (hhhh) SEQ ID NOs: 854 and 942, respectively;
- (iiii) SEQ ID NOs: 855 and 943, respectively; and,
- (jjjj) SEQ ID NOs: 856 and 944, respectively.

Embodiment 47. The RNAi oligonucleotide of any one of embodiments 1 to 46, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 786, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 874.

Embodiment 48. The RNAi oligonucleotide of any one of embodiments 1 to 46, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 787, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 875.

Embodiment 49. The RNAi oligonucleotide of any one of embodiments 1 to 46, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 1537, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 929.

Embodiment 50. The RNAi oligonucleotide of any one of embodiments 1 to 46, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 813, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 901.

Embodiment 51. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein all nucleotides comprising the sense strand and

antisense strand are modified, wherein the antisense strand comprises a region of complementarity to a *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

Embodiment 52. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein all nucleotides comprising the sense strand and antisense strand are modified, wherein the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog, wherein the antisense strand comprises a region of complementarity to a *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

Embodiment 53. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein all nucleotides comprising the sense strand and antisense strand are modified, wherein the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog, wherein the antisense strand comprises a region of complementarity to a *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

Embodiment 54. An RNAi oligonucleotide for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein all nucleotides comprising the sense strand and the antisense strand are modified, wherein the antisense strand and the sense strand comprise one or more 2'-fluoro and 2'-O-methyl modified nucleotides and at least one phosphorothioate linkage, wherein the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog, wherein the antisense strand comprises a region of complementarity to a *NR1H3* mRNA target sequence of any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

Embodiment 55. The RNAi oligonucleotide of any one of embodiments 1-54, wherein the sense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 945-1032.

Embodiment 56. The RNAi oligonucleotide of any one of embodiments 1-55, wherein the antisense strand comprises a nucleotide sequence of any one of SEQ ID NOs: 1033-1120.

Embodiment 57. The RNAi oligonucleotide of any one of embodiments 1-56, wherein the sense and antisense strands comprise nucleotide sequences selected from the group consisting of:

- (a) SEQ ID NOs: 945 and 1033, respectively;
- (b) SEQ ID NOs: 946 and 1034, respectively;
- (c) SEQ ID NOs: 947 and 1035, respectively;
- (d) SEQ ID NOs: 948 and 1036, respectively;
- (e) SEQ ID NOs: 949 and 1037, respectively;
- (f) SEQ ID NOs: 950 and 1038, respectively;
- (g) SEQ ID NOs: 951 and 1039, respectively;
- (h) SEQ ID NOs: 952 and 1040, respectively;
- (i) SEQ ID NOs: 953 and 1041, respectively;
- (j) SEQ ID NOs: 954 and 1042, respectively;
- (k) SEQ ID NOs: 955 and 1043, respectively;
- (l) SEQ ID NOs: 956 and 1044 respectively;
- (m) SEQ ID NOs: 957 and 1045, respectively;
- (n) SEQ ID NOs: 958 and 1046, respectively;
- (o) SEQ ID NOs: 959 and 1047, respectively;
- (p) SEQ ID NOs: 960 and 1048, respectively;
- (q) SEQ ID NOs: 961 and 1049, respectively;
- (r) SEQ ID NOs: 962 and 1050, respectively;
- (s) SEQ ID NOs: 963 and 1051, respectively;
- (t) SEQ ID NOs: 964 and 1052, respectively;
- (u) SEQ ID NOs: 965 and 1053, respectively;
- (v) SEQ ID NOs: 966 and 1054, respectively;

- (w) SEQ ID NOs: 967 and 1055, respectively;
- (x) SEQ ID NOs: 968 and 1056, respectively;
- (y) SEQ ID NOs: 969 and 1057, respectively;
- (z) SEQ ID NOs: 970 and 1058, respectively;
- (aa) SEQ ID NOs: 971 and 1059, respectively;
- (bb) SEQ ID NOs: 972 and 1060, respectively;
- (cc) SEQ ID NOs: 973 and 1061, respectively;
- (dd) SEQ ID NOs: 974 and 1062, respectively;
- (ee) SEQ ID NOs: 975 and 1063, respectively;
- (ff) SEQ ID NOs: 976 and 1064, respectively;
- (gg) SEQ ID NOs: 977 and 1065, respectively;
- (hh) SEQ ID NOs: 978 and 1066, respectively;
- (ii) SEQ ID NOs: 979 and 1067, respectively;
- (jj) SEQ ID NOs: 980 and 1068, respectively;
- (kk) SEQ ID NOs: 981 and 1069, respectively;
- (ll) SEQ ID NOs: 982 and 1070, respectively;
- (mm) SEQ ID NOs: 983 and 1071, respectively;
- (nn) SEQ ID NOs: 984 and 1072, respectively;
- (oo) SEQ ID NOs: 985 and 1073, respectively;
- (pp) SEQ ID NOs: 986 and 1074, respectively;
- (qq) SEQ ID NOs: 987 and 1075, respectively;
- (rr) SEQ ID NOs: 988 and 1076, respectively;
- (ss) SEQ ID NOs: 989 and 1077, respectively;
- (tt) SEQ ID NOs: 990 and 1078, respectively;
- (uu) SEQ ID NOs: 991 and 1079, respectively;
- (vv) SEQ ID NOs: 992 and 1080, respectively;
- (ww) SEQ ID NOs: 993 and 1081, respectively;
- (xx) SEQ ID NOs: 994 and 1082, respectively;
- (yy) SEQ ID NOs: 995 and 1083, respectively;
- (zz) SEQ ID NOs: 996 and 1084, respectively;

- (aaa) SEQ ID NOs: 997 and 1085, respectively;
- (bbb) SEQ ID NOs: 998 and 1086, respectively;
- (ccc) SEQ ID NOs: 999 and 1087, respectively;
- (ddd) SEQ ID NOs: 1000 and 1088, respectively;
- (eee) SEQ ID NOs: 1001 and 1089, respectively;
- (fff) SEQ ID NOs: 1002 and 1090, respectively;
- (ggg) SEQ ID NOs: 1003 and 1091, respectively;
- (hhh) SEQ ID NOs: 1004 and 1092 respectively;
- (iii) SEQ ID NOs: 1005 and 1093 respectively;
- (jjj) SEQ ID NOs: 1006 and 1094, respectively;
- (kkk) SEQ ID NOs: 1007 and 1095, respectively;
- (lll) SEQ ID NOs: 1008 and 1096, respectively;
- (mmm)SEQ ID NOs: 1009 and 1097, respectively;
- (nnn) SEQ ID NOs: 1010 and 1098, respectively;
- (ooo) SEQ ID NOs: 1011 and 1099, respectively;
- (ppp) SEQ ID NOs: 1012 and 1100, respectively;
- (qqq) SEQ ID NOs: 1013 and 1101, respectively;
- (rrr) SEQ ID NOs: 1014 and 1102 respectively;
- (sss) SEQ ID NOs: 1015 and 1103, respectively;
- (ttt) SEQ ID NOs: 1016 and 1104, respectively;
- (uuu) SEQ ID NOs: 1017 and 1105, respectively;
- (vvv) SEQ ID NOs: 1018 and 1106, respectively;
- (www) SEQ ID NOs: 1019 and 1107, respectively;
- (xxx) SEQ ID NOs: 1020 and 1108, respectively;
- (yyy) SEQ ID NOs: 1021 and 1109, respectively;
- (zzz) SEQ ID NOs: 1022 and 1110, respectively;
- (aaaa) SEQ ID NOs: 1023 and 1111, respectively;
- (bbbb) SEQ ID NOs: 1024 and 1112, respectively;
- (cccc) SEQ ID NOs: 1025 and 1113, respectively;
- (dddd) SEQ ID NOs: 1026 and 1114, respectively;

- (eeee) SEQ ID NOs: 1027 and 1115, respectively;
- (ffff) SEQ ID NOs: 1028 and 1116, respectively;
- (gggg) SEQ ID NOs: 1029 and 1117, respectively;
- (hhhh) SEQ ID NOs: 1030 and 1118, respectively;
- (iiii) SEQ ID NOs: 1031 and 1119, respectively; and,
- (jjjj) SEQ ID NOs: 1032 and 1120, respectively.

Embodiment 58. The RNAi oligonucleotide of any one of embodiments 1-57, wherein the sense and antisense strands comprise the nucleotide sequences set forth in SEQ ID NOs: 963 and 1051, respectively.

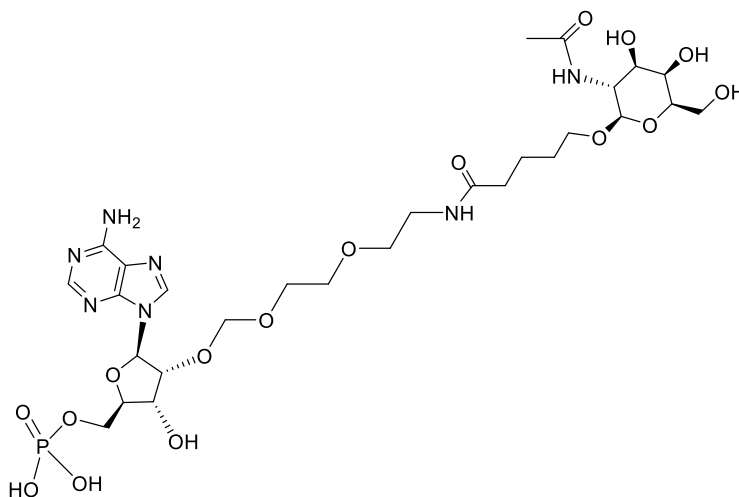
Embodiment 59. The RNAi oligonucleotide of any one of embodiments 1-57, wherein the sense and antisense strands comprise the nucleotide sequences set forth in SEQ ID NOs: 964 and 1052, respectively.

Embodiment 60. The RNAi oligonucleotide of any one of embodiments 1-57, wherein the sense and antisense strands comprise the nucleotide sequences set forth in SEQ ID NOs: 1006 and 1094, respectively.

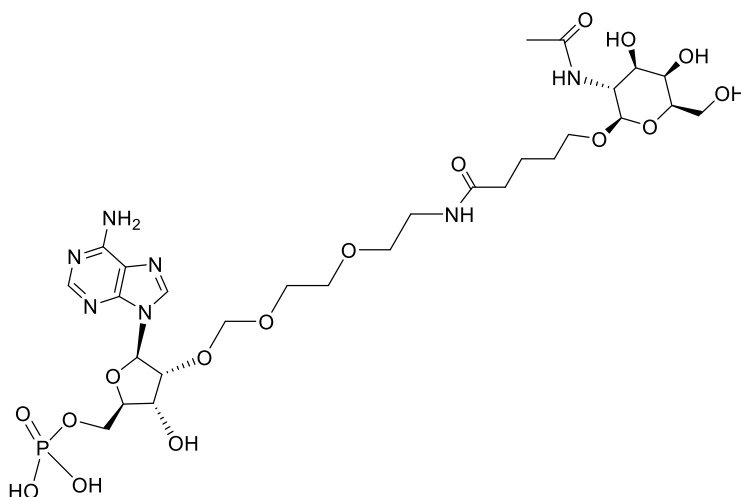
Embodiment 61. The RNAi oligonucleotide of any one of embodiments 1-57, wherein the sense and antisense strands comprise the nucleotide sequences set forth in SEQ ID NOs: 1018 and 1106, respectively.

Embodiment 62. An RNAi oligonucleotide for inhibiting expression of NR1H3, wherein said dsRNA comprises a sense strand and an antisense strand, the antisense strand comprising a region of complementarity to a NR1H3 RNA transcript, wherein the sense strand comprises the sequence and all of the modifications of 5'-mCs-mU-mC-mA-mA-mG-mG-fA-fU-fU-mC-mA-mG-mU-mU-mA-mU-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: 963), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-

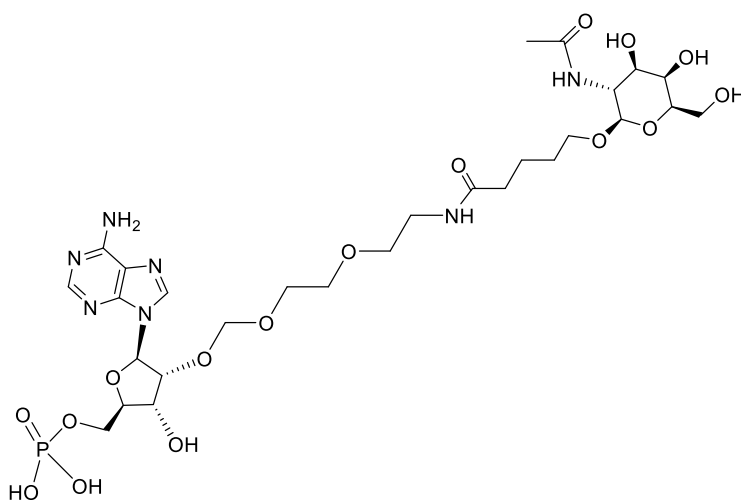
mUs]-fUs-fAs-fU-fA-mA-fC-mU-mG-fA-mA-mA-mU-fC-mC-mU-mU-mG-mA-mGs-mGs-mG-3' (SEQ ID NO: 1051), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU = 2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =



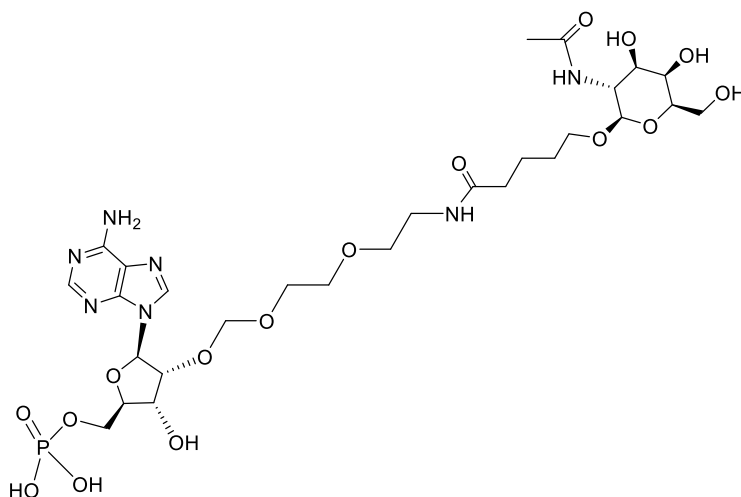
Embodiment 63. An RNAi oligonucleotide for inhibiting expression of NR1H3, wherein said dsRNA comprises a sense strand and an antisense strand, the antisense strand comprising a region of complementarity to a NR1H3 RNA transcript, wherein the sense strand comprises the sequence and all of the modifications of 5'-mUs-mC-mA-mA-mG-mG-mA-fU-fU-fU-fC-mA-mG-mU-mU-mA-mU-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: 964) and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs]-fUs-fUs-fA-fU-mA-fA-mC-mU-fG-mA-mA-mA-fU-mC-mC-mU-mU-mG-mAs-mGs-mG-3' (SEQ ID NO: 1052), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU=2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =



Embodiment 64. An RNAi oligonucleotide for inhibiting expression of NR1H3, wherein said dsRNA comprises a sense strand and an antisense strand, the antisense strand comprising a region of complementarity to a NR1H3 RNA transcript, wherein the sense strand comprises the sequence and all of the modifications of 5'-mAs-mG-mC-mA-mG-mC-mG-fU-fC-fC-fA-mC-mU-mC-mA-mG-mA-mG-mC-mA-mG-mC-mA-mG-mC-mC-mG-[ademA-GalNAc]-[ademA-GalNAc]-[ademA-GalNAc]-mG-mG-mC-mU-mG-mC-3' (SEQ ID NO: 1006), and wherein the antisense strand comprises the sequence and all of the modifications of 5'[MePhosphonate-4O-mUs]-fGs-fCs-fU-fC-mU-fG-mA-mG-fU-mG-mG-mA-fC-mG-mC-mU-mG-mC-mUs-mGs-mG-3' (SEQ ID NO: 1094), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU=2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =



Embodiment 65. A double stranded RNAi oligonucleotide (dsRNAi) for inhibiting expression of NR1H3, wherein said dsRNA comprises a sense strand and an antisense strand, the antisense strand comprising a region of complementarity to a NR1H3 RNA transcript, wherein the sense strand comprises the sequence and all of the modifications of 5'-mAs-mU-mG-mU-mG-mC-mA-fC-fG-fA-fA-mU-mG-mA-mC-mU-mG-mU-mU-mA-mG-mC-mA-mG-mC-mC-mG-[ademA-GalNAc]-[ademA-GalNAc]-[ademA-GalNAc]-mG-mG-mC-mU-mG-mC-3' (SEQ ID NO: 1018), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs]-fAs-fAs-fC-fA-mG-fU-mC-mA-fU-mU-mC-mG-fU-mG-mC-mA-mC-mA-mUs-mGs-mG-3' (SEQ ID NO: 1106), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU=2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =



Embodiment 66. A method for treating a subject having a disease, disorder or condition associated with NR1H3 expression, the method comprising administering to the subject a therapeutically effective amount of the RNAi oligonucleotide of any one of the preceding embodiments, or pharmaceutical composition thereof, thereby treating the subject.

Embodiment 67. A pharmaceutical composition comprising the RNAi oligonucleotide of any one of embodiments 1 to 65, and a pharmaceutically acceptable carrier, delivery agent or excipient.

Embodiment 68. A method of delivering an oligonucleotide to a subject, the method comprising administering pharmaceutical composition of embodiment 67 to the subject.

Embodiment 69. A method for reducing *NR1H3* 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 embodiments 1 to 65, or the pharmaceutical composition of embodiment 67; or
- ii. administering to the subject the RNAi oligonucleotide of any one of embodiments 1 to 65, or the pharmaceutical composition of embodiment 67.

Embodiment 70. The method of embodiment 69, wherein reducing *NR1H3* expression comprises reducing an amount or level of *NR1H3* mRNA, an amount or level of NR1H3 protein, or both.

Embodiment 71. The method of embodiment 69 or 70, wherein the subject has a disease, disorder or condition associated with *NR1H3* expression.

Embodiment 72. The method of embodiment 66 or 71, wherein the disease, disorder or condition associated with *NR1H3* expression is non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), multiple sclerosis, or systemic lupus erythematosus.

Embodiment 73. The method of any one of embodiments 66 and 69 to 72, wherein the RNAi oligonucleotide, or pharmaceutical composition, is administered in combination with a second composition or therapeutic agent.

Embodiment 74. A method for treating a subject having a disease, disorder or condition associated with *NR1H3* expression, the method comprising administering to the subject a therapeutically effective amount of an RNAi 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 *NR1H3* mRNA target sequence of

any one of SEQ ID NOs: 1-384, and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

Embodiment 75. A method for treating a subject having a disease, disorder or condition associated with *NR1H3* expression, the method comprising administering to the subject a therapeutically effective amount of an RNAi oligonucleotide comprising a sense strand and an antisense strand selected from a row set forth in **Table 4 or Table 5**, or pharmaceutical composition thereof, thereby treating the subject.

Embodiment 76. A method for treating a subject having a disease, disorder or condition associated with *NR1H3* expression, the method comprising administering to the subject a therapeutically effective amount of an RNAi oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

- (a) SEQ ID NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;

- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;
- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;

(uu) SEQ ID NOs: 815 and 903, respectively;
(vv) SEQ ID NOs: 816 and 904, respectively;
(ww) SEQ ID NOs: 817 and 905, respectively;
(xx) SEQ ID NOs: 818 and 906, respectively;
(yy) SEQ ID NOs: 819 and 907, respectively;
(zz) SEQ ID NOs: 820 and 908, respectively;
(aaa) SEQ ID NOs: 821 and 909, respectively;
(bbb) SEQ ID NOs: 822 and 910, respectively;
(ccc) SEQ ID NOs: 823 and 911, respectively;
(ddd) SEQ ID NOs: 824 and 912, respectively;
(eee) SEQ ID NOs: 825 and 913, respectively;
(fff) SEQ ID NOs: 826 and 914, respectively;
(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm)SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;
(ooo) SEQ ID NOs: 835 and 923, respectively;
(ppp) SEQ ID NOs: 836 and 924, respectively;
(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;
(uuu) SEQ ID NOs: 1537 and 929, respectively;
(vvv) SEQ ID NOs: 842 and 930, respectively;
(www) SEQ ID NOs: 843 and 931, respectively;
(xxx) SEQ ID NOs: 844 and 932, respectively;

- (yyy) SEQ ID NOs: 845 and 933, respectively;
- (zzz) SEQ ID NOs: 846 and 934, respectively;
- (aaaa) SEQ ID NOs: 847 and 935, respectively;
- (bbbb) SEQ ID NOs: 848 and 936, respectively;
- (cccc) SEQ ID NOs: 849 and 937, respectively;
- (dddd) SEQ ID NOs: 850 and 938, respectively;
- (eeee) SEQ ID NOs: 851 and 939, respectively;
- (ffff) SEQ ID NOs: 852 and 940, respectively;
- (gggg) SEQ ID NOs: 853 and 941, respectively;
- (hhhh) SEQ ID NOs: 854 and 942, respectively;
- (iii) SEQ ID NOs: 855 and 943, respectively; and,
- (jjjj) SEQ ID NOs: 856 and 944, respectively.

Embodiment 77. The method of embodiment 76, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 786, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 874.

Embodiment 78. The method of embodiment 76, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 787, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 875.

Embodiment 79. The method of embodiment 76, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 1537, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 929.

Embodiment 80. The method of embodiment 76, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 813, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 901.

Embodiment 81. A method for treating a subject having a disease, disorder or condition associated with *NR1H3* expression, the method comprising administering to the subject a therapeutically effective amount of an RNAi oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

- (a) SEQ ID NOs: 945 and 1033, respectively;
- (b) SEQ ID NOs: 946 and 1034, respectively;
- (c) SEQ ID NOs: 947 and 1035, respectively;
- (d) SEQ ID NOs: 948 and 1036, respectively;
- (e) SEQ ID NOs: 949 and 1037, respectively;
- (f) SEQ ID NOs: 950 and 1038, respectively;
- (g) SEQ ID NOs: 951 and 1039, respectively;
- (h) SEQ ID NOs: 952 and 1040, respectively;
- (i) SEQ ID NOs: 953 and 1041, respectively;
- (j) SEQ ID NOs: 954 and 1042, respectively;
- (k) SEQ ID NOs: 955 and 1043, respectively;
- (l) SEQ ID NOs: 956 and 1044 respectively;
- (m) SEQ ID NOs: 957 and 1045, respectively;
- (n) SEQ ID NOs: 958 and 1046, respectively;
- (o) SEQ ID NOs: 959 and 1047, respectively;
- (p) SEQ ID NOs: 960 and 1048, respectively;
- (q) SEQ ID NOs: 961 and 1049, respectively;
- (r) SEQ ID NOs: 962 and 1050, respectively;
- (s) SEQ ID NOs: 963 and 1051, respectively;
- (t) SEQ ID NOs: 964 and 1052, respectively;
- (u) SEQ ID NOs: 965 and 1053, respectively;
- (v) SEQ ID NOs: 966 and 1054, respectively;
- (w) SEQ ID NOs: 967 and 1055, respectively;
- (x) SEQ ID NOs: 968 and 1056, respectively;
- (y) SEQ ID NOs: 969 and 1057, respectively;

- (z) SEQ ID NOs: 970 and 1058, respectively;
- (aa) SEQ ID NOs: 971 and 1059, respectively;
- (bb) SEQ ID NOs: 972 and 1060, respectively;
- (cc) SEQ ID NOs: 973 and 1061, respectively;
- (dd) SEQ ID NOs: 974 and 1062, respectively;
- (ee) SEQ ID NOs: 975 and 1063, respectively;
- (ff) SEQ ID NOs: 976 and 1064, respectively;
- (gg) SEQ ID NOs: 977 and 1065, respectively;
- (hh) SEQ ID NOs: 978 and 1066, respectively;
- (ii) SEQ ID NOs: 979 and 1067, respectively;
- (jj) SEQ ID NOs: 980 and 1068, respectively;
- (kk) SEQ ID NOs: 981 and 1069, respectively;
- (ll) SEQ ID NOs: 982 and 1070, respectively;
- (mm) SEQ ID NOs: 983 and 1071, respectively;
- (nn) SEQ ID NOs: 984 and 1072, respectively;
- (oo) SEQ ID NOs: 985 and 1073, respectively;
- (pp) SEQ ID NOs: 986 and 1074, respectively;
- (qq) SEQ ID NOs: 987 and 1075, respectively;
- (rr) SEQ ID NOs: 988 and 1076, respectively;
- (ss) SEQ ID NOs: 989 and 1077, respectively;
- (tt) SEQ ID NOs: 990 and 1078, respectively;
- (uu) SEQ ID NOs: 991 and 1079, respectively;
- (vv) SEQ ID NOs: 992 and 1080, respectively;
- (ww) SEQ ID NOs: 993 and 1081, respectively;
- (xx) SEQ ID NOs: 994 and 1082, respectively;
- (yy) SEQ ID NOs: 995 and 1083, respectively;
- (zz) SEQ ID NOs: 996 and 1084, respectively;
- (aaa) SEQ ID NOs: 997 and 1085, respectively;
- (bbb) SEQ ID NOs: 998 and 1086, respectively;
- (ccc) SEQ ID NOs: 999 and 1087, respectively;

(ddd) SEQ ID NOs: 1000 and 1088, respectively;
(eee) SEQ ID NOs: 1001 and 1089, respectively;
(fff) SEQ ID NOs: 1002 and 1090, respectively;
(ggg) SEQ ID NOs: 1003 and 1091, respectively;
(hhh) SEQ ID NOs: 1004 and 1092 respectively;
(iii) SEQ ID NOs: 1005 and 1093 respectively;
(jjj) SEQ ID NOs: 1006 and 1094, respectively;
(kkk) SEQ ID NOs: 1007 and 1095, respectively;
(lll) SEQ ID NOs: 1008 and 1096, respectively;
(mmm)SEQ ID NOs: 1009 and 1097, respectively;
(nnn) SEQ ID NOs: 1010 and 1098, respectively;
(ooo) SEQ ID NOs: 1011 and 1099, respectively;
(ppp) SEQ ID NOs: 1012 and 1100, respectively;
(qqq) SEQ ID NOs: 1013 and 1101, respectively;
(rrr) SEQ ID NOs: 1014 and 1102 respectively;
(sss) SEQ ID NOs: 1015 and 1103, respectively;
(ttt) SEQ ID NOs: 1016 and 1104, respectively;
(uuu) SEQ ID NOs: 1017 and 1105, respectively;
(vvv) SEQ ID NOs: 1018 and 1106, respectively;
(www) SEQ ID NOs: 1019 and 1107, respectively;
(xxx) SEQ ID NOs: 1020 and 1108, respectively;
(yyy) SEQ ID NOs: 1021 and 1109, respectively;
(zzz) SEQ ID NOs: 1022 and 1110, respectively;
(aaaa) SEQ ID NOs: 1023 and 1111, respectively;
(bbbb) SEQ ID NOs: 1024 and 1112, respectively;
(cccc) SEQ ID NOs: 1025 and 1113, respectively;
(dddd) SEQ ID NOs: 1026 and 1114, respectively;
(eeee) SEQ ID NOs: 1027 and 1115, respectively;
(ffff) SEQ ID NOs: 1028 and 1116, respectively;
(gggg) SEQ ID NOs: 1029 and 1117, respectively;

- (hhhh) SEQ ID NOs: 1030 and 1118, respectively;
- (iiii) SEQ ID NOs: 1031 and 1119, respectively, and;
- (jjjj) SEQ ID NOs: 1032 and 1120, respectively.

Embodiment 82. The method of embodiment 81, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 963, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 1051.

Embodiment 83. The method of embodiment 81, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 964, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 1052.

Embodiment 84. The method of embodiment 81, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 1006, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 1094.

Embodiment 85. The method of embodiment 81, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 1018, wherein the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 1106.

Embodiment 86. The method of any one of embodiments 74 to 85, wherein the disease, disorder or condition associated with *NR1H3* expression is non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), multiple sclerosis, or systemic lupus erythematosus.

Embodiment 87. Use of the RNAi oligonucleotide of any one of embodiments 1 to 65, or the pharmaceutical composition of embodiment 67, in the manufacture of a medicament for the treatment of a disease, disorder or condition associated with *NR1H3* expression, optionally for the treatment of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), multiple sclerosis, or systemic lupus erythematosus.

Embodiment 88. The RNAi oligonucleotide of any one of embodiments 1 to 65, or the pharmaceutical composition of embodiment 67, for use, or adaptable for use, in the treatment of a disease, disorder or condition associated with *NR1H3* expression, optionally for the treatment of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), multiple sclerosis, or systemic lupus erythematosus.

Embodiment 89. A kit comprising the RNAi oligonucleotide of any one of embodiments 1 to 65, an optional pharmaceutically acceptable carrier, and a package insert comprising instructions for administration to a subject having a disease, disorder or condition associated with *NR1H3* expression.

Embodiment 90. The use of embodiment 87, the RNAi oligonucleotide or pharmaceutical composition for use, or adaptable for use, of embodiment 88, or the kit of embodiment 89, wherein the disease, disorder or condition associated with *NR1H3* expression is non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), multiple sclerosis, or systemic lupus erythematosus.

Embodiment 91. A double stranded RNAi oligonucleotide (dsRNAi) for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein

(i) the sense strand comprises a nucleotide sequence comprising at least 15, 17, or 19 contiguous nucleotides, with 0, 1, 2, or 3 mismatches, of a portion of a nucleotide sequence of any one of SEQ ID NOs: 1-384, SEQ ID NOs: 1125-1511, SEQ ID NOs: 769-856, SEQ ID NOs: 1519-1552 or SEQ ID NOs: 945-1032; and

(ii) the antisense strand comprises a nucleotide sequence comprising at least 15, 17, or 19 contiguous nucleotides, with 0, 1, 2, or 3 mismatches, of a portion of a nucleotide sequence of any one of SEQ ID NOs: 385-768, SEQ ID NOs 857-944, SEQ ID NOs 1512-1515, or SEQ ID NOs: 1033-1120.

Embodiment 92. The RNA oligonucleotide of embodiment 91, wherein the sense strand and antisense strands comprise nucleotide sequences selected from the group consisting of:

- (a) SEQ ID NOs: 769 and 857, respectively;
- (b) SEQ ID NOs: 770 and 858, respectively;
- (c) SEQ ID NOs: 771 and 859, respectively;
- (d) SEQ ID NOs: 772 and 860, respectively;
- (e) SEQ ID NOs: 773 and 861, respectively;
- (f) SEQ ID NOs: 774 and 862, respectively;
- (g) SEQ ID NOs: 775 and 863, respectively;
- (h) SEQ ID NOs: 776 and 864, respectively;
- (i) SEQ ID NOs: 777 and 865, respectively;
- (j) SEQ ID NOs: 778 and 866, respectively;
- (k) SEQ ID NOs: 779 and 867, respectively;
- (l) SEQ ID NOs: 780 and 868, respectively;
- (m) SEQ ID NOs: 781 and 869, respectively;
- (n) SEQ ID NOs: 782 and 870, respectively;
- (o) SEQ ID NOs: 783 and 871, respectively;
- (p) SEQ ID NOs: 784 and 872, respectively;
- (q) SEQ ID NOs: 785 and 873, respectively;
- (r) SEQ ID NOs: 786 and 874, respectively;
- (s) SEQ ID NOs: 787 and 875, respectively;
- (t) SEQ ID NOs: 788 and 876, respectively;
- (u) SEQ ID NOs: 789 and 877, respectively;
- (v) SEQ ID NOs: 790 and 878, respectively;
- (w) SEQ ID NOs: 791 and 879, respectively;
- (x) SEQ ID NOs: 792 and 880, respectively;
- (y) SEQ ID NOs: 793 and 881, respectively;
- (z) SEQ ID NOs: 794 and 882, respectively;
- (aa) SEQ ID NOs: 795 and 883, respectively;
- (bb) SEQ ID NOs: 796 and 884, respectively;

- (cc) SEQ ID NOs: 797 and 885, respectively;
- (dd) SEQ ID NOs: 798 and 886, respectively;
- (ee) SEQ ID NOs: 799 and 887, respectively;
- (ff) SEQ ID NOs: 800 and 888, respectively;
- (gg) SEQ ID NOs: 801 and 889, respectively;
- (hh) SEQ ID NOs: 802 and 890, respectively;
- (ii) SEQ ID NOs: 803 and 891, respectively;
- (jj) SEQ ID NOs: 804 and 892, respectively;
- (kk) SEQ ID NOs: 805 and 893, respectively;
- (ll) SEQ ID NOs: 806 and 894, respectively;
- (mm) SEQ ID NOs: 807 and 895, respectively;
- (nn) SEQ ID NOs: 808 and 896, respectively;
- (oo) SEQ ID NOs: 809 and 897, respectively;
- (pp) SEQ ID NOs: 810 and 898, respectively;
- (qq) SEQ ID NOs: 811 and 899, respectively;
- (rr) SEQ ID NOs: 812 and 900, respectively;
- (ss) SEQ ID NOs: 813 and 901, respectively;
- (tt) SEQ ID NOs: 814 and 902, respectively;
- (uu) SEQ ID NOs: 815 and 903, respectively;
- (vv) SEQ ID NOs: 816 and 904, respectively;
- (ww) SEQ ID NOs: 817 and 905, respectively;
- (xx) SEQ ID NOs: 818 and 906, respectively;
- (yy) SEQ ID NOs: 819 and 907, respectively;
- (zz) SEQ ID NOs: 820 and 908, respectively;
- (aaa) SEQ ID NOs: 821 and 909, respectively;
- (bbb) SEQ ID NOs: 822 and 910, respectively;
- (ccc) SEQ ID NOs: 823 and 911, respectively;
- (ddd) SEQ ID NOs: 824 and 912, respectively;
- (eee) SEQ ID NOs: 825 and 913, respectively;
- (fff) SEQ ID NOs: 826 and 914, respectively;

(ggg) SEQ ID NOs: 827 and 915, respectively;
(hhh) SEQ ID NOs: 828 and 916, respectively;
(iii) SEQ ID NOs: 829 and 917, respectively;
(jjj) SEQ ID NOs: 830 and 918, respectively;
(kkk) SEQ ID NOs: 831 and 919, respectively;
(lll) SEQ ID NOs: 832 and 920, respectively;
(mmm)SEQ ID NOs: 833 and 921, respectively;
(nnn) SEQ ID NOs: 834 and 922, respectively;
(ooo) SEQ ID NOs: 835 and 923, respectively;
(ppp) SEQ ID NOs: 836 and 924, respectively;
(qqq) SEQ ID NOs: 837 and 925, respectively;
(rrr) SEQ ID NOs: 838 and 926, respectively;
(sss) SEQ ID NOs: 839 and 927, respectively;
(ttt) SEQ ID NOs: 840 and 928, respectively;
(uuu) SEQ ID NOs: 1537 and 929, respectively;
(vvv) SEQ ID NOs: 842 and 930, respectively;
(www) SEQ ID NOs: 843 and 931, respectively;
(xxx) SEQ ID NOs: 844 and 932, respectively;
(yyy) SEQ ID NOs: 845 and 933, respectively;
(zzz) SEQ ID NOs: 846 and 934, respectively;
(aaaa) SEQ ID NOs: 847 and 935, respectively;
(bbbb) SEQ ID NOs: 848 and 936, respectively;
(cccc) SEQ ID NOs: 849 and 937, respectively;
(dddd) SEQ ID NOs: 850 and 938, respectively;
(eeee) SEQ ID NOs: 851 and 939, respectively;
(ffff) SEQ ID NOs: 852 and 940, respectively;
(gggg) SEQ ID NOs: 853 and 941, respectively;
(hhhh) SEQ ID NOs: 854 and 942, respectively;
(iiii) SEQ ID NOs: 855 and 943, respectively; and,
(jjjj) SEQ ID NOs: 856 and 944, respectively.

Embodiment 93. An RNAi oligonucleotide for reducing growth (NR1H3) 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 NR1H3 mRNA target sequence of any one of SEQ ID NOs: 1125-1511 and wherein the region of complementarity is at least 15 contiguous nucleotides in length.

Embodiment 94. The RNAi oligonucleotide of any one of embodiments 91 to 93, wherein the 3' end of the sense strand comprises a stem-loop set forth as S1-L-S2, wherein

(i) S1 is complementary to S2, optionally wherein S1 and S2 are each 1-10 nucleotides in length and have the same length, optionally wherein S1 and S2 are each 1, 2, 3, 4, 5, 6, 7, 8, 9, or, 10 nucleotides in length, further optionally wherein S1 and S2 are 6 nucleotides in length; and

(ii) L forms a loop between S1 and S2 of 3-5 nucleotides in length, optionally wherein L is a triloop or a tetraloop, optionally wherein the tetraloop comprises the sequence 5'-GAAA-3', optionally wherein the stem-loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 1121).

Embodiment 95. The RNAi oligonucleotide of any one of embodiments 91 to 94, wherein at least one nucleotide of the oligonucleotide is conjugated to one or more targeting ligands, optionally wherein:

(a) each targeting ligand comprises a carbohydrate, amino sugar, cholesterol, polypeptide or lipid;

(b) the stem loop comprises one or more targeting ligands conjugated to one or more nucleotides of the stem loop;

(c) the one or more targeting ligands is conjugated to one or more nucleotides of the loop, optionally 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, wherein the targeting ligands are the same or different;

(d) the targeting ligand is a hepatocyte targeting ligand and each targeting ligand comprises a N-acetylgalactosamine (GalNAc) moiety, optionally wherein the GalNAc moiety is a

monovalent GalNAc moiety, a bivalent GalNAc moiety, a trivalent GalNAc moiety or a tetravalent GalNAc moiety; and/or

(e) the targeting ligand is a hepatocyte targeting ligand and up to 4 nucleotides of L of the stem-loop are each conjugated to a monovalent GalNAc moiety.

Embodiment 96. The RNAi oligonucleotide of any one of embodiments 91 to 95, wherein:

(i) the oligonucleotide comprises at least one modified nucleotide, optionally wherein the modified nucleotide comprises a 2'-modification, optionally wherein

(a) 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, optionally wherein the modification is selected from 2'-fluoro and 2'-O-methyl, optionally wherein all nucleotides of the oligonucleotide are modified, wherein the modification is 2'-fluoro and 2'-O-methyl;

(b) about 10-15%, 10%, 11%, 12%, 13%, 14%, or 15% of the nucleotides of the sense strand comprise a 2'-fluoro modification;

(c) 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;

(d) 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;

(e) the sense strand comprises 36 nucleotides with positions 1-36 from 5' to 3', wherein positions 8-11 comprise a 2'-fluoro modification;

(f) the antisense strand comprises 22 nucleotides with positions 1-22 from 5' to 3', and wherein positions 2, 3, 4, 5, 7, 10, and 14 comprise a 2'-fluoro modification; and/or

(g) the remaining nucleotides comprise a 2'-O-methyl modification, and/or

(ii) the oligonucleotide comprises at least one modified internucleotide linkage, optionally wherein the at least one modified internucleotide linkage is a phosphorothioate linkage, optionally wherein:

(a) 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'; and/or

(b) 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', and/or

(iii) the antisense strand comprises a phosphorylated nucleotide at the 5' terminus, wherein the phosphorylated nucleotide is selected from uridine and adenosine, optionally wherein the phosphorylated nucleotide is uridine, and/or

(iv) the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog, optionally wherein the phosphate analog is oxymethylphosphonate, vinylphosphonate or malonylphosphonate, optionally wherein the phosphate analog is a 4'-phosphate analog comprising 5'-methoxyphosphonate-4'-oxy, and/or

(v) the antisense strand comprises an overhang sequence of one or more nucleotides in length at the 3' terminus, optionally wherein the overhang comprises purine nucleotides, optionally wherein the overhang sequence is 2 nucleotides in length, optionally wherein the overhang is selected from AA, GG, AG, and GA, optionally wherein the overhang is GG.

Embodiment 97. The RNAi oligonucleotide of any one of embodiments 91 to 94, wherein at least one nucleotide of the oligonucleotide is conjugated to one or more hepatocyte targeting ligands.

Embodiment 98. The RNAi oligonucleotide of embodiment 97, wherein each hepatocyte targeting ligand comprises a N-acetylgalactosamine (GalNAc) moiety, optionally wherein the GalNAc moiety is a monovalent GalNAc moiety, a bivalent GalNAc moiety, a trivalent GalNAc moiety or a tetravalent GalNAc moiety.

Embodiment 99. A pharmaceutical composition comprising the RNAi oligonucleotide of any one of embodiments 91 to 98, and a pharmaceutically acceptable carrier, delivery agent or excipient.

Embodiment 100. A RNAi oligonucleotide of any one of embodiments 91-98, or the pharmaceutical composition of embodiment 99, for use in the treatment non-alcoholic fatty liver

disease (NAFLD), non-alcoholic steatohepatitis (NASH), multiple sclerosis, or systemic lupus erythematosus.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety.

Name	Species	Description	Sequence	SEQ ID NO
NR1H3-764-784-861	Artificial Sequence	25 mer sense strand	UGUCCUGUCAGAAGAACAGAUCCGC	1
NR1H3-766-786-863	Artificial Sequence	25 mer sense strand	UCCUGUCAGAAGAACAGAUACGC	2
NR1H3-789-809-886	Artificial Sequence	25 mer sense strand	CUGAAGAAACUGAAGCGGCAAGAGG	3
NR1H3-790-810-887	Artificial Sequence	25 mer sense strand	UGAAGAAACUGAAGCGGCAAGAGGA	4
NR1H3-791-811-888	Artificial Sequence	25 mer sense strand	GAAGAAACUGAAGCGGCAAAAGGAG	5
NR1H3-792-812-889	Artificial Sequence	25 mer sense strand	AAGAAACUGAAGCGGCAAGAGGAGG	6
NR1H3-793-813-890	Artificial Sequence	25 mer sense strand	AGAAACUGAAGCGGCAAGAAGAGGA	7
NR1H3-795-815-892	Artificial Sequence	25 mer sense strand	AAACUGAAGCGGCAAGAGGAGGAGG	8
NR1H3-796-816-893	Artificial Sequence	25 mer sense strand	AACUGAAGCGGCAAGAGGAAGAGGA	9
NR1H3-797-817-894	Artificial Sequence	25 mer sense strand	ACUGAAGCGGCAAGAGGAGAGAAA	10
NR1H3-798-818-895	Artificial Sequence	25 mer sense strand	CUGAAGCGGCAAGAGGAGGAACAGG	11
NR1H3-799-819-896	Artificial Sequence	25 mer sense strand	UGAAGCGGCAAGAGGAGGAACAAGG	12
NR1H3-802-822-899	Artificial Sequence	25 mer sense strand	AGCGGCAAGAGGAGGAACAAGC	13
NR1H3-803-823-900	Artificial Sequence	25 mer sense strand	GCGGCAAGAGGAGGAACAGACUC	14
NR1H3-804-824-901	Artificial Sequence	25 mer sense strand	CGGCAAGAGGAGGAACAGGAUC	15
NR1H3-806-826-903	Artificial Sequence	25 mer sense strand	GCAAGAGGAGGAACAGGCUAAU	16

NR1H3-808-828-905	Artificial Sequence	25 mer sense strand	AAGAGGAGGAACAGGCUCAAGCCAC	17
NR1H3-809-829-906	Artificial Sequence	25 mer sense strand	AGAGGAGGAACAGGCUCAUACCA	18
NR1H3-810-830-907	Artificial Sequence	25 mer sense strand	GAGGAGGAACAGGCUCAUGACAC	19
NR1H3-811-831-908	Artificial Sequence	25 mer sense strand	AGGAGGAACAGGCUCAUGCAACA	20
NR1H3-813-833-910	Artificial Sequence	25 mer sense strand	GAGGAACAGGCUCAUGCCAAAUC	21
NR1H3-844	Artificial Sequence	25 mer sense strand	CCAGGGCUUCCUCACCCCCACAA	22
NR1H3-895-915-992	Artificial Sequence	25 mer sense strand	UGGGCAUGAUCGAGAAGCUAGU	23
NR1H3-898-918-995	Artificial Sequence	25 mer sense strand	GCAUGAUCGAGAAGCUCGUAGCU	24
NR1H3-915-935	Artificial Sequence	25 mer sense strand	GUCGCUGCCCAGCAACAGUAUAA	25
NR1H3-917-937	Artificial Sequence	25 mer sense strand	CGCUGCCCAGCAACAGUGUAACC	26
NR1H3-922-942	Artificial Sequence	25 mer sense strand	CCCAGCAACAGUGUAACCGACGC	27
NR1H3-924-944	Artificial Sequence	25 mer sense strand	CAGCAACAGUGUAACCGGCACUC	28
NR1H3-925-945	Artificial Sequence	25 mer sense strand	AGCAACAGUGUAACCGGCGAUCC	29
NR1H3-927-947	Artificial Sequence	25 mer sense strand	CAACAGUGUAACCGGCGCUACUU	30
NR1H3-928-948	Artificial Sequence	25 mer sense strand	AACAGUGUAACCGGCGCUCAUUU	31
NR1H3-929-949	Artificial Sequence	25 mer sense strand	ACAGUGUAACCGGCGCUCCAUUU	32
NR1H3-930-950	Artificial Sequence	25 mer sense strand	CAGUGUAACCGGCGCUCCUAUUC	33
NR1H3-931-951	Artificial Sequence	25 mer sense strand	AGUGUAACCGGCGCUCCUUAUCU	34
NR1H3-932-952	Artificial Sequence	25 mer sense strand	GUGUAACCGGCGCUCCUUUACUG	35
NR1H3-933-953	Artificial Sequence	25 mer sense strand	UGUAACCGGCGCUCCUUUUAUGA	36
NR1H3-941-961	Artificial Sequence	25 mer sense strand	GCGCUCCUUUUCUGACCGGAUUC	37

NR1H3-944-964	Artificial Sequence	25 mer sense strand	CUCCUUUUCUGACCGGCUUAGAGUC	38
NR1H3-945-965	Artificial Sequence	25 mer sense strand	UCCUUUUCUGACCGGCUUCAAGUCA	39
NR1H3-946-966	Artificial Sequence	25 mer sense strand	CCUUUUCUGACCGGCUUCGAGUCAC	40
NR1H3-947-967	Artificial Sequence	25 mer sense strand	CUUUUUCUGACCGGCUUCGAAUCA	41
NR1H3-949-969	Artificial Sequence	25 mer sense strand	UUUCUGACCGGCUUCGAGUAACGCC	42
NR1H3-951-971	Artificial Sequence	25 mer sense strand	UCUGACCGGCUUCGAGUCAAGCCUU	43
NR1H3-952-972	Artificial Sequence	25 mer sense strand	CUGACCGGCUUCGAGUCACACCUUG	44
NR1H3-953-973	Artificial Sequence	25 mer sense strand	UGACCGGCUUCGAGUCACGACUUGG	45
NR1H3-1151-1171	Artificial Sequence	25 mer sense strand	GGUGAUGCUUCUGGAGACAACUCGG	46
NR1H3-1153-1173	Artificial Sequence	25 mer sense strand	UGAUGCUUCUGGAGACAUCACGGAG	47
NR1H3-1154-1174	Artificial Sequence	25 mer sense strand	GAUGCUUCUGGAGACAUCUAGGAGG	48
NR1H3-1155-1175	Artificial Sequence	25 mer sense strand	AUGCUUCUGGAGACAUCUCAGAGGU	49
NR1H3-1156-1176	Artificial Sequence	25 mer sense strand	UGCUUCUGGAGACAUCUCGAAGGUA	50
NR1H3-1157-1177	Artificial Sequence	25 mer sense strand	GCUUCUGGAGACAUCUCGGAGGUAC	51
NR1H3-1158-1178	Artificial Sequence	25 mer sense strand	CUUCUGGAGACAUCUCGGAAGUACA	52
NR1H3-1159-1179	Artificial Sequence	25 mer sense strand	UUCUGGAGACAUCUCGGAGAUACAA	53
NR1H3-1160-1180	Artificial Sequence	25 mer sense strand	UCUGGAGACAUCUCGGAGGAACAAC	54
NR1H3-1161-1181	Artificial Sequence	25 mer sense strand	CUGGAGACAUCUCGGAGGUACAAAC	55
NR1H3-1162-1182	Artificial Sequence	25 mer sense strand	UGGAGACAUCUCGGAGGUAAAAAC	56
NR1H3-1163-1183	Artificial Sequence	25 mer sense strand	GGAGACAUCUCGGAGGUACAACCCU	57
NR1H3-1164-1184	Artificial Sequence	25 mer sense strand	GAGACAUCUCGGAGGUACAACCCUG	58

NR1H3-1165-1185	Artificial Sequence	25 mer sense strand	AGACAUCUCGGAGGUACAAACCU GG	59
NR1H3-1166-1186	Artificial Sequence	25 mer sense strand	GACAUCUCGGAGGUACAACACUG GG	60
NR1H3-1167-1187	Artificial Sequence	25 mer sense strand	ACAUCUCGGAGGUACAACCAUGG GA	61
NR1H3-1169-1189	Artificial Sequence	25 mer sense strand	AUCUCGGAGGUACAACCCUAGGA GU	62
NR1H3-1170-1190	Artificial Sequence	25 mer sense strand	UCUCGGAGGUACAACCCUGAGAG UG	63
NR1H3-1171-1191	Artificial Sequence	25 mer sense strand	CUCGGAGGUACAACCCUGGAAGU GA	64
NR1H3-1173-1193	Artificial Sequence	25 mer sense strand	CGGAGGUACAACCCUGGGAAUGA GA	65
NR1H3-1175-1195	Artificial Sequence	25 mer sense strand	GAGGUACAACCCUGGGAGUAAG AGU	66
NR1H3-1176-1196	Artificial Sequence	25 mer sense strand	AGGUACAACCCUGGGAGUGAGA GUA	67
NR1H3-1177-1197	Artificial Sequence	25 mer sense strand	GGUACAACCCUGGGAGUGAAAG UAU	68
NR1H3-1178-1198	Artificial Sequence	25 mer sense strand	GUACAACCCUGGGAGUGAGAGU AUC	69
NR1H3-1179-1199	Artificial Sequence	25 mer sense strand	UACAACCCUGGGAGUGAGAAUA UCA	70
NR1H3-1180-1200	Artificial Sequence	25 mer sense strand	ACAACCCUGGGAGUGAGAGAAUC AC	71
NR1H3-1181-1201	Artificial Sequence	25 mer sense strand	CAACCCUGGGAGUGAGAGUAUCA CC	72
NR1H3-1182-1202	Artificial Sequence	25 mer sense strand	AACCCUGGGAGUGAGAGUAACAC CU	73
NR1H3-1183-1203	Artificial Sequence	25 mer sense strand	ACCCUGGGAGUGAGAGUAUAACC UU	74
NR1H3-1184-1204	Artificial Sequence	25 mer sense strand	CCCUGGGAGUGAGAGUAUCACCU UC	75
NR1H3-1185-1205	Artificial Sequence	25 mer sense strand	CCUGGGAGUGAGAGUAUCAACU UCC	76
NR1H3-1186-1206	Artificial Sequence	25 mer sense strand	CUGGGAGUGAGAGUAUCACAUU CCU	77
NR1H3-1187-1207	Artificial Sequence	25 mer sense strand	UGGGAGUGAGAGUAUCACCAUCC UC	78
NR1H3-1188-1208	Artificial Sequence	25 mer sense strand	GGGAGUGAGAGUAUCACCUACCU CA	79

NR1H3-1190-1210	Artificial Sequence	25 mer sense strand	GAGUGAGAGUAUCACCUUCAUCAAG	80
NR1H3-1191-1211	Artificial Sequence	25 mer sense strand	AGUGAGAGUAUCACCUUCCACAA GG	81
NR1H3-1192-1212	Artificial Sequence	25 mer sense strand	GUGAGAGUAUCACCUUCCUAAAG GA	82
NR1H3-1193-1213	Artificial Sequence	25 mer sense strand	UGAGAGUAUCACCUUCCUCAAGG AU	83
NR1H3-1194-1214	Artificial Sequence	25 mer sense strand	GAGAGUAUCACCUUCCUCAAGGA UU	84
NR1H3-1196-1216	Artificial Sequence	25 mer sense strand	GAGUAUCACCUUCCUCAAGAAUU UC	85
NR1H3-1197-1217	Artificial Sequence	25 mer sense strand	AGUAUCACCUUCCUCAAGGAUUU CA	86
NR1H3-1198-1218	Artificial Sequence	25 mer sense strand	GUAUCACCUUCCUCAAGGAAUUC AG	87
NR1H3-1199-1219	Artificial Sequence	25 mer sense strand	UAUCACCUUCCUCAAGGAUAUCA GU	88
NR1H3-1200-1220	Artificial Sequence	25 mer sense strand	AUCACCUUCCUCAAGGAUUACAG UU	89
NR1H3-1203-1223	Artificial Sequence	25 mer sense strand	ACCUUCCUCAAGGAUUUCAAUUA UA	90
NR1H3-1204-1224	Artificial Sequence	25 mer sense strand	CCUUCCUCAAGGAUUUCAGAUUAU AA	91
NR1H3-1207-1227	Artificial Sequence	25 mer sense strand	UCCUCAAGGAUUUCAGUUAACAC CG	92
NR1H3-1211-1231	Artificial Sequence	25 mer sense strand	CAAGGAUUUCAGUUAUAACAGG GAA	93
NR1H3-1212-1232	Artificial Sequence	25 mer sense strand	AAGGAUUUCAGUUAUAACAGG AAG	94
NR1H3-1213-1233	Artificial Sequence	25 mer sense strand	AGGAUUUCAGUUAUAACCGAGA AGA	95
NR1H3-1214-1234	Artificial Sequence	25 mer sense strand	GGAUUUCAGUUAUAACCGGAAA GAC	96
NR1H3-1215-1235	Artificial Sequence	25 mer sense strand	GAUUUCAGUUAUAACCGGGAAG ACU	97
NR1H3-1216-1236	Artificial Sequence	25 mer sense strand	AUUUCAGUUAUAACCGGGAAGA CUU	98
NR1H3-1217-1237	Artificial Sequence	25 mer sense strand	UUUCAGUUAUAACCGGGAAAAC UUU	99
NR1H3-1218-1238	Artificial Sequence	25 mer sense strand	UUCAGUUAUAACCGGGAAGACU UUG	100

NR1H3-1219-1239	Artificial Sequence	25 mer sense strand	UCAGUUAUAACCGGGAAGAAUU UGC	101
NR1H3-1220-1240	Artificial Sequence	25 mer sense strand	CAGUUAUAACCGGGAAGACAUU GCC	102
NR1H3-1222-1242	Artificial Sequence	25 mer sense strand	GUUAUAACCGGGAAGACUUAGCC AA	103
NR1H3-1223-1243	Artificial Sequence	25 mer sense strand	UUAUAACCGGGAAGACUUUACCA AA	104
NR1H3-1224-1244	Artificial Sequence	25 mer sense strand	UAUAACCGGGAAGACUUUGACA AAG	105
NR1H3-1225-1245	Artificial Sequence	25 mer sense strand	AUAACCGGGAAGACUUUGCAAA AGC	106
NR1H3-1226-1246	Artificial Sequence	25 mer sense strand	UAACCGGGAAGACUUUGCCAAAG CA	107
NR1H3-1227-1247	Artificial Sequence	25 mer sense strand	AACCGGGAAGACUUUGCCAAAGC AG	108
NR1H3-1228-1248	Artificial Sequence	25 mer sense strand	ACCGGGAAGACUUUGCCAAAGCA GG	109
NR1H3-1229-1249	Artificial Sequence	25 mer sense strand	CCGGGAAGACUUUGCCAAAACAG GG	110
NR1H3-1232-1252	Artificial Sequence	25 mer sense strand	GGAAGACUUUGCCAAAGCAAGGC UG	111
NR1H3-1233-1253	Artificial Sequence	25 mer sense strand	GAAGACUUUGCCAAAGCAGAGCU GC	112
NR1H3-1234-1254	Artificial Sequence	25 mer sense strand	AAGACUUUGCCAAAGCAGGACUG CA	113
NR1H3-1235-1255	Artificial Sequence	25 mer sense strand	AGACUUUGCCAAAGCAGGGAUGC AA	114
NR1H3-1236-1256	Artificial Sequence	25 mer sense strand	GACUUUGCCAAAGCAGGGCAGCA AG	115
NR1H3-1237-1257	Artificial Sequence	25 mer sense strand	ACUUUGCCAAAGCAGGGCUACAA GU	116
NR1H3-1238-1258	Artificial Sequence	25 mer sense strand	CUUUGCCAAAGCAGGGCUGAAAG UG	117
NR1H3-1241-1261	Artificial Sequence	25 mer sense strand	UGCCAAAGCAGGGCUGCAA AUGG AA	118
NR1H3-1242-1262	Artificial Sequence	25 mer sense strand	GCCAAAGCAGGGCUGCAAGAGGA AU	119
NR1H3-1243-1263	Artificial Sequence	25 mer sense strand	CCAAAGCAGGGCUGCAAGUAGAA UU	120
NR1H3-1244-1264	Artificial Sequence	25 mer sense strand	CAAAGCAGGGCUGCAAGUGAAA UUC	121

NR1H3-1245-1265	Artificial Sequence	25 mer sense strand	AAAGCAGGGCUGCAAGUGGAAU UCA	122
NR1H3-1246-1266	Artificial Sequence	25 mer sense strand	AAGCAGGGCUGCAAGUGGAAU CAU	123
NR1H3-1247-1267	Artificial Sequence	25 mer sense strand	AGCAGGGCUGCAAGUGGAAA AUC	124
NR1H3-1248-1268	Artificial Sequence	25 mer sense strand	GCAGGGCUGCAAGUGGAAU ACA UCA	125
NR1H3-1250-1270	Artificial Sequence	25 mer sense strand	AGGGCUGCAAGUGGAAU UCAUC AAC	126
NR1H3-1251-1271	Artificial Sequence	25 mer sense strand	GGGCUGCAAGUGGAAU UCAACA ACC	127
NR1H3-1252-1272	Artificial Sequence	25 mer sense strand	GGCUGCAAGUGGAAU UCAUAAA CCC	128
NR1H3-1253-1273	Artificial Sequence	25 mer sense strand	GCUGCAAGUGGAAU UCAUCAACC CC	129
NR1H3-1256-1276	Artificial Sequence	25 mer sense strand	GCAAGUGGAAU UCAUCAACACCA UC	130
NR1H3-1258-1278	Artificial Sequence	25 mer sense strand	AAGUGGAAU UCAUCAACCCAAUC UU	131
NR1H3-1259-1279	Artificial Sequence	25 mer sense strand	AGUGGAAU UCAUCAACCCCAUCU UC	132
NR1H3-1261-1281	Artificial Sequence	25 mer sense strand	UGGAAU UCAUCAACCCCAUAUUC GA	133
NR1H3-1262-1282	Artificial Sequence	25 mer sense strand	GGAAU UCAUCAACCCCAUCAUCG AG	134
NR1H3-1265-1285	Artificial Sequence	25 mer sense strand	AUUCAUCAACCCCAUCU UCAAGU UC	135
NR1H3-1266-1286	Artificial Sequence	25 mer sense strand	UUCAUCAACCCCAUCU UCGAGUU CU	136
NR1H3-1267-1287	Artificial Sequence	25 mer sense strand	UCAUCAACCCCAUCU UCGAAUUC UC	137
NR1H3-1268-1288	Artificial Sequence	25 mer sense strand	CAUCAACCCCAUCU UCGAGAUCU CC	138
NR1H3-1269-1289	Artificial Sequence	25 mer sense strand	AUCAACCCCAUCU UCGAGUACUC CA	139
NR1H3-1270-1290	Artificial Sequence	25 mer sense strand	UCAACCCCAUCU UCGAGUUAUCC AG	140
NR1H3-1271-1291	Artificial Sequence	25 mer sense strand	CAACCCCAUCU UCGAGUUCACCA GG	141
NR1H3-1272-1292	Artificial Sequence	25 mer sense strand	AACCCCAUCU UCGAGUUCUACAG GG	142

NR1H3-1273-1293	Artificial Sequence	25 mer sense strand	ACCCCAUCUUCGAGUUCUCAAGG GC	143
NR1H3-1275-1295	Artificial Sequence	25 mer sense strand	CCCAUCUUCGAGUUCUCCAAGGC CA	144
NR1H3-1276-1296	Artificial Sequence	25 mer sense strand	CCAUCUUCGAGUUCUCCAGAGCC AU	145
NR1H3-1277-1297	Artificial Sequence	25 mer sense strand	CAUCUUCGAGUUCUCCAGGACCA UG	146
NR1H3-1278-1298	Artificial Sequence	25 mer sense strand	AUCUUCGAGUUCUCCAGGGACA UG	147
NR1H3-1279-1299	Artificial Sequence	25 mer sense strand	UCUUCGAGUUCUCCAGGGCAAUG AA	148
NR1H3-1280-1300	Artificial Sequence	25 mer sense strand	CUUCGAGUUCUCCAGGGCCAUGA AU	149
NR1H3-1281-1301	Artificial Sequence	25 mer sense strand	UUCGAGUUCUCCAGGGCCAAGAA UG	150
NR1H3-1282-1302	Artificial Sequence	25 mer sense strand	UCGAGUUCUCCAGGGCCAUAUAU GA	151
NR1H3-1283-1303	Artificial Sequence	25 mer sense strand	CGAGUUCUCCAGGGCCAUGAAUG AG	152
NR1H3-1284-1304	Artificial Sequence	25 mer sense strand	GAGUUCUCCAGGGCCAUGAAUGA GC	153
NR1H3-1285-1305	Artificial Sequence	25 mer sense strand	AGUUCUCCAGGGCCAUGAAAGAG CU	154
NR1H3-1286-1306	Artificial Sequence	25 mer sense strand	GUUCUCCAGGGCCAUGAAUAAGC UG	155
NR1H3-1288-1308	Artificial Sequence	25 mer sense strand	UCUCCAGGGCCAUGAAUGAACUG CA	156
NR1H3-1289-1309	Artificial Sequence	25 mer sense strand	CUCCAGGGCCAUGAAUGAGAU GC	157
NR1H3-1290-1310	Artificial Sequence	25 mer sense strand	UCCAGGGCCAUGAAUGAGCAGCA AC	158
NR1H3-1291-1311	Artificial Sequence	25 mer sense strand	CCAGGGCCAUGAAUGAGCUACAA CU	159
NR1H3-1292-1312	Artificial Sequence	25 mer sense strand	CAGGGCCAUGAAUGAGCUGAAAC UC	160
NR1H3-1293-1313	Artificial Sequence	25 mer sense strand	AGGGCCAUGAAUGAGCUGCAACU CA	161
NR1H3-1294-1314	Artificial Sequence	25 mer sense strand	GGGCCAUGAAUGAGCUGCAACUC AA	162
NR1H3-1295-1315	Artificial Sequence	25 mer sense strand	GGCCAUGAAUGAGCUGCAAAUCA AU	163

NR1H3-1296-1316	Artificial Sequence	25 mer sense strand	GCCAUGAAUGAGCUGCAACACAAUG	164
NR1H3-1297-1317	Artificial Sequence	25 mer sense strand	CCAUGAAUGAGCUGCAACUAAAUGA	165
NR1H3-1338-1358	Artificial Sequence	25 mer sense strand	CUCAUUGCUAUCAGCAUCUACUCUG	166
NR1H3-1339-1359	Artificial Sequence	25 mer sense strand	UCAUUGCUAUCAGCAUCUUAUCUGC	167
NR1H3-1340-1360	Artificial Sequence	25 mer sense strand	CAUUGCUAUCAGCAUCUUCACUGCA	168
NR1H3-1341-1361	Artificial Sequence	25 mer sense strand	AUUGCUAUCAGCAUCUUCUAUGCAG	169
NR1H3-1342-1362	Artificial Sequence	25 mer sense strand	UUGCUAUCAGCAUCUUCUCAGCAGA	170
NR1H3-1343-1363	Artificial Sequence	25 mer sense strand	UGCUAUCAGCAUCUUCUCUACAGAC	171
NR1H3-1344-1364	Artificial Sequence	25 mer sense strand	GCUAUCAGCAUCUUCUCUGAAGACC	172
NR1H3-1345-1365	Artificial Sequence	25 mer sense strand	CUAUCAGCAUCUUCUCUGCAGACCG	173
NR1H3-1346-1366	Artificial Sequence	25 mer sense strand	UAUCAGCAUCUUCUCUGCAAACCGG	174
NR1H3-1347-1367	Artificial Sequence	25 mer sense strand	AUCAGCAUCUUCUCUGCAGACCGGC	175
NR1H3-1377-1443	Artificial Sequence	25 mer sense strand	GUGCAGGACCAGCUCCAGGAAGAGA	176
NR1H3-1379-1445	Artificial Sequence	25 mer sense strand	GCAGGACCAGCUCCAGGUAAAGAGG	177
NR1H3-1383-1449	Artificial Sequence	25 mer sense strand	GACCAGCUCCAGGUAGAGAAGCUGC	178
NR1H3-1384-1450	Artificial Sequence	25 mer sense strand	ACCAGCUCCAGGUAGAGAGACUGCA	179
NR1H3-1385-1451	Artificial Sequence	25 mer sense strand	CCAGCUCCAGGUAGAGAGGAUGCAG	180
NR1H3-1387-1453	Artificial Sequence	25 mer sense strand	AGCUCCAGGUAGAGAGGCUACAGCA	181
NR1H3-1388-1454	Artificial Sequence	25 mer sense strand	GCUCCAGGUAGAGAGGCUGAAGCAC	182
NR1H3-1391-1457	Artificial Sequence	25 mer sense strand	CCAGGUAGAGAGGCUGCAGAACA CA	183
NR1H3-1393-1459	Artificial Sequence	25 mer sense strand	AGGUAGAGAGGCUGCAGCAAACAUA	184

NR1H3-1394-1460	Artificial Sequence	25 mer sense strand	GGUAGAGAGGCUGCAGCACACAU AU	185
NR1H3-1395-1461	Artificial Sequence	25 mer sense strand	GUAGAGAGGCUGCAGCACAAAU AUG	186
NR1H3-1396-1462	Artificial Sequence	25 mer sense strand	UAGAGAGGCUGCAGCACACAU AU GU	187
NR1H3-1397-1463	Artificial Sequence	25 mer sense strand	AGAGAGGCUGCAGCACACAAAUG UG	188
NR1H3-1398-1464	Artificial Sequence	25 mer sense strand	GAGAGGCUGCAGCACACAU AUGU GG	189
NR1H3-1399-1465	Artificial Sequence	25 mer sense strand	AGAGGCUGCAGCACACAU AAGUG GA	190
NR1H3-1400-1466	Artificial Sequence	25 mer sense strand	GAGGCUGCAGCACACAU AU AUGG AA	191
NR1H3-1401-1467	Artificial Sequence	25 mer sense strand	AGGCUGCAGCACACAU AUGAGGA AG	192
NR1H3-1402-1468	Artificial Sequence	25 mer sense strand	GGCUGCAGCACACAU AUGUAGAA GC	193
NR1H3-1403-1469	Artificial Sequence	25 mer sense strand	GCUGCAGCACACAU AUGUGAAAG CC	194
NR1H3-1404-1470	Artificial Sequence	25 mer sense strand	CUGCAGCACACAU AUGUGGAAGC CC	195
NR1H3-1406-1472	Artificial Sequence	25 mer sense strand	GCAGCACACAU AUGUGGAAACCC UG	196
NR1H3-1407-1473	Artificial Sequence	25 mer sense strand	CAGCACACAU AUGUGGAAGACCU GC	197
NR1H3-1408-1474	Artificial Sequence	25 mer sense strand	AGCACACAU AUGUGGAAGCACUG CA	198
NR1H3-1410-1476	Artificial Sequence	25 mer sense strand	CACACAU AUGUGGAAGCCCAGCA UG	199
NR1H3-1411-1477	Artificial Sequence	25 mer sense strand	ACACAU AUGUGGAAGCCCUACAU GC	200
NR1H3-1412-1478	Artificial Sequence	25 mer sense strand	CACAU AUGUGGAAGCCCUGAAUG CC	201
NR1H3-1413-1479	Artificial Sequence	25 mer sense strand	ACAU AUGUGGAAGCCCUGCAUGC CU	202
NR1H3-1414-1480	Artificial Sequence	25 mer sense strand	CAU AUGUGGAAGCCCUGCAAGCC UA	203
NR1H3-1415-1481	Artificial Sequence	25 mer sense strand	AU AUGUGGAAGCCCUGCAUACCU AC	204
NR1H3-1416-1482	Artificial Sequence	25 mer sense strand	UAU AUGUGGAAGCCCUGCAUGACUA CG	205

NR1H3-1417-1483	Artificial Sequence	25 mer sense strand	AUGUGGAAGCCCUGCAUGCAUACGU	206
NR1H3-1418-1484	Artificial Sequence	25 mer sense strand	UGUGGAAGCCCUGCAUGCCAACGUC	207
NR1H3-1419-1485	Artificial Sequence	25 mer sense strand	GUGGAAGCCCUGCAUGCCUACGUCU	208
NR1H3-1420-1486	Artificial Sequence	25 mer sense strand	UGGAAGCCCUGCAUGCCUAAGUCUC	209
NR1H3-1421-1487	Artificial Sequence	25 mer sense strand	GGAAGCCCUGCAUGCCUACAUCUCC	210
NR1H3-1422-1488	Artificial Sequence	25 mer sense strand	GAAGCCCUGCAUGCCUACGACUCCA	211
NR1H3-1423-1489	Artificial Sequence	25 mer sense strand	AAGCCCUGCAUGCCUACGUAUCCAU	212
NR1H3-1424-1490	Artificial Sequence	25 mer sense strand	AGCCCUGCAUGCCUACGUCACCAUC	213
NR1H3-1425-1491	Artificial Sequence	25 mer sense strand	GCCCUGCAUGCCUACGUCUACAUC	214
NR1H3-1426-1492	Artificial Sequence	25 mer sense strand	CCCUGCAUGCCUACGUCUCAAUCC	215
NR1H3-1427-1493	Artificial Sequence	25 mer sense strand	CCUGCAUGCCUACGUCUCCAUCCAC	216
NR1H3-1428-1494	Artificial Sequence	25 mer sense strand	CUGCAUGCCUACGUCUCCAACCA	217
NR1H3-1429-1495	Artificial Sequence	25 mer sense strand	UGCAUGCCUACGUCUCCAUACACCA	218
NR1H3-1430-1496	Artificial Sequence	25 mer sense strand	GCAUGCCUACGUCUCCAUCAACCAU	219
NR1H3-1431-1497	Artificial Sequence	25 mer sense strand	CAUGCCUACGUCUCCAUCCACCAUC	220
NR1H3-1432-1498	Artificial Sequence	25 mer sense strand	AUGCCUACGUCUCCAUCCAACAUC	221
NR1H3-1433-1499	Artificial Sequence	25 mer sense strand	UGCCUACGUCUCCAUCCACAAUCC	222
NR1H3-1434-1500	Artificial Sequence	25 mer sense strand	GCCUACGUCUCCAUCCACCAUCC	223
NR1H3-1435-1501	Artificial Sequence	25 mer sense strand	CCUACGUCUCCAUCCACCAACCC	224
NR1H3-1436-1502	Artificial Sequence	25 mer sense strand	CUACGUCUCCAUCCACCAUACCC	225
NR1H3-1437-1503	Artificial Sequence	25 mer sense strand	UACGUCUCCAUCCACCAUCACCAUG	226

NR1H3-1438-1504	Artificial Sequence	25 mer sense strand	ACGUCUCCAUCCACCAUCCACAUGA	227
NR1H3-1439-1505	Artificial Sequence	25 mer sense strand	CGUCUCCAUCCACCAUCCCAAUGAC	228
NR1H3-1440-1506	Artificial Sequence	25 mer sense strand	GUCUCCAUCCACCAUCCCCAUGACC	229
NR1H3-1442-1508	Artificial Sequence	25 mer sense strand	CUCCAUCCACCAUCCCCAUAACCGA	230
NR1H3-1443-1509	Artificial Sequence	25 mer sense strand	UCCAUCCACCAUCCCCAUGACCGAC	231
NR1H3-1444-1510	Artificial Sequence	25 mer sense strand	CCAUCCACCAUCCCCAUGAACGACU	232
NR1H3-1445-1511	Artificial Sequence	25 mer sense strand	CAUCCACCAUCCCCAUGACAGACUG	233
NR1H3-1446-1512	Artificial Sequence	25 mer sense strand	AUCCACCAUCCCCAUGACCAACUGA	234
NR1H3-1447-1513	Artificial Sequence	25 mer sense strand	UCCACCAUCCCCAUGACCGACUGAU	235
NR1H3-1448-1514	Artificial Sequence	25 mer sense strand	CCACCAUCCCCAUGACCGAAUGAUG	236
NR1H3-1449-1515	Artificial Sequence	25 mer sense strand	CACCAUCCCCAUGACCGACAGAUGU	237
NR1H3-1450-1516	Artificial Sequence	25 mer sense strand	ACCAUCCCCAUGACCGACUAAUGUU	238
NR1H3-1451-1517	Artificial Sequence	25 mer sense strand	CCAUCCCCAUGACCGACUGAUGUUC	239
NR1H3-1452-1518	Artificial Sequence	25 mer sense strand	CAUCCCCAUGACCGACUGAAGUUC	240
NR1H3-1453-1519	Artificial Sequence	25 mer sense strand	AUCCCCAUGACCGACUGAUUUC	241
NR1H3-1454-1520	Artificial Sequence	25 mer sense strand	UCCCCAUGACCGACUGAUGAUCCCA	242
NR1H3-1455-1521	Artificial Sequence	25 mer sense strand	CCCCAUGACCGACUGAUGUACCCAC	243
NR1H3-1456-1522	Artificial Sequence	25 mer sense strand	CCCAUGACCGACUGAUGUUACCA	244
NR1H3-1457-1523	Artificial Sequence	25 mer sense strand	CCAUGACCGACUGAUGUUCACACGG	245
NR1H3-1459-1525	Artificial Sequence	25 mer sense strand	AUGACCGACUGAUGUUCCCACGGAU	246
NR1H3-1460-1526	Artificial Sequence	25 mer sense strand	UGACCGACUGAUGUUCCCAAGGAUG	247

NR1H3-1461-1527	Artificial Sequence	25 mer sense strand	GACCGACUGAUGUUCCCACAGAU GC	248
NR1H3-1462-1528	Artificial Sequence	25 mer sense strand	ACCGACUGAUGUUCCCACGAAUG CU	249
NR1H3-1463-1529	Artificial Sequence	25 mer sense strand	CCGACUGAUGUUCCCACGGAUGC UA	250
NR1H3-1465-1531	Artificial Sequence	25 mer sense strand	GACUGAUGUUCCCACGGAUACUA AU	251
NR1H3-1466-1532	Artificial Sequence	25 mer sense strand	ACUGAUGUUCCCACGGAUGAUAA UG	252
NR1H3-1468-1534	Artificial Sequence	25 mer sense strand	UGAUGUUCCCACGGAUGCUA AUG AA	253
NR1H3-1469-1535	Artificial Sequence	25 mer sense strand	GAUGUUCCCACGGAUGCUA AUG AA	254
NR1H3-1471-1537	Artificial Sequence	25 mer sense strand	UGUUCCCACGGAUGCUA AUG AAA CU	255
NR1H3-1472-1538	Artificial Sequence	25 mer sense strand	GUUCCCACGGAUGCUA AUG AA UG	256
NR1H3-1473-1539	Artificial Sequence	25 mer sense strand	UUCCCACGGAUGCUA AUG AA CU GG	257
NR1H3-1474-1540	Artificial Sequence	25 mer sense strand	UCCCACGGAUGCUA AUG AA CU GU	258
NR1H3-1475-1541	Artificial Sequence	25 mer sense strand	CCCACGGAUGCUA AUG AAA UG	259
NR1H3-1476-1542	Artificial Sequence	25 mer sense strand	CCACGGAUGCUA AUG AA CAG GU	260
NR1H3-1477-1543	Artificial Sequence	25 mer sense strand	CACGGAUGCUA AUG AA CU AGU GAG	261
NR1H3-1478-1544	Artificial Sequence	25 mer sense strand	ACGGAUGCUA AUG AA CUG AGC	262
NR1H3-1479-1545	Artificial Sequence	25 mer sense strand	CGGAUGCUA AUG AA CUG GAG GCC	263
NR1H3-1480-1546	Artificial Sequence	25 mer sense strand	GGAUGCUA AUG AA CUG GUA AG CCU	264
NR1H3-1481-1547	Artificial Sequence	25 mer sense strand	GAUGCUA AUG AA CUG GUG AGC CUC	265
NR1H3-1483-1549	Artificial Sequence	25 mer sense strand	UGCUA AUG AA CUG GUG AGA CU CCG	266
NR1H3-1484-1550	Artificial Sequence	25 mer sense strand	GCUA AUG AA CUG GUG AGA CU CC GG	267
NR1H3-1485-1551	Artificial Sequence	25 mer sense strand	CUA AUG AA CUG GUG AGC CAC CG GA	268

NR1H3-1486-1552	Artificial Sequence	25 mer sense strand	UAAUGAAACUGGUGAGCCUACG GAC	269
NR1H3-1487-1553	Artificial Sequence	25 mer sense strand	AAUGAAACUGGUGAGCCUCAGG ACC	270
NR1H3-1488-1554	Artificial Sequence	25 mer sense strand	AUGAAACUGGUGAGCCUCCAGAC CC	271
NR1H3-1489-1555	Artificial Sequence	25 mer sense strand	UGAAACUGGUGAGCCUCCGAACC CU	272
NR1H3-1491-1557	Artificial Sequence	25 mer sense strand	AAACUGGUGAGCCUCCGGAACCU GA	273
NR1H3-1492-1558	Artificial Sequence	25 mer sense strand	AACUGGUGAGCCUCCGGACACUG AG	274
NR1H3-1494-1560	Artificial Sequence	25 mer sense strand	CUGGUGAGCCUCCGGACCCAGAG CA	275
NR1H3-1505-1571	Artificial Sequence	25 mer sense strand	CCGGACCCUGAGCAGCGUCAACU CA	276
NR1H3-1507-1573	Artificial Sequence	25 mer sense strand	GGACCCUGAGCAGCGUCCAAUCA GA	277
NR1H3-1508-1574	Artificial Sequence	25 mer sense strand	GACCCUGAGCAGCGUCCACACAG AG	278
NR1H3-1509-1575	Artificial Sequence	25 mer sense strand	ACCCUGAGCAGCGUCCACUAAGA GC	279
NR1H3-1510-1576	Artificial Sequence	25 mer sense strand	CCCUGAGCAGCGUCCACUCAGAG CA	280
NR1H3-1511-1577	Artificial Sequence	25 mer sense strand	CCUGAGCAGCGUCCACUCAAAGC AA	281
NR1H3-1512-1578	Artificial Sequence	25 mer sense strand	CUGAGCAGCGUCCACUCAGAGCA AG	282
NR1H3-1513-1579	Artificial Sequence	25 mer sense strand	UGAGCAGCGUCCACUCAGAACAA GU	283
NR1H3-1514-1580	Artificial Sequence	25 mer sense strand	GAGCAGCGUCCACUCAGAGAAAG UG	284
NR1H3-1515-1581	Artificial Sequence	25 mer sense strand	AGCAGCGUCCACUCAGAGCAAGU GU	285
NR1H3-1516-1582	Artificial Sequence	25 mer sense strand	GCAGCGUCCACUCAGAGCAAGUG UU	286
NR1H3-1517-1583	Artificial Sequence	25 mer sense strand	CAGCGUCCACUCAGAGCAAAUGU UU	287
NR1H3-1518-1584	Artificial Sequence	25 mer sense strand	AGCGUCCACUCAGAGCAAGAGUU UG	288
NR1H3-1519-1585	Artificial Sequence	25 mer sense strand	GCGUCCACUCAGAGCAAGUAUUU GC	289

NR1H3-1520-1586	Artificial Sequence	25 mer sense strand	CGUCCACUCAGAGCAAGUGAUUGCA	290
NR1H3-1521-1587	Artificial Sequence	25 mer sense strand	GUCCACUCAGAGCAAGUGUAUGCAC	291
NR1H3-1522-1588	Artificial Sequence	25 mer sense strand	UCCACUCAGAGCAAGUGUUAGCA	292
NR1H3-1523-1589	Artificial Sequence	25 mer sense strand	CCACUCAGAGCAAGUGUUUACACUG	293
NR1H3-1525-1591	Artificial Sequence	25 mer sense strand	ACUCAGAGCAAGUGUUUGCACUGCG	294
NR1H3-1526-1592	Artificial Sequence	25 mer sense strand	CUCAGAGCAAGUGUUUGCAAUGCGU	295
NR1H3-1527-1593	Artificial Sequence	25 mer sense strand	UCAGAGCAAGUGUUUGCACAGCGUC	296
NR1H3-1528-1594	Artificial Sequence	25 mer sense strand	CAGAGCAAGUGUUUGCACUACGUCU	297
NR1H3-1529-1595	Artificial Sequence	25 mer sense strand	AGAGCAAGUGUUUGCACUGAGUCUG	298
NR1H3-1530-1596	Artificial Sequence	25 mer sense strand	GAGCAAGUGUUUGCACUGCAUCU	299
NR1H3-1531-1597	Artificial Sequence	25 mer sense strand	AGCAAGUGUUUGCACUGCGACUGCA	300
NR1H3-1532-1598	Artificial Sequence	25 mer sense strand	GCAAGUGUUUGCACUGCGUAUGCAG	301
NR1H3-1533-1599	Artificial Sequence	25 mer sense strand	CAAGUGUUUGCACUGCGUCAGCAGG	302
NR1H3-1534-1600	Artificial Sequence	25 mer sense strand	AAGUGUUUGCACUGCGUCUACAGGA	303
NR1H3-1535-1601	Artificial Sequence	25 mer sense strand	AGUGUUUGCACUGCGUCUGAAGGAC	304
NR1H3-1536-1602	Artificial Sequence	25 mer sense strand	GUGUUUGCACUGCGUCUGCAGGACA	305
NR1H3-1537-1603	Artificial Sequence	25 mer sense strand	UGUUUGCACUGCGUCUGCAAGACAA	306
NR1H3-1538-1604	Artificial Sequence	25 mer sense strand	GUUUGCACUGCGUCUGCAGAACA	307
NR1H3-1539-1605	Artificial Sequence	25 mer sense strand	UUUGCACUGCGUCUGCAGGACAA	308
NR1H3-1540-1606	Artificial Sequence	25 mer sense strand	UUGCACUGCGUCUGCAGGAAAAAA	309
NR1H3-1541-1607	Artificial Sequence	25 mer sense strand	UGCACUGCGUCUGCAGGACAAAAAG	310

NR1H3-1542-1608	Artificial Sequence	25 mer sense strand	GCACUGCGUCUGCAGGACAAAAA GC	311
NR1H3-1543-1609	Artificial Sequence	25 mer sense strand	CACUGCGUCUGCAGGACAAAAAAG CU	312
NR1H3-1544-1610	Artificial Sequence	25 mer sense strand	ACUGCGUCUGCAGGACAAAAAAGC UC	313
NR1H3-1545-1611	Artificial Sequence	25 mer sense strand	CUGCGUCUGCAGGACAAAAAAGCU CC	314
NR1H3-1546-1612	Artificial Sequence	25 mer sense strand	UGCGUCUGCAGGACAAAAAACUC CC	315
NR1H3-1547-1613	Artificial Sequence	25 mer sense strand	GCGUCUGCAGGACAAAAAGA UCC CA	316
NR1H3-1548-1614	Artificial Sequence	25 mer sense strand	CGUCUGCAGGACAAAAAGCACCC AC	317
NR1H3-1549-1615	Artificial Sequence	25 mer sense strand	GUCUGCAGGACAAAAAGCUACCA CC	318
NR1H3-1550-1616	Artificial Sequence	25 mer sense strand	UCUGCAGGACAAAAAGCUCACAC CG	319
NR1H3-1551-1617	Artificial Sequence	25 mer sense strand	CUGCAGGACAAAAAGCUCCAACC GC	320
NR1H3-1553-1619	Artificial Sequence	25 mer sense strand	GCAGGACAAAAAGCUCCCAACGC UG	321
NR1H3-1554-1620	Artificial Sequence	25 mer sense strand	CAGGACAAAAAGCUCCCACAGCU GC	322
NR1H3-1555-1621	Artificial Sequence	25 mer sense strand	AGGACAAAAAGCUCCCACCACUG CU	323
NR1H3-1556-1622	Artificial Sequence	25 mer sense strand	GGACAAAAAGCUCCCACCGAUGC UC	324
NR1H3-1558-1624	Artificial Sequence	25 mer sense strand	ACAAAAAGCUCCCACCGCUACUC UC	325
NR1H3-1559-1625	Artificial Sequence	25 mer sense strand	CAAAAAGCUCCCACCGCUGAUCU CU	326
NR1H3-1560-1626	Artificial Sequence	25 mer sense strand	AAAAAGCUCCCACCGCUGCACUC UG	327
NR1H3-1561-1627	Artificial Sequence	25 mer sense strand	AAAAGCUCCCACCGCUGCUAUCU GA	328
NR1H3-1562-1628	Artificial Sequence	25 mer sense strand	AAAGCUCCCACCGCUGCUCACUG AG	329
NR1H3-1563-1629	Artificial Sequence	25 mer sense strand	AAGCUCCCACCGCUGCUCUAUGA GA	330
NR1H3-1564-1630	Artificial Sequence	25 mer sense strand	AGCUCCCACCGCUGCUCUCAGAG AU	331

NR1H3-1565-1631	Artificial Sequence	25 mer sense strand	GCUCCACCGCUGCUCUCUAAGAUC	332
NR1H3-1567-1633	Artificial Sequence	25 mer sense strand	UCCACCGCUGCUCUCUGAAAUCUG	333
NR1H3-1569-1635	Artificial Sequence	25 mer sense strand	CCACCGCUGCUCUCUGAGAACUGGG	334
NR1H3-1570-1636	Artificial Sequence	25 mer sense strand	CACCGCUGCUCUCUGAGAUAUGGGA	335
NR1H3-1572-1638	Artificial Sequence	25 mer sense strand	CCGCUGCUCUCUGAGAUCUAGGAUG	336
NR1H3-1573-1639	Artificial Sequence	25 mer sense strand	CGCUGCUCUCUGAGAUCUGAGAU GU	337
NR1H3-1574-1640	Artificial Sequence	25 mer sense strand	GCUGCUCUCUGAGAUCUGGAAUGUG	338
NR1H3-1577-1643	Artificial Sequence	25 mer sense strand	GCUCUCUGAGAUCUGGGAUAUGCAC	339
NR1H3-1579-1645	Artificial Sequence	25 mer sense strand	UCUCUGAGAUCUGGGAUGUACACGA	340
NR1H3-1580-1646	Artificial Sequence	25 mer sense strand	CUCUGAGAUCUGGGAUGUGAACGAA	341
NR1H3-1581-1647	Artificial Sequence	25 mer sense strand	UCUGAGAUCUGGGAUGUGCACGAAU	342
NR1H3-1582-1648	Artificial Sequence	25 mer sense strand	CUGAGAUCUGGGAUGUGCAAGAAUG	343
NR1H3-1583-1649	Artificial Sequence	25 mer sense strand	UGAGAUCUGGGAUGUGCACAAAUGA	344
NR1H3-1584-1650	Artificial Sequence	25 mer sense strand	GAGAUCUGGGAUGUGCACGAAUGAC	345
NR1H3-1585-1651	Artificial Sequence	25 mer sense strand	AGAUCUGGGAUGUGCACGAAUGACU	346
NR1H3-1586-1652	Artificial Sequence	25 mer sense strand	GAUCUGGGAUGUGCACGAAAGACUG	347
NR1H3-1587-1653	Artificial Sequence	25 mer sense strand	AUCUGGGAUGUGCACGAAUAACUGU	348
NR1H3-1588-1654	Artificial Sequence	25 mer sense strand	UCUGGGAUGUGCACGAAUGACUGU	349
NR1H3-1589-1655	Artificial Sequence	25 mer sense strand	CUGGGAUGUGCACGAAUGAAUGUUC	350
NR1H3-1590-1656	Artificial Sequence	25 mer sense strand	UGGGAUGUGCACGAAUGACAGUUCU	351
NR1H3-1591-1657	Artificial Sequence	25 mer sense strand	GGGAUGUGCACGAAUGACUAUUCUG	352

NR1H3-1592-1658	Artificial Sequence	25 mer sense strand	GGAUGUGCACGAAUGACUGAUCUGU	353
NR1H3-1593-1659	Artificial Sequence	25 mer sense strand	GAUGUGCACGAAUGACUGUACUGUC	354
NR1H3-1656-1720	Artificial Sequence	25 mer sense strand	UGGUGGCUGCCUCCUAGAAAUGGAA	355
NR1H3-1657-1721	Artificial Sequence	25 mer sense strand	GGUGGCUGCCUCCUAGAAGAGGAC	356
NR1H3-1658-1722	Artificial Sequence	25 mer sense strand	GUGGCUGCCUCCUAGAAGUAGAA	357
NR1H3-1659-1723	Artificial Sequence	25 mer sense strand	UGGCUGCCUCCUAGAAGUGAAACAG	358
NR1H3-1660-1724	Artificial Sequence	25 mer sense strand	GGCUGCCUCCUAGAAGUGGAACAGA	359
NR1H3-1661-1725	Artificial Sequence	25 mer sense strand	GCUGCCUCCUAGAAGUGGAACAGAC	360
NR1H3-1662-1726	Artificial Sequence	25 mer sense strand	CUGCCUCCUAGAAGUGGAAAAGACU	361
NR1H3-1663-1727	Artificial Sequence	25 mer sense strand	UGCCUCCUAGAAGUGGAACAGACUG	362
NR1H3-1664-1728	Artificial Sequence	25 mer sense strand	GCCUCCUAGAAGUGGAACAAACUGA	363
NR1H3-1665-1729	Artificial Sequence	25 mer sense strand	CCUCCUAGAAGUGGAACAGACUGAG	364
NR1H3-1666-1730	Artificial Sequence	25 mer sense strand	CUCCUAGAAGUGGAACAGAAUGAGA	365
NR1H3-1667-1731	Artificial Sequence	25 mer sense strand	UCCUAGAAGUGGAACAGACAGAGAA	366
NR1H3-1668-1732	Artificial Sequence	25 mer sense strand	CCUAGAAGUGGAACAGACUAAGAAG	367
NR1H3-1669-1733	Artificial Sequence	25 mer sense strand	CUAGAAGUGGAACAGACUGAGAGAGG	368
NR1H3-1671-1735	Artificial Sequence	25 mer sense strand	AGAAGUGGAACAGACUGAGAGAGGGC	369
NR1H3-1677-1741	Artificial Sequence	25 mer sense strand	GGAACAGACUGAGAAGGGCAAA	370
NR1H3-1679-1743	Artificial Sequence	25 mer sense strand	AACAGACUGAGAAGGGCAAACA	371
NR1H3-1680-1744	Artificial Sequence	25 mer sense strand	ACAGACUGAGAAGGGCAAAAAU	372
NR1H3-1681-1745	Artificial Sequence	25 mer sense strand	CAGACUGAGAAGGGCAAACAUCU	373

NR1H3-1682-1746	Artificial Sequence	25 mer sense strand	AGACUGAGAAGGGCAAACAAUCCUG	374
NR1H3-1683-1747	Artificial Sequence	25 mer sense strand	GACUGAGAAGGGCAAACAUACCU	375
NR1H3-1684-1748	Artificial Sequence	25 mer sense strand	ACUGAGAAGGGCAAACAUUACU	376
NR1H3-1685-1749	Artificial Sequence	25 mer sense strand	CUGAGAAGGGCAAACAUUCAUG	377
NR1H3-1686-1750	Artificial Sequence	25 mer sense strand	UGAGAAGGGCAAACAUUCCAGG	378
NR1H3-1687-1751	Artificial Sequence	25 mer sense strand	GAGAAGGGCAAACAUUCCUAGG	379
NR1H3-1728-1792	Artificial Sequence	25 mer sense strand	CCCGUGGCAUUAAGAGAAUCA	380
NR1H3-1729-1793	Artificial Sequence	25 mer sense strand	CCGUGGCAUUAAGAGAGACA	381
NR1H3-1730-1794	Artificial Sequence	25 mer sense strand	CGUGGCAUUAAGAGAGUAAA	382
NR1H3-1731-1795	Artificial Sequence	25 mer sense strand	GUGGCAUUAAGAGAGUCAAA	383
NR1H3-1732-1796	Artificial Sequence	25 mer sense strand	UGGCAUUAAGAGAGUCAAAAG	384
NR1H3-764-784-861	Artificial Sequence	27 mer antisense strand	GCGGAUCUGUUCUUCUGACAGGA	385
NR1H3-766-786-863	Artificial Sequence	27 mer antisense strand	AGGCGUAUCUGUUCUUCUGACAG	386
NR1H3-789-809-886	Artificial Sequence	27 mer antisense strand	CCUCUUGCCGCUUCAGUUUCUUC	387
NR1H3-790-810-887	Artificial Sequence	27 mer antisense strand	UCCUCUUGCCGCUUCAGUUUCU	388
NR1H3-791-811-888	Artificial Sequence	27 mer antisense strand	CUCCUUUUGCCGCUUCAGUUUCU	389
NR1H3-792-812-889	Artificial Sequence	27 mer antisense strand	CCUCCUCUUGCCGCUUCAGUUUC	390
NR1H3-793-813-890	Artificial Sequence	27 mer antisense strand	UCCUCUUCUUGCCGCUUCAGUUU	391

NR1H3-795-815-892	Artificial Sequence	27 mer antisense strand	GUUCCUCCUCUUGCCGCUUCAGU UUCU	392
NR1H3-796-816-893	Artificial Sequence	27 mer antisense strand	UGUUCUUCCUCUUGCCGCUUCAG UUUC	393
NR1H3-797-817-894	Artificial Sequence	27 mer antisense strand	CUGUUUCUCCUCUUGCCGCUUCA GUUU	394
NR1H3-798-818-895	Artificial Sequence	27 mer antisense strand	CCUGUUCCUCCUCUUGCCGCUUC AGUU	395
NR1H3-799-819-896	Artificial Sequence	27 mer antisense strand	GCCUGUUCCUCCUCUUGCCGCUU CAGU	396
NR1H3-802-822-899	Artificial Sequence	27 mer antisense strand	UGAGCUUGUUCCUCCUCUUGCCG CUUC	397
NR1H3-803-823-900	Artificial Sequence	27 mer antisense strand	AUGAGUCUGUUCCUCCUCUUGCC GCUU	398
NR1H3-804-824-901	Artificial Sequence	27 mer antisense strand	CAUGAUCCUGUUCCUCCUCUUGC CGCU	399
NR1H3-806-826-903	Artificial Sequence	27 mer antisense strand	GGCAUUAGCCUGUUCCUCCUCUU GCCG	400
NR1H3-808-828-905	Artificial Sequence	27 mer antisense strand	GUGGCUUGAGCCUGUUCCUCCUC UUGC	401
NR1H3-809-829-906	Artificial Sequence	27 mer antisense strand	UGUGGUAUGAGCCUGUUCCUCCU CUUG	402
NR1H3-810-830-907	Artificial Sequence	27 mer antisense strand	AUGUGUCAUGAGCCUGUUCCUCC UCUU	403
NR1H3-811-831-908	Artificial Sequence	27 mer antisense strand	GAUGUUGCAUGAGCCUGUUCCUC CUCU	404
NR1H3-813-833-910	Artificial Sequence	27 mer antisense strand	AGGAUUUGGCAUGAGCCUGUUCC UCCU	405

NR1H3-844	Artificial Sequence	27 mer antisense strand	AUUUGUGGGGGUGAGGAAGCCC UGGGG	406
NR1H3-895-915-992	Artificial Sequence	27 mer antisense strand	GCGACUAGCUUCUCGAUCAUGCC CAGU	407
NR1H3-898-918-995	Artificial Sequence	27 mer antisense strand	GCAGCUACGAGCUUCUCGAUCAU GCCC	408
NR1H3-915-935	Artificial Sequence	27 mer antisense strand	GGUUAUACUGUUGCUGGGCAGC GACGA	409
NR1H3-917-937	Artificial Sequence	27 mer antisense strand	CCGGUUACACUGUUGCUGGGCAG CGAC	410
NR1H3-922-942	Artificial Sequence	27 mer antisense strand	GAGCGUCGGUUACACUGUUGCUG GGCA	411
NR1H3-924-944	Artificial Sequence	27 mer antisense strand	AGGAGUGCCGGUUACACUGUUGC UGGG	412
NR1H3-925-945	Artificial Sequence	27 mer antisense strand	AAGGAUCGCCGGUUACACUGUUG CUGG	413
NR1H3-927-947	Artificial Sequence	27 mer antisense strand	AAAAGUAGCGCCGGUUACACUGU UGCU	414
NR1H3-928-948	Artificial Sequence	27 mer antisense strand	GAAAAUGAGCGCCGGUUACACUG UUGC	415
NR1H3-929-949	Artificial Sequence	27 mer antisense strand	AGAAAUUGGAGCGCCGGUUACACU GUUG	416
NR1H3-930-950	Artificial Sequence	27 mer antisense strand	CAGAAUAGGAGCGCCGGUUACAC UGUU	417
NR1H3-931-951	Artificial Sequence	27 mer antisense strand	UCAGAUAAAGGAGCGCCGGUUACA CUGU	418
NR1H3-932-952	Artificial Sequence	27 mer antisense strand	GUCAGUAAAGGAGCGCCGGUUAC ACUG	419

NR1H3-933-953	Artificial Sequence	27 mer antisense strand	GGUCAUAAAAGGAGCGCCGGUU ACACU	420
NR1H3-941-961	Artificial Sequence	27 mer antisense strand	UCGAAUCCGGUCAGAAAAGGAGC GCCG	421
NR1H3-944-964	Artificial Sequence	27 mer antisense strand	GACUCUAAGCCGGUCAGAAAAGG AGCG	422
NR1H3-945-965	Artificial Sequence	27 mer antisense strand	UGACUUGAAGCCGGUCAGAAAA GGAGC	423
NR1H3-946-966	Artificial Sequence	27 mer antisense strand	GUGACUCGAAGCCGGUCAGAAAA GGAG	424
NR1H3-947-967	Artificial Sequence	27 mer antisense strand	CGUGAUUCGAAGCCGGUCAGAAA AGGA	425
NR1H3-949-969	Artificial Sequence	27 mer antisense strand	GGCGUUACUCGAAGCCGGUCAGA AAAG	426
NR1H3-951-971	Artificial Sequence	27 mer antisense strand	AAGGCUUGACUCGAAGCCGGUCA GAAA	427
NR1H3-952-972	Artificial Sequence	27 mer antisense strand	CAAGGUGUGACUCGAAGCCGGUC AGAA	428
NR1H3-953-973	Artificial Sequence	27 mer antisense strand	CCAAGUCGUGACUCGAAGCCGGU CAGA	429
NR1H3-1151-1171	Artificial Sequence	27 mer antisense strand	CCGAGUUGUCUCCAGAAGCAUCA CCUG	430
NR1H3-1153-1173	Artificial Sequence	27 mer antisense strand	CUCCGUGAUGUCUCCAGAAGCAU CACC	431
NR1H3-1154-1174	Artificial Sequence	27 mer antisense strand	CCUCCUAGAUGUCUCCAGAAGCA UCAC	432
NR1H3-1155-1175	Artificial Sequence	27 mer antisense strand	ACCUCUGAGAUGUCUCCAGAAGC AUCA	433

NR1H3-1156-1176	Artificial Sequence	27 mer antisense strand	UACCUUCGAGAUGUCUCCAGAAG CAUC	434
NR1H3-1157-1177	Artificial Sequence	27 mer antisense strand	GUACCUCCGAGAUGUCUCCAGAA GCAU	435
NR1H3-1158-1178	Artificial Sequence	27 mer antisense strand	UGUACUCCGAGAUGUCUCCAGA AGCA	436
NR1H3-1159-1179	Artificial Sequence	27 mer antisense strand	UUGUAUCUCCGAGAUGUCUCCAG AAGC	437
NR1H3-1160-1180	Artificial Sequence	27 mer antisense strand	GUUGUCCUCCGAGAUGUCUCCA GAAG	438
NR1H3-1161-1181	Artificial Sequence	27 mer antisense strand	GGUUGUACCUCCGAGAUGUCUCC AGAA	439
NR1H3-1162-1182	Artificial Sequence	27 mer antisense strand	GGGUUUUACCUCCGAGAUGUCUC CAGA	440
NR1H3-1163-1183	Artificial Sequence	27 mer antisense strand	AGGGUUGUACCUCCGAGAUGUCU CCAG	441
NR1H3-1164-1184	Artificial Sequence	27 mer antisense strand	CAGGGUUGUACCUCCGAGAUGUC UCCA	442
NR1H3-1165-1185	Artificial Sequence	27 mer antisense strand	CCAGGUUUGUACCUCCGAGAUGU CUCC	443
NR1H3-1166-1186	Artificial Sequence	27 mer antisense strand	CCCAGUGUUGUACCUCCGAGAUG UCUC	444
NR1H3-1167-1187	Artificial Sequence	27 mer antisense strand	UCCCAUGGUUGUACCUCCGAGAU GUCU	445
NR1H3-1169-1189	Artificial Sequence	27 mer antisense strand	ACUCCUAGGGUUGUACCUCCGAG AUGU	446
NR1H3-1170-1190	Artificial Sequence	27 mer antisense strand	CACUCUCAGGGUUGUACCUCCGA GAUG	447

NR1H3-1171-1191	Artificial Sequence	27 mer antisense strand	UCACUUCCAGGGUUGUACCUCCG AGAU	448
NR1H3-1173-1193	Artificial Sequence	27 mer antisense strand	UCUCAUUCCCAGGGUUGUACCUC CGAG	449
NR1H3-1175-1195	Artificial Sequence	27 mer antisense strand	ACUCUUACUCCCAGGGUUGUACC UCCG	450
NR1H3-1176-1196	Artificial Sequence	27 mer antisense strand	UACUCUCACUCCCAGGGUUGUAC CUCC	451
NR1H3-1177-1197	Artificial Sequence	27 mer antisense strand	AUACUUUCACUCCCAGGGUUGUA CCUC	452
NR1H3-1178-1198	Artificial Sequence	27 mer antisense strand	GAUACUCUCACUCCCAGGGUUGU ACCU	453
NR1H3-1179-1199	Artificial Sequence	27 mer antisense strand	UGAUAUUCUCACUCCCAGGGUUG UACC	454
NR1H3-1180-1200	Artificial Sequence	27 mer antisense strand	GUGAUUCUCUCACUCCCAGGGUU GUAC	455
NR1H3-1181-1201	Artificial Sequence	27 mer antisense strand	GGUGAUACUCUCACUCCCAGGGU UGUA	456
NR1H3-1182-1202	Artificial Sequence	27 mer antisense strand	AGGUGUUACUCUCACUCCCAGGG UUGU	457
NR1H3-1183-1203	Artificial Sequence	27 mer antisense strand	AAGGUUAUACUCUCACUCCCAGG GUUG	458
NR1H3-1184-1204	Artificial Sequence	27 mer antisense strand	GAAGGUGAUACUCUCACUCCCAG GGUU	459
NR1H3-1185-1205	Artificial Sequence	27 mer antisense strand	GGAAGUUGAUACUCUCACUCCCA GGGU	460
NR1H3-1186-1206	Artificial Sequence	27 mer antisense strand	AGGAAUGUGAUACUCUCACUCCC AGGG	461

NR1H3-1187-1207	Artificial Sequence	27 mer antisense strand	GAGGAUGGUGAUACUCUCACUCC CAGG	462
NR1H3-1188-1208	Artificial Sequence	27 mer antisense strand	UGAGGUAGGUGAUACUCUCACUC CCAG	463
NR1H3-1190-1210	Artificial Sequence	27 mer antisense strand	CUUGAUGAAGGUGAUACUCUCAC UCCC	464
NR1H3-1191-1211	Artificial Sequence	27 mer antisense strand	CCUUGUGGAAGGUGAUACUCUCA CUCC	465
NR1H3-1192-1212	Artificial Sequence	27 mer antisense strand	UCCUUUAGGAAGGUGAUACUCUC ACUC	466
NR1H3-1193-1213	Artificial Sequence	27 mer antisense strand	AUCCUUGAGGAAGGUGAUACUC UCACU	467
NR1H3-1194-1214	Artificial Sequence	27 mer antisense strand	AAUCCUUGAGGAAGGUGAUACU CUCAC	468
NR1H3-1196-1216	Artificial Sequence	27 mer antisense strand	GAAAUUCUUGAGGAAGGUGAUA CUCUC	469
NR1H3-1197-1217	Artificial Sequence	27 mer antisense strand	UGAAAUCCUUGAGGAAGGUGAU ACUCU	470
NR1H3-1198-1218	Artificial Sequence	27 mer antisense strand	CUGAAUCCUUGAGGAAGGUGA UACUC	471
NR1H3-1199-1219	Artificial Sequence	27 mer antisense strand	ACUGAUAUCCUUGAGGAAGGUG AUACU	472
NR1H3-1200-1220	Artificial Sequence	27 mer antisense strand	AACUGUAAUCCUUGAGGAAGGU GAUAC	473
NR1H3-1203-1223	Artificial Sequence	27 mer antisense strand	UAUAAUUGAAAUCCUUGAGGAA GGUGA	474
NR1H3-1204-1224	Artificial Sequence	27 mer antisense strand	UUAUAUCUGAAAUCCUUGAGGA AGGUG	475

NR1H3-1207-1227	Artificial Sequence	27 mer antisense strand	CGGUUUUAAACUGAAAUCCUUGA GGAAG	476
NR1H3-1211-1231	Artificial Sequence	27 mer antisense strand	UUCCCUGUUUAUAAACUGAAAUCCU UGAG	477
NR1H3-1212-1232	Artificial Sequence	27 mer antisense strand	CUUCCUGGUUAUAAACUGAAAUCC UUGA	478
NR1H3-1213-1233	Artificial Sequence	27 mer antisense strand	UCUUCUCGGUUAUAAACUGAAAUC CUUG	479
NR1H3-1214-1234	Artificial Sequence	27 mer antisense strand	GUCUUUCCGGUUAUAAACUGAAA UCCUU	480
NR1H3-1215-1235	Artificial Sequence	27 mer antisense strand	AGUCUUCCCGGUUAUAAACUGAAA UCCU	481
NR1H3-1216-1236	Artificial Sequence	27 mer antisense strand	AAGUCUUCCCGGUUAUAAACUGAA AUCC	482
NR1H3-1217-1237	Artificial Sequence	27 mer antisense strand	AAAGUUUUCCCGGUUAUAAACUG AAAUC	483
NR1H3-1218-1238	Artificial Sequence	27 mer antisense strand	CAAAGUCUUCCCGGUUAUAAACUG AAAU	484
NR1H3-1219-1239	Artificial Sequence	27 mer antisense strand	GCAAAUUCUUCCCGGUUAUAACU GAAA	485
NR1H3-1220-1240	Artificial Sequence	27 mer antisense strand	GGCAAUGUCUUCCCGGUUAUAAC UGAA	486
NR1H3-1222-1242	Artificial Sequence	27 mer antisense strand	UUGGCUAAGUCUUCCCGGUUAUA ACUG	487
NR1H3-1223-1243	Artificial Sequence	27 mer antisense strand	UUUGGUAAGUCUUCCCGGUUA UAACU	488
NR1H3-1224-1244	Artificial Sequence	27 mer antisense strand	CUUUGUCAAGUCUUCCCGGUUA UAAC	489

NR1H3-1225-1245	Artificial Sequence	27 mer antisense strand	GCUUUUGCAAAGUCUUCCCCGGUU AUAA	490
NR1H3-1226-1246	Artificial Sequence	27 mer antisense strand	UGC UUUGGCAAAGUCUUCCCCGGU UAUA	491
NR1H3-1227-1247	Artificial Sequence	27 mer antisense strand	CUGCUUUGGCAAAGUCUUCCCCGG UUAU	492
NR1H3-1228-1248	Artificial Sequence	27 mer antisense strand	CCUGCUUUGGCAAAGUCUUCCCCG GUUA	493
NR1H3-1229-1249	Artificial Sequence	27 mer antisense strand	CCCUGUUUUGGCAAAGUCUUCCC GG UU	494
NR1H3-1232-1252	Artificial Sequence	27 mer antisense strand	CAGCCUUGC UUUGGCAAAGUCUU CCGG	495
NR1H3-1233-1253	Artificial Sequence	27 mer antisense strand	GCAGCUCUGCUUUGGCAAAGUCU UCCC	496
NR1H3-1234-1254	Artificial Sequence	27 mer antisense strand	UGCAGUCCUGCUUUGGCAAAGUC UCC	497
NR1H3-1235-1255	Artificial Sequence	27 mer antisense strand	UUGCAUCCCUGCUUUGGCAAAGU CUUC	498
NR1H3-1236-1256	Artificial Sequence	27 mer antisense strand	CUUGCUGCCCUGCUUUGGCAAAG UCUU	499
NR1H3-1237-1257	Artificial Sequence	27 mer antisense strand	ACUUGUAGCCCUGCUUUGGCAAA GUCU	500
NR1H3-1238-1258	Artificial Sequence	27 mer antisense strand	CACUUUCAGCCCUGCUUUGGCAA AGUC	501
NR1H3-1241-1261	Artificial Sequence	27 mer antisense strand	UUCCA UUUGCAGCCCUGCUUUGG CAAA	502
NR1H3-1242-1262	Artificial Sequence	27 mer antisense strand	AUUCCUCUUGCAGCCCUGCUUUG GCAA	503

NR1H3-1243-1263	Artificial Sequence	27 mer antisense strand	AAUUCUACUUGCAGCCCUGCUUU GGCA	504
NR1H3-1244-1264	Artificial Sequence	27 mer antisense strand	GAAUUUCACUUGCAGCCCUGCUU UGGC	505
NR1H3-1245-1265	Artificial Sequence	27 mer antisense strand	UGAAUUCCACUUGCAGCCCUGCU UUGG	506
NR1H3-1246-1266	Artificial Sequence	27 mer antisense strand	AUGAAUUCCACUUGCAGCCCUGC UUUG	507
NR1H3-1247-1267	Artificial Sequence	27 mer antisense strand	GAUGAUUUCCACUUGCAGCCCUG CUUU	508
NR1H3-1248-1268	Artificial Sequence	27 mer antisense strand	UGAUGUAUUCCACUUGCAGCCCU GCUU	509
NR1H3-1250-1270	Artificial Sequence	27 mer antisense strand	GUUGAUGAAUUCCACUUGCAGCC CUGC	510
NR1H3-1251-1271	Artificial Sequence	27 mer antisense strand	GGUUGUUGAAUUCCACUUGCAGC CCUG	511
NR1H3-1252-1272	Artificial Sequence	27 mer antisense strand	GGGUUUAUGAAUUCCACUUGCA GCCCU	512
NR1H3-1253-1273	Artificial Sequence	27 mer antisense strand	GGGGUUGAUGAAUUCCACUUGC AGCCC	513
NR1H3-1256-1276	Artificial Sequence	27 mer antisense strand	GAUGGUGUUGAUGAAUUCCACU UGCAG	514
NR1H3-1258-1278	Artificial Sequence	27 mer antisense strand	AAGAUUGGGUUGAUGAAUUCCA CUUGC	515
NR1H3-1259-1279	Artificial Sequence	27 mer antisense strand	GAAGAUGGGGUUGAUGAAUUCC ACUUG	516
NR1H3-1261-1281	Artificial Sequence	27 mer antisense strand	UCGAAUAUGGGGUUGAUGAAU CCACU	517

NR1H3-1262-1282	Artificial Sequence	27 mer antisense strand	CUCGAUGAUGGGGUUGAUGAAU UCCAC	518
NR1H3-1265-1285	Artificial Sequence	27 mer antisense strand	GAACUUGAAGAUGGGGUUGAUG AAUUC	519
NR1H3-1266-1286	Artificial Sequence	27 mer antisense strand	AGAACUCGAAGAUGGGGUUGAU GAAUU	520
NR1H3-1267-1287	Artificial Sequence	27 mer antisense strand	GAGAAUUCGAAGAUGGGGUUGA UGAAU	521
NR1H3-1268-1288	Artificial Sequence	27 mer antisense strand	GGAGAUCUCGAAGAUGGGGUUG AUGAA	522
NR1H3-1269-1289	Artificial Sequence	27 mer antisense strand	UGGAGUACUCGAAGAUGGGGUU GAUGA	523
NR1H3-1270-1290	Artificial Sequence	27 mer antisense strand	CUGGAUAACUCGAAGAUGGGGU UGAUG	524
NR1H3-1271-1291	Artificial Sequence	27 mer antisense strand	CCUGGUGAACUCGAAGAUGGGG UUGAU	525
NR1H3-1272-1292	Artificial Sequence	27 mer antisense strand	CCCUGUAGAACUCGAAGAUGGGG UUGA	526
NR1H3-1273-1293	Artificial Sequence	27 mer antisense strand	GCCCUUGAGAACUCGAAGAUGGG GUUG	527
NR1H3-1275-1295	Artificial Sequence	27 mer antisense strand	UGGCCUUGGAGAACUCGAAGAU GGGGU	528
NR1H3-1276-1296	Artificial Sequence	27 mer antisense strand	AUGGCUCUGGAGAACUCGAAGA UGGGG	529
NR1H3-1277-1297	Artificial Sequence	27 mer antisense strand	CAUGGUCCUGGAGAACUCGAAGA UGGG	530
NR1H3-1278-1298	Artificial Sequence	27 mer antisense strand	UCAUGUCCCUGGAGAACUCGAAG AUGG	531

NR1H3-1279-1299	Artificial Sequence	27 mer antisense strand	UUCAUUGCCCUGGAGAACUCGAA GAUG	532
NR1H3-1280-1300	Artificial Sequence	27 mer antisense strand	AUUCAUGGCCCUGGAGAACUCGA AGAU	533
NR1H3-1281-1301	Artificial Sequence	27 mer antisense strand	CAUUCUUGGCCCUGGAGAACUCG AAGA	534
NR1H3-1282-1302	Artificial Sequence	27 mer antisense strand	UCAUUUAUGGCCCUGGAGAACUC GAAG	535
NR1H3-1283-1303	Artificial Sequence	27 mer antisense strand	CUCAUUCAUGGCCCUGGAGAACU CGAA	536
NR1H3-1284-1304	Artificial Sequence	27 mer antisense strand	GCUCAUUCAUGGCCCUGGAGAAC UCGA	537
NR1H3-1285-1305	Artificial Sequence	27 mer antisense strand	AGCUCUUUCAUGGCCCUGGAGAA CUCG	538
NR1H3-1286-1306	Artificial Sequence	27 mer antisense strand	CAGCUUAUUCAUGGCCCUGGAGA ACUC	539
NR1H3-1288-1308	Artificial Sequence	27 mer antisense strand	UGCAGUUCAUUCAUGGCCCUGGA GAAC	540
NR1H3-1289-1309	Artificial Sequence	27 mer antisense strand	UUGCAUCUCAUUCAUGGCCCUGG AGAA	541
NR1H3-1290-1310	Artificial Sequence	27 mer antisense strand	GUUGCUGCUCAUUCAUGGCCCUG GAGA	542
NR1H3-1291-1311	Artificial Sequence	27 mer antisense strand	AGUUGUAGCUCAUUCAUGGCCC UGAG	543
NR1H3-1292-1312	Artificial Sequence	27 mer antisense strand	GAGUUUCAGCUCAUUCAUGGCCC UGGA	544
NR1H3-1293-1313	Artificial Sequence	27 mer antisense strand	UGAGUUGCAGCUCAUUCAUGGCC CUGG	545

NR1H3-1294-1314	Artificial Sequence	27 mer antisense strand	UUGAGUUGCAGCUCAUUCAUGGC CCUG	546
NR1H3-1295-1315	Artificial Sequence	27 mer antisense strand	AUUGAUUUGCAGCUCAUUCAUG GCCCU	547
NR1H3-1296-1316	Artificial Sequence	27 mer antisense strand	CAUUGUGUUGCAGCUCAUUCAUG GCCC	548
NR1H3-1297-1317	Artificial Sequence	27 mer antisense strand	UCAUUUAGUUGCAGCUCAUUCAU GGCC	549
NR1H3-1338-1358	Artificial Sequence	27 mer antisense strand	CAGAGUAGAUGCUGAUAGCAAU GAGCA	550
NR1H3-1339-1359	Artificial Sequence	27 mer antisense strand	GCAGAUAGAUGCUGAUAGCAA UGAGC	551
NR1H3-1340-1360	Artificial Sequence	27 mer antisense strand	UGCAGUGAAGAUGCUGAUAGCA AUGAG	552
NR1H3-1341-1361	Artificial Sequence	27 mer antisense strand	CUGCAUAGAAGAUGCUGAUAGC AAUGA	553
NR1H3-1342-1362	Artificial Sequence	27 mer antisense strand	UCUGCUGAGAAGAUGCUGAUAG CAAUG	554
NR1H3-1343-1363	Artificial Sequence	27 mer antisense strand	GUCUGUAGAGAAGAUGCUGAUA GCAAU	555
NR1H3-1344-1364	Artificial Sequence	27 mer antisense strand	GGUCUUCAGAGAAGAUGCUGAU AGCAA	556
NR1H3-1345-1365	Artificial Sequence	27 mer antisense strand	CGGUCUGCAGAGAAGAUGCUGA UAGCA	557
NR1H3-1346-1366	Artificial Sequence	27 mer antisense strand	CCGGUUUGCAGAGAAGAUGCUG AUAGC	558
NR1H3-1347-1367	Artificial Sequence	27 mer antisense strand	GCCGGUCUGCAGAGAAGAUGCUG AUAG	559

NR1H3-1377-1443	Artificial Sequence	27 mer antisense strand	UCUCUUCCUGGAGCUGGUCCUGC ACGU	560
NR1H3-1379-1445	Artificial Sequence	27 mer antisense strand	CCUCUUUACCUGGAGCUGGUCCU GCAC	561
NR1H3-1383-1449	Artificial Sequence	27 mer antisense strand	GCAGCUUCUCUACCUGGAGCUGG UCCU	562
NR1H3-1384-1450	Artificial Sequence	27 mer antisense strand	UGCAGUCUCUCUACCUGGAGCUG GUCC	563
NR1H3-1385-1451	Artificial Sequence	27 mer antisense strand	CUGCAUCCUCUCUACCUGGAGCU GGUC	564
NR1H3-1387-1453	Artificial Sequence	27 mer antisense strand	UGCUGUAGCCUCUCUACCUGGAG CUGG	565
NR1H3-1388-1454	Artificial Sequence	27 mer antisense strand	GUGCUUCAGCCUCUCUACCUGGA GCUG	566
NR1H3-1391-1457	Artificial Sequence	27 mer antisense strand	UGUGUUCUGCAGCCUCUCUACCU GGAG	567
NR1H3-1393-1459	Artificial Sequence	27 mer antisense strand	UAUGUUUGCUGCAGCCUCUCUAC CUGG	568
NR1H3-1394-1460	Artificial Sequence	27 mer antisense strand	AUAUGUGUGCUGCAGCCUCUCUA CCUG	569
NR1H3-1395-1461	Artificial Sequence	27 mer antisense strand	CAUAUUUGUGCUGCAGCCUCUCU ACCU	570
NR1H3-1396-1462	Artificial Sequence	27 mer antisense strand	ACAUAUGUGUGCUGCAGCCUCUC UACC	571
NR1H3-1397-1463	Artificial Sequence	27 mer antisense strand	CACAUUUGUGUGCUGCAGCCUCU CUAC	572
NR1H3-1398-1464	Artificial Sequence	27 mer antisense strand	CCACAUAUGUGUGCUGCAGCCUC UCUA	573

NR1H3-1399-1465	Artificial Sequence	27 mer antisense strand	UCCACUUAUGUGUGCUGCAGCCU CUCU	574
NR1H3-1400-1466	Artificial Sequence	27 mer antisense strand	UCCAUUAUAUGUGUGCUGCAGCC UCUC	575
NR1H3-1401-1467	Artificial Sequence	27 mer antisense strand	CUUCCUCAUAUGUGUGCUGCAGC CUCU	576
NR1H3-1402-1468	Artificial Sequence	27 mer antisense strand	GCUUCUACAUAUGUGUGCUGCAG CCUC	577
NR1H3-1403-1469	Artificial Sequence	27 mer antisense strand	GGCUUUCACAUAUGUGUGCUGCA GCCU	578
NR1H3-1404-1470	Artificial Sequence	27 mer antisense strand	GGGCUUCCACAUAUGUGUGCUGC AGCC	579
NR1H3-1406-1472	Artificial Sequence	27 mer antisense strand	CAGGGUUUCCACAUAUGUGUGCU GCAG	580
NR1H3-1407-1473	Artificial Sequence	27 mer antisense strand	GCAGGUCUCCACAUAUGUGUGC UGCA	581
NR1H3-1408-1474	Artificial Sequence	27 mer antisense strand	UGCAGUGCUUCCACAUAUGUGUG CUGC	582
NR1H3-1410-1476	Artificial Sequence	27 mer antisense strand	CAUGCUGGGCUUCCACAUAUGUG UGCU	583
NR1H3-1411-1477	Artificial Sequence	27 mer antisense strand	GCAUGUAGGGCUUCCACAUAUGU GUGC	584
NR1H3-1412-1478	Artificial Sequence	27 mer antisense strand	GGCAUUCAGGGCUUCCACAUAUG UGUG	585
NR1H3-1413-1479	Artificial Sequence	27 mer antisense strand	AGGCAUGCAGGGCUUCCACAUAU GUGU	586
NR1H3-1414-1480	Artificial Sequence	27 mer antisense strand	UAGGCUUGCAGGGCUUCCACAUA UGUG	587

NR1H3-1415-1481	Artificial Sequence	27 mer antisense strand	GUAGGUAUGCAGGGCUUCCACAU AUGU	588
NR1H3-1416-1482	Artificial Sequence	27 mer antisense strand	CGUAGUCAUGCAGGGCUUCCACA UAUG	589
NR1H3-1417-1483	Artificial Sequence	27 mer antisense strand	ACGUAUGCAUGCAGGGCUUCCAC AUAU	590
NR1H3-1418-1484	Artificial Sequence	27 mer antisense strand	GACGUUGGCAUGCAGGGCUUCCA CAUA	591
NR1H3-1419-1485	Artificial Sequence	27 mer antisense strand	AGACGUAGGCAUGCAGGGCUUCC ACAU	592
NR1H3-1420-1486	Artificial Sequence	27 mer antisense strand	GAGACUUAGGCAUGCAGGGCUUC CACA	593
NR1H3-1421-1487	Artificial Sequence	27 mer antisense strand	GGAGAUGUAGGCAUGCAGGGCU UCCAC	594
NR1H3-1422-1488	Artificial Sequence	27 mer antisense strand	UGGAGUCGUAGGCAUGCAGGGC UUCCA	595
NR1H3-1423-1489	Artificial Sequence	27 mer antisense strand	AUGGAUACGUAGGCAUGCAGGG CUUCC	596
NR1H3-1424-1490	Artificial Sequence	27 mer antisense strand	GAUGGUGACGUAGGCAUGCAGG GCUUC	597
NR1H3-1425-1491	Artificial Sequence	27 mer antisense strand	GGAUGUAGACGUAGGCAUGCAG GGC UU	598
NR1H3-1426-1492	Artificial Sequence	27 mer antisense strand	UGGAUUGAGACGUAGGCAUGCA GGGCU	599
NR1H3-1427-1493	Artificial Sequence	27 mer antisense strand	GUGGAUGGAGACGUAGGCAUGC AGGGC	600
NR1H3-1428-1494	Artificial Sequence	27 mer antisense strand	GGUGGUUGGAGACGUAGGCAUG CAGGG	601

NR1H3-1429-1495	Artificial Sequence	27 mer antisense strand	UGGUGUAUGGAGACGUAGGCAU GCAGG	602
NR1H3-1430-1496	Artificial Sequence	27 mer antisense strand	AUGGUUGAUGGAGACGUAGGCA UGCAG	603
NR1H3-1431-1497	Artificial Sequence	27 mer antisense strand	GAUGGUGGAUGGAGACGUAGGC AUGCA	604
NR1H3-1432-1498	Artificial Sequence	27 mer antisense strand	GGAUGUUGGAUGGAGACGUAGG CAUGC	605
NR1H3-1433-1499	Artificial Sequence	27 mer antisense strand	GGGAUUGUGGAUGGAGACGUAG GCAUG	606
NR1H3-1434-1500	Artificial Sequence	27 mer antisense strand	GGGGAUGGUGGAUGGAGACGUA GGCAU	607
NR1H3-1435-1501	Artificial Sequence	27 mer antisense strand	UGGGGUUGGUGGAUGGAGACGU AGGCA	608
NR1H3-1436-1502	Artificial Sequence	27 mer antisense strand	AUGGGUAUGGUGGAUGGAGACG UAGGC	609
NR1H3-1437-1503	Artificial Sequence	27 mer antisense strand	CAUGGUGAUGGUGGAUGGAGAC GUAGG	610
NR1H3-1438-1504	Artificial Sequence	27 mer antisense strand	UCAUGUGGAUGGUGGAUGGAGA CGUAG	611
NR1H3-1439-1505	Artificial Sequence	27 mer antisense strand	GUCAUUGGGAUGGUGGAUGGAG ACGUA	612
NR1H3-1440-1506	Artificial Sequence	27 mer antisense strand	GGUCAUGGGGAUGGUGGAUGGA GACGU	613
NR1H3-1442-1508	Artificial Sequence	27 mer antisense strand	UCGGUUAUGGGGAUGGUGGAUG GAGAC	614
NR1H3-1443-1509	Artificial Sequence	27 mer antisense strand	GUCGGUCAUGGGGAUGGUGGAU GGAGA	615

NR1H3-1444-1510	Artificial Sequence	27 mer antisense strand	AGUCGUUCAUGGGGAUGGUGGAUGGAG	616
NR1H3-1445-1511	Artificial Sequence	27 mer antisense strand	CAGUCUGUCAUGGGGAUGGUGGAUGGA	617
NR1H3-1446-1512	Artificial Sequence	27 mer antisense strand	UCAGUUGGUCAUGGGGAUGGUGGAUGG	618
NR1H3-1447-1513	Artificial Sequence	27 mer antisense strand	AUCAGUCGGUCAUGGGGAUGGUGGAUG	619
NR1H3-1448-1514	Artificial Sequence	27 mer antisense strand	CAUCAUUCGGUCAUGGGGAUGGUGGAU	620
NR1H3-1449-1515	Artificial Sequence	27 mer antisense strand	ACAUCUGUCGGUCAUGGGGAUGGUGGA	621
NR1H3-1450-1516	Artificial Sequence	27 mer antisense strand	AACAUUAGUCGGUCAUGGGGAUGGUGG	622
NR1H3-1451-1517	Artificial Sequence	27 mer antisense strand	GAACAUCAGUCGGUCAUGGGGAUGGUG	623
NR1H3-1452-1518	Artificial Sequence	27 mer antisense strand	GGAACUUCAGUCGGUCAUGGGGAUGGU	624
NR1H3-1453-1519	Artificial Sequence	27 mer antisense strand	GGGAUAUCAGUCGGUCAUGGGGAUGG	625
NR1H3-1454-1520	Artificial Sequence	27 mer antisense strand	UGGGAUCAUCAGUCGGUCAUGGGAUG	626
NR1H3-1455-1521	Artificial Sequence	27 mer antisense strand	GUGGGUACAUCAGUCGGUCAUGGGGAU	627
NR1H3-1456-1522	Artificial Sequence	27 mer antisense strand	CGUGGUAACAUCAGUCGGUCAUGGGGA	628
NR1H3-1457-1523	Artificial Sequence	27 mer antisense strand	CCGUGUGAACAUCAGUCGGUCAUGGGG	629

NR1H3-1459-1525	Artificial Sequence	27 mer antisense strand	AUCCGUGGGAACAUCAGUCGGUC AUGG	630
NR1H3-1460-1526	Artificial Sequence	27 mer antisense strand	CAUCCUUGGGAACAUCAGUCGGU CAUG	631
NR1H3-1461-1527	Artificial Sequence	27 mer antisense strand	GCAUCUGUGGGAACAUCAGUCGG UCAU	632
NR1H3-1462-1528	Artificial Sequence	27 mer antisense strand	AGCAUUCGUGGGAACAUCAGUCG GUCA	633
NR1H3-1463-1529	Artificial Sequence	27 mer antisense strand	UAGCAUCCGUGGGAACAUCAGUC GGUC	634
NR1H3-1465-1531	Artificial Sequence	27 mer antisense strand	AUUAGUAUCCGUGGGAACAUCA GUCGG	635
NR1H3-1466-1532	Artificial Sequence	27 mer antisense strand	CAUUAUCAUCCGUGGGAACAUCA GUCG	636
NR1H3-1468-1534	Artificial Sequence	27 mer antisense strand	UUCAUUAGCAUCCGUGGGAACAU CAGU	637
NR1H3-1469-1535	Artificial Sequence	27 mer antisense strand	UUUCAUUAGCAUCCGUGGGAACA UCAG	638
NR1H3-1471-1537	Artificial Sequence	27 mer antisense strand	AGUUUUUUUAGCAUCCGUGGGA ACAUC	639
NR1H3-1472-1538	Artificial Sequence	27 mer antisense strand	CAGUUUCAUUAGCAUCCGUGGGA ACAU	640
NR1H3-1473-1539	Artificial Sequence	27 mer antisense strand	CCAGUUUCAUUAGCAUCCGUGGG AACA	641
NR1H3-1474-1540	Artificial Sequence	27 mer antisense strand	ACCAGUUUCAUUAGCAUCCGUGG GAAC	642
NR1H3-1475-1541	Artificial Sequence	27 mer antisense strand	CACCAUUUUUCAUUAGCAUCCGUG GGAA	643

NR1H3-1476-1542	Artificial Sequence	27 mer antisense strand	UCACCUGUUUCAUUAGCAUCCGU GGGA	644
NR1H3-1477-1543	Artificial Sequence	27 mer antisense strand	CUCACUAGUUUCAUUAGCAUCCG UGGG	645
NR1H3-1478-1544	Artificial Sequence	27 mer antisense strand	GCUCAUCAGUUUCAUUAGCAUCC GUGG	646
NR1H3-1479-1545	Artificial Sequence	27 mer antisense strand	GGCUCUCCAGUUUCAUUAGCAUC CGUG	647
NR1H3-1480-1546	Artificial Sequence	27 mer antisense strand	AGGCUUACCAGUUUCAUUAGCAU CCGU	648
NR1H3-1481-1547	Artificial Sequence	27 mer antisense strand	GAGGCUCACCAGUUUCAUUAGCA UCCG	649
NR1H3-1483-1549	Artificial Sequence	27 mer antisense strand	CGGAGUCUCACCAGUUUCAUUAG CAUC	650
NR1H3-1484-1550	Artificial Sequence	27 mer antisense strand	CCGGAUGCUCACCAGUUUCAUUA GCAU	651
NR1H3-1485-1551	Artificial Sequence	27 mer antisense strand	UCCGGUGGCUCACCAGUUUCAUU AGCA	652
NR1H3-1486-1552	Artificial Sequence	27 mer antisense strand	GUCCGUAGGCUCACCAGUUUCAU UAGC	653
NR1H3-1487-1553	Artificial Sequence	27 mer antisense strand	GGUCCUGAGGCUCACCAGUUUCA UUAG	654
NR1H3-1488-1554	Artificial Sequence	27 mer antisense strand	GGGUCUGGAGGCUCACCAGUUUC AUUA	655
NR1H3-1489-1555	Artificial Sequence	27 mer antisense strand	AGGGUUCGGAGGCUCACCAGUUU CAUU	656
NR1H3-1491-1557	Artificial Sequence	27 mer antisense strand	UCAGGUUCCGGAGGCUCACCAGU UUCA	657

NR1H3-1492-1558	Artificial Sequence	27 mer antisense strand	CUCAGUGUCCGGAGGCUCACCAGUUUC	658
NR1H3-1494-1560	Artificial Sequence	27 mer antisense strand	UGCUCUGGGUCCGGAGGCUCACCAGUU	659
NR1H3-1505-1571	Artificial Sequence	27 mer antisense strand	UGAGUUGACGCUGCUCAGGGUCCGGAG	660
NR1H3-1507-1573	Artificial Sequence	27 mer antisense strand	UCUGAUUGGACGCUGCUCAGGGUCCGG	661
NR1H3-1508-1574	Artificial Sequence	27 mer antisense strand	CUCUGUGUGGACGCUGCUCAGGGUCCG	662
NR1H3-1509-1575	Artificial Sequence	27 mer antisense strand	GCUCUUAGUGGACGCUGCUCAGGGUCC	663
NR1H3-1510-1576	Artificial Sequence	27 mer antisense strand	UGCUCUGAGUGGACGCUGCUCAGGGUC	664
NR1H3-1511-1577	Artificial Sequence	27 mer antisense strand	UUGCUUUGAGUGGACGCUGCUCAGGGU	665
NR1H3-1512-1578	Artificial Sequence	27 mer antisense strand	CUUGCUCUGAGUGGACGCUGCUCAGGG	666
NR1H3-1513-1579	Artificial Sequence	27 mer antisense strand	ACUUGUUCUGAGUGGACGCUGCUCAGG	667
NR1H3-1514-1580	Artificial Sequence	27 mer antisense strand	CACUUUCUCUGAGUGGACGCUGCUCAG	668
NR1H3-1515-1581	Artificial Sequence	27 mer antisense strand	ACACUUGCUCUGAGUGGACGCUGCUCAC	669
NR1H3-1516-1582	Artificial Sequence	27 mer antisense strand	AACACUUGCUCUGAGUGGACGCUGCUC	670
NR1H3-1517-1583	Artificial Sequence	27 mer antisense strand	AAACAUUUGCUCUGAGUGGACGCUGCUC	671

NR1H3-1518-1584	Artificial Sequence	27 mer antisense strand	CAAACUCUUGCUCUGAGUGGACG CUGC	672
NR1H3-1519-1585	Artificial Sequence	27 mer antisense strand	GCAAAUACUUGCUCUGAGUGGAC GCUG	673
NR1H3-1520-1586	Artificial Sequence	27 mer antisense strand	UGCAAUCACUUGCUCUGAGUGGA CGCU	674
NR1H3-1521-1587	Artificial Sequence	27 mer antisense strand	GUGCAUACACUUGCUCUGAGUGG ACGC	675
NR1H3-1522-1588	Artificial Sequence	27 mer antisense strand	AGUGCUAACACUUGCUCUGAGUG GACG	676
NR1H3-1523-1589	Artificial Sequence	27 mer antisense strand	CAGUGUAAACACUUGCUCUGAGU GGAC	677
NR1H3-1525-1591	Artificial Sequence	27 mer antisense strand	CGCAGUGCAAACACUUGCUCUGA GUGG	678
NR1H3-1526-1592	Artificial Sequence	27 mer antisense strand	ACGCAUUGCAAACACUUGCUCUG AGUG	679
NR1H3-1527-1593	Artificial Sequence	27 mer antisense strand	GACGCUGUGCAAACACUUGCUCU GAGU	680
NR1H3-1528-1594	Artificial Sequence	27 mer antisense strand	AGACGUAGUGCAAACACUUGCUC UGAG	681
NR1H3-1529-1595	Artificial Sequence	27 mer antisense strand	CAGACUCAGUGCAAACACUUGCU CUGA	682
NR1H3-1530-1596	Artificial Sequence	27 mer antisense strand	GCAGAUGCAGUGCAAACACUUGC UCUG	683
NR1H3-1531-1597	Artificial Sequence	27 mer antisense strand	UGCAGUCGCAGUGCAAACACUUG CUCU	684
NR1H3-1532-1598	Artificial Sequence	27 mer antisense strand	CUGCAUACGCAGUGCAAACACUU GCUC	685

NR1H3-1533-1599	Artificial Sequence	27 mer antisense strand	CCUGCUGACGCAGUGCAAACACU UGCU	686
NR1H3-1534-1600	Artificial Sequence	27 mer antisense strand	UCCUGUAGACGCAGUGCAAACAC UUGC	687
NR1H3-1535-1601	Artificial Sequence	27 mer antisense strand	GUCCUUCAGACGCAGUGCAAACA CUUG	688
NR1H3-1536-1602	Artificial Sequence	27 mer antisense strand	UGUCCUGCAGACGCAGUGCAAAC ACUU	689
NR1H3-1537-1603	Artificial Sequence	27 mer antisense strand	UUGUCUUGCAGACGCAGUGCAAA CACU	690
NR1H3-1538-1604	Artificial Sequence	27 mer antisense strand	UUUGUUCUGCAGACGCAGUGCAA ACAC	691
NR1H3-1539-1605	Artificial Sequence	27 mer antisense strand	UUUUGUCCUGCAGACGCAGUGCA AACA	692
NR1H3-1540-1606	Artificial Sequence	27 mer antisense strand	UUUUUUUCCUGCAGACGCAGUGC AAAC	693
NR1H3-1541-1607	Artificial Sequence	27 mer antisense strand	CUUUUUGUCCUGCAGACGCAGUG CAAA	694
NR1H3-1542-1608	Artificial Sequence	27 mer antisense strand	GCUUUUUGUCCUGCAGACGCAGU GCAA	695
NR1H3-1543-1609	Artificial Sequence	27 mer antisense strand	AGCUUUUUGUCCUGCAGACGCAG UGCA	696
NR1H3-1544-1610	Artificial Sequence	27 mer antisense strand	GAGCUUUUUGUCCUGCAGACGCA GUGC	697
NR1H3-1545-1611	Artificial Sequence	27 mer antisense strand	GGAGCUUUUUGUCCUGCAGACGC AGUG	698
NR1H3-1546-1612	Artificial Sequence	27 mer antisense strand	GGGAGUUUUUUGUCCUGCAGAC GCAGU	699

NR1H3-1547-1613	Artificial Sequence	27 mer antisense strand	UGGGAUCUUUUUGUCCUGCAGACGCAG	700
NR1H3-1548-1614	Artificial Sequence	27 mer antisense strand	GUGGGUGCUUUUUGUCCUGCAGACGCA	701
NR1H3-1549-1615	Artificial Sequence	27 mer antisense strand	GGUGGUAGCUUUUUGUCCUGCAGACGC	702
NR1H3-1550-1616	Artificial Sequence	27 mer antisense strand	CGGUGUGAGCUUUUUGUCCUGCAGACG	703
NR1H3-1551-1617	Artificial Sequence	27 mer antisense strand	GCGGUUGGAGCUUUUUGUCCUGCAGAC	704
NR1H3-1553-1619	Artificial Sequence	27 mer antisense strand	CAGCGUUGGGAGCUUUUUGUCCUGCAG	705
NR1H3-1554-1620	Artificial Sequence	27 mer antisense strand	GCAGCUGUGGGAGCUUUUUGUCCUGCA	706
NR1H3-1555-1621	Artificial Sequence	27 mer antisense strand	AGCAGUGGUGGGAGCUUUUUGUCCUGC	707
NR1H3-1556-1622	Artificial Sequence	27 mer antisense strand	GAGCAUCGGUGGGAGCUUUUUGUCCUG	708
NR1H3-1558-1624	Artificial Sequence	27 mer antisense strand	GAGAGUAGCGGUGGGAGCUUUUUGUCC	709
NR1H3-1559-1625	Artificial Sequence	27 mer antisense strand	AGAGAUCAGCGGUGGGAGCUUUUUGUC	710
NR1H3-1560-1626	Artificial Sequence	27 mer antisense strand	CAGAGUGCAGCGGUGGGAGCUUUUUGU	711
NR1H3-1561-1627	Artificial Sequence	27 mer antisense strand	UCAGAUAGCAGCGGUGGGAGCUUUUUG	712
NR1H3-1562-1628	Artificial Sequence	27 mer antisense strand	CUCAGUGAGCAGCGGUGGGAGCUUUUU	713

NR1H3-1563-1629	Artificial Sequence	27 mer antisense strand	UCUCAUAGAGCAGCGGUGGGAGC UUUU	714
NR1H3-1564-1630	Artificial Sequence	27 mer antisense strand	AUCUCUGAGAGCAGCGGUGGGA GCUUU	715
NR1H3-1565-1631	Artificial Sequence	27 mer antisense strand	GAUCUUAGAGAGCAGCGGUGGG AGCUU	716
NR1H3-1567-1633	Artificial Sequence	27 mer antisense strand	CAGAUUUCAGAGAGCAGCGGUG GGAGC	717
NR1H3-1569-1635	Artificial Sequence	27 mer antisense strand	CCCAGUUCUCAGAGAGCAGCGGU GGGA	718
NR1H3-1570-1636	Artificial Sequence	27 mer antisense strand	UCCCAUAUCUCAGAGAGCAGCGG UGGG	719
NR1H3-1572-1638	Artificial Sequence	27 mer antisense strand	CAUCCUAGAUCUCAGAGAGCAGC GGUG	720
NR1H3-1573-1639	Artificial Sequence	27 mer antisense strand	ACAUCUCAGAUCUCAGAGAGCAG CGGU	721
NR1H3-1574-1640	Artificial Sequence	27 mer antisense strand	CACAUUCCAGAUCUCAGAGAGCA GCGG	722
NR1H3-1577-1643	Artificial Sequence	27 mer antisense strand	GUGCAUAUCCCAGAUCUCAGAGA GCAG	723
NR1H3-1579-1645	Artificial Sequence	27 mer antisense strand	UCGUGUACAUCCCAGAUCUCAGA GAGC	724
NR1H3-1580-1646	Artificial Sequence	27 mer antisense strand	UUCGUUCACAUCCCAGAUCUCAG AGAG	725
NR1H3-1581-1647	Artificial Sequence	27 mer antisense strand	AUUCGUGCACAUCCCAGAUCUCA GAGA	726
NR1H3-1582-1648	Artificial Sequence	27 mer antisense strand	CAUUCUUGCACAUCCCAGAUCUC AGAG	727

NR1H3-1583-1649	Artificial Sequence	27 mer antisense strand	UCAUUUGUGCACAUCCCAGAUCU CAGA	728
NR1H3-1584-1650	Artificial Sequence	27 mer antisense strand	GUCAUUCGUGCACAUCCCAGAUC UCAG	729
NR1H3-1585-1651	Artificial Sequence	27 mer antisense strand	AGUCAUUCGUGCACAUCCCAGAU CUCA	730
NR1H3-1586-1652	Artificial Sequence	27 mer antisense strand	CAGUCUUUCGUGCACAUCCCAGA UCUC	731
NR1H3-1587-1653	Artificial Sequence	27 mer antisense strand	ACAGUUAUUCGUGCACAUCCCAG AUCU	732
NR1H3-1588-1654	Artificial Sequence	27 mer antisense strand	AACAGUCAUUCGUGCACAUCCCA GAUC	733
NR1H3-1589-1655	Artificial Sequence	27 mer antisense strand	GAACAUUCAUUCGUGCACAUCCC AGAU	734
NR1H3-1590-1656	Artificial Sequence	27 mer antisense strand	AGAACUGUCAUUCGUGCACAUCC CAGA	735
NR1H3-1591-1657	Artificial Sequence	27 mer antisense strand	CAGAAUAGUCAUUCGUGCACAUC CCAG	736
NR1H3-1592-1658	Artificial Sequence	27 mer antisense strand	ACAGAUCAGUCAUUCGUGCACAU CCCA	737
NR1H3-1593-1659	Artificial Sequence	27 mer antisense strand	GACAGUACAGUCAUUCGUGCACA UCCC	738
NR1H3-1656-1720	Artificial Sequence	27 mer antisense strand	UUCCAUUUCUAGGAGGCAGCCAC CAGG	739
NR1H3-1657-1721	Artificial Sequence	27 mer antisense strand	GUUCCUCUUCUAGGAGGCAGCCA CCAG	740
NR1H3-1658-1722	Artificial Sequence	27 mer antisense strand	UGUUCUACUUCUAGGAGGCAGCC ACCA	741

NR1H3-1659-1723	Artificial Sequence	27 mer antisense strand	CUGUUUCACUUCUAGGAGGCAGC CACC	742
NR1H3-1660-1724	Artificial Sequence	27 mer antisense strand	UCUGUUCCACUUCUAGGAGGCAG CCAC	743
NR1H3-1661-1725	Artificial Sequence	27 mer antisense strand	GUCUGUUCCACUUCUAGGAGGCA GCCA	744
NR1H3-1662-1726	Artificial Sequence	27 mer antisense strand	AGUCUUUUCCACUUCUAGGAGGC AGCC	745
NR1H3-1663-1727	Artificial Sequence	27 mer antisense strand	CAGUCUGUUCCACUUCUAGGAGG CAGC	746
NR1H3-1664-1728	Artificial Sequence	27 mer antisense strand	UCAGUUUGUUCCACUUCUAGGAG GCAG	747
NR1H3-1665-1729	Artificial Sequence	27 mer antisense strand	CUCAGUCUGUUCCACUUCUAGGA GGCA	748
NR1H3-1666-1730	Artificial Sequence	27 mer antisense strand	UCUCAUUCUGUUCCACUUCUAGG AGGC	749
NR1H3-1667-1731	Artificial Sequence	27 mer antisense strand	UUCUCUGUCUGUUCCACUUCUAG GAGG	750
NR1H3-1668-1732	Artificial Sequence	27 mer antisense strand	CUUCUUAGUCUGUUCCACUUCUA GGAG	751
NR1H3-1669-1733	Artificial Sequence	27 mer antisense strand	CCUUCUCAGUCUGUUCCACUUCU AGGA	752
NR1H3-1671-1735	Artificial Sequence	27 mer antisense strand	GCCCUUCUCAGUCUGUUCCACUU CUAG	753
NR1H3-1677-1741	Artificial Sequence	27 mer antisense strand	AUGUUUGCCCUUCUCAGUCUGUU CCAC	754
NR1H3-1679-1743	Artificial Sequence	27 mer antisense strand	GAAUGUUUGCCCUUCUCAGUCUG UUCC	755

NR1H3-1680-1744	Artificial Sequence	27 mer antisense strand	GGAAUUUUUGCCCUUCUCAGUCU GUUC	756
NR1H3-1681-1745	Artificial Sequence	27 mer antisense strand	AGGAAUGUUUGCCCUUCUCAGUC UGUU	757
NR1H3-1682-1746	Artificial Sequence	27 mer antisense strand	CAGGAUUGUUUGCCCUUCUCAGU CUGU	758
NR1H3-1683-1747	Artificial Sequence	27 mer antisense strand	CCAGGUAUGUUUGCCCUUCUCAG UCUG	759
NR1H3-1684-1748	Artificial Sequence	27 mer antisense strand	CCCAGUAAUGUUUGCCCUUCUCA GUCU	760
NR1H3-1685-1749	Artificial Sequence	27 mer antisense strand	UCCCAUGAAUGUUUGCCCUUCUC AGUC	761
NR1H3-1686-1750	Artificial Sequence	27 mer antisense strand	CUCCCUGGAAUGUUUGCCCUUCU CAGU	762
NR1H3-1687-1751	Artificial Sequence	27 mer antisense strand	GCUCCUAGGAAUGUUUGCCCUUC UCAG	763
NR1H3-1728-1792	Artificial Sequence	27 mer antisense strand	UUUGAUUCUCUUUUAAUGCCACG GGAG	764
NR1H3-1729-1793	Artificial Sequence	27 mer antisense strand	CUUUGUCUCUCUUUUAAUGCCAC GGGA	765
NR1H3-1730-1794	Artificial Sequence	27 mer antisense strand	CCUUUUACUCUCUUUUAAUGCCA CGGG	766
NR1H3-1731-1795	Artificial Sequence	27 mer antisense strand	CCCUUUGACUCUCUUUUAAUGCC ACGG	767
NR1H3-1732-1796	Artificial Sequence	27 mer antisense strand	ACCCUUUGACUCUCUUUUAAUGC CACG	768
NR1H3-763-783-860	Artificial Sequence	36 mer sense strand	GUGUCCUGUCAGAAGAACAAGCA GCCGAAAGGCUGC	769
NR1H3-765-785-862	Artificial Sequence	36 mer sense strand	GUCCUGUCAGAAGAACAAGCA GCCGAAAGGCUGC	770

NR1H3-767-787-864	Artificial Sequence	36 mer sense strand	CCUGUCAGAAGAACAGAUUCAGCA GCCGAAAGGCUGC	771
NR1H3-768-788-865	Artificial Sequence	36 mer sense strand	CUGUCAGAAGAACAGAUCCAGCA GCCGAAAGGCUGC	772
NR1H3-769-789-866	Artificial Sequence	36 mer sense strand	UGUCAGAAGAACAGAUCCGAGCA GCCGAAAGGCUGC	773
NR1H3-794-814-891	Artificial Sequence	36 mer sense strand	GAAACUGAAGCGGCAAGAGAGC AGCCGAAAGGCUGC	774
NR1H3-1152-1172-1249	Artificial Sequence	36 mer sense strand	GUGAUGCUUCUGGAGACAUAGC AGCCGAAAGGCUGC	775
NR1H3-1189-1209-1286	Artificial Sequence	36 mer sense strand	GGAGUGAGAGUAUCACCUUAGC AGCCGAAAGGCUGC	776
NR1H3-1195-1215-1292	Artificial Sequence	36 mer sense strand	AGAGUAUCACCUUCCUCAAAAGCA GCCGAAAGGCUGC	777
NR1H3-1200-1220-1297	Artificial Sequence	36 mer sense strand	AUCACCUUCCUCAAGGAUUAGCA GCCGAAAGGCUGC	778
NR1H3-1201-1221-1298	Artificial Sequence	36 mer sense strand	UCACCUUCCUCAAGGAUUUAGCA GCCGAAAGGCUGC	779
NR1H3-1202-1222-1299	Artificial Sequence	36 mer sense strand	CACCUUCCUCAAGGAUUUCAGCA GCCGAAAGGCUGC	780
NR1H3-1203-1223-1300	Artificial Sequence	36 mer sense strand	ACCUUCCUCAAGGAUUUCAAGCA GCCGAAAGGCUGC	781
NR1H3-1204-1224-1301	Artificial Sequence	36 mer sense strand	CCUUCCUCAAGGAUUUCAGAGCA GCCGAAAGGCUGC	782
NR1H3-1205-1225-1302	Artificial Sequence	36 mer sense strand	CUUCCUCAAGGAUUUCAGUAGCA GCCGAAAGGCUGC	783
NR1H3-1206-1226-1303	Artificial Sequence	36 mer sense strand	UUCCUCAAGGAUUUCAGUUAGCA GCCGAAAGGCUGC	784
NR1H3-1208-1228-1305	Artificial Sequence	36 mer sense strand	CCUCAAGGAUUUCAGUUAUAGCA GCCGAAAGGCUGC	785
NR1H3-1209-1229-1306	Artificial Sequence	36 mer sense strand	CUCAAGGAUUUCAGUUAUAAGC AGCCGAAAGGCUGC	786
NR1H3-1210-1230-1307	Artificial Sequence	36 mer sense strand	UCAAGGAUUUCAGUUAUAAAGC AGCCGAAAGGCUGC	787
NR1H3-1211-1231-1308	Artificial Sequence	36 mer sense strand	CAAGGAUUUCAGUUAUAACAGC AGCCGAAAGGCUGC	788
NR1H3-1212-1232-1309	Artificial Sequence	36 mer sense strand	AAGGAUUUCAGUUAUAACCAGC AGCCGAAAGGCUGC	789
NR1H3-1213-1233-1310	Artificial Sequence	36 mer sense strand	AGGAUUUCAGUUAUAACCGAGC AGCCGAAAGGCUGC	790
NR1H3-1214-1234-1311	Artificial Sequence	36 mer sense strand	GGAUUUCAGUUAUAACCGGAGC AGCCGAAAGGCUGC	791

NR1H3-1221-1241-1318	Artificial Sequence	36 mer sense strand	AGUUAUAACCGGGAAGACUAGC AGCCGAAAGGCUGC	792
NR1H3-1249-1269-1346	Artificial Sequence	36 mer sense strand	CAGGGCUGCAAGUGGAAUUAGC AGCCGAAAGGCUGC	793
NR1H3-1254-1274-1351	Artificial Sequence	36 mer sense strand	CUGCAAGUGGAAUUCAUCAAGCA GCCGAAAGGCUGC	794
NR1H3-1255-1275-1352	Artificial Sequence	36 mer sense strand	UGCAAGUGGAAUUCAUCAAAGC AGCCGAAAGGCUGC	795
NR1H3-1256-1276-1353	Artificial Sequence	36 mer sense strand	GCAAGUGGAAUUCAUCAAAGCA GCCGAAAGGCUGC	796
NR1H3-1257-1277-1354	Artificial Sequence	36 mer sense strand	CAAGUGGAAUUCAUCAAAGCA GCCGAAAGGCUGC	797
NR1H3-1260-1280-1357	Artificial Sequence	36 mer sense strand	GUGGAAUUCAUCAAACCCCAAGCA GCCGAAAGGCUGC	798
NR1H3-1261-1281-1358	Artificial Sequence	36 mer sense strand	UGGAAUUCAUCAAACCCCAUAGCA GCCGAAAGGCUGC	799
NR1H3-1263-1283-1360	Artificial Sequence	36 mer sense strand	GAAUUCAUCAAACCCCAUCUAGCA GCCGAAAGGCUGC	800
NR1H3-1264-1284-1361	Artificial Sequence	36 mer sense strand	AAUUCAUCAAACCCCAUCUUAGCA GCCGAAAGGCUGC	801
NR1H3-1405-1471-1502	Artificial Sequence	36 mer sense strand	UGCAGCACACAUUAUGUGGAAGCA GCCGAAAGGCUGC	802
NR1H3-1409-1475-1506	Artificial Sequence	36 mer sense strand	GCACACAUUAUGUGGAAGCCAGCA GCCGAAAGGCUGC	803
NR1H3-1458-1524-1555	Artificial Sequence	36 mer sense strand	CAUGACCGACUGAUGUCCAGCA GCCGAAAGGCUGC	804
NR1H3-1464-1530-1561	Artificial Sequence	36 mer sense strand	CGACUGAUGUUCCCACGGAAGCA GCCGAAAGGCUGC	805
NR1H3-1465-1531-1562	Artificial Sequence	36 mer sense strand	GACUGAUGUUCCCACGGAUAGCA GCCGAAAGGCUGC	806
NR1H3-1467-1533-1564	Artificial Sequence	36 mer sense strand	CUGAUGUUCCCACGGAUGCAGCA GCCGAAAGGCUGC	807
NR1H3-1469-1535-1566	Artificial Sequence	36 mer sense strand	GAUGUUCCCACGGAUGCUAAGCA GCCGAAAGGCUGC	808
NR1H3-1470-1536-1567	Artificial Sequence	36 mer sense strand	AUGUUCCCACGGAUGCUGAAAGCA GCCGAAAGGCUGC	809
NR1H3-1480-1546-1577	Artificial Sequence	36 mer sense strand	GGAUGCUGAAUGAAACUGGUAGC AGCCGAAAGGCUGC	810
NR1H3-1482-1548-1579	Artificial Sequence	36 mer sense strand	AUGCUGAAUGAAACUGGUGAAGC AGCCGAAAGGCUGC	811
NR1H3-1524-1590-1621	Artificial Sequence	36 mer sense strand	CACUCAGAGCAAGUGUUUGAGCA GCCGAAAGGCUGC	812

NR1H3-1594-1660-1691	Artificial Sequence	36 mer sense strand	AUGUGCACGAAUGACUGUUAGC AGCCGAAAGGCUGC	813
NR1H3-1595-1661-1692	Artificial Sequence	36 mer sense strand	UGUGCACGAAUGACUGUUCAGCA GCCGAAAGGCUGC	814
NR1H3-1596-1662	Artificial Sequence	36 mer sense strand	GUGCACGAAUGACUGUUCUAGCA GCCGAAAGGCUGC	815
NR1H3-1670-1734	Artificial Sequence	36 mer sense strand	UAGAAGUGGAACAGACUGAAGC AGCCGAAAGGCUGC	816
NR1H3-1672-1736	Artificial Sequence	36 mer sense strand	GAAGUGGAACAGACUGAGAAGC AGCCGAAAGGCUGC	817
NR1H3-1673-1737	Artificial Sequence	36 mer sense strand	AAGUGGAACAGACUGAGAAAGC AGCCGAAAGGCUGC	818
NR1H3-1674-1738	Artificial Sequence	36 mer sense strand	AGUGGAACAGACUGAGAAGAGC AGCCGAAAGGCUGC	819
NR1H3-1675-1739-1766	Artificial Sequence	36 mer sense strand	GUGGAACAGACUGAGAAGGAGC AGCCGAAAGGCUGC	820
NR1H3-1676-1740-1767	Artificial Sequence	36 mer sense strand	UGGAACAGACUGAGAAGGGAGC AGCCGAAAGGCUGC	821
NR1H3-1678-1742-1769	Artificial Sequence	36 mer sense strand	GAACAGACUGAGAAGGGCAAGC AGCCGAAAGGCUGC	822
NR1H3-1207-1227	Artificial Sequence	36 mer sense strand	UCCUCAAGGAUUUCAGUUAAGCA GCCGGGCUGC	823
NR1H3-1220-1240	Artificial Sequence	36 mer sense strand	CAGUUUAUAACCGGGAAGACAGCA GCCGGGCUGC	824
NR1H3-1224-1244	Artificial Sequence	36 mer sense strand	UAUAACCGGGAAGACUUUGAGC AGCCGGGCUGC	825
NR1H3-1244-1264	Artificial Sequence	36 mer sense strand	CAAAGCAGGGCUGCAAGUGAGCA GCCGGGCUGC	826
NR1H3-1252-1272	Artificial Sequence	36 mer sense strand	GGCUGCAAGUGGAAUUCAUAGC AGCCGGGCUGC	827
NR1H3-1259-1279	Artificial Sequence	36 mer sense strand	AGUGGAAUUCAUCAACCCCAGCA GCCGGGCUGC	828
NR1H3-1265-1285	Artificial Sequence	36 mer sense strand	AUUCAUCAACCCCAUCUUCAGCA GCCGGGCUGC	829
NR1H3-1266-1286	Artificial Sequence	36 mer sense strand	UUCAUCAACCCCAUCUUCGAGCA GCCGGGCUGC	830
NR1H3-1429-1495	Artificial Sequence	36 mer sense strand	UGCAUGCCUACGUCUCCAUAAGCA GCCGGGCUGC	831
NR1H3-1433-1499	Artificial Sequence	36 mer sense strand	UGCCUACGUCUCCAUCCACAGCA GCCGGGCUGC	832
NR1H3-1437-1503	Artificial Sequence	36 mer sense strand	UACGUCUCCAUCCACCAUCAGCA GCCGGGCUGC	833
NR1H3-1439-1505	Artificial Sequence	36 mer sense strand	CGUCUCCAUCCACCAUCCCAGCA GCCGGGCUGC	834

NR1H3-1446-1512	Artificial Sequence	36 mer sense strand	AUCCACCAUCCCCAUGACCAGCA GCCGGGCUGC	835
NR1H3-1463-1529	Artificial Sequence	36 mer sense strand	CCGACUGAUGUUCCCACGGAGCA GCCGGGCUGC	836
NR1H3-1475-1541	Artificial Sequence	36 mer sense strand	CCCACGGAUGC UAAUGAAAAGCA GCCGGGCUGC	837
NR1H3-1479-1545	Artificial Sequence	36 mer sense strand	CGGAUGC UAAUGAAACUGGAGC AGCCGGGCUGC	838
NR1H3-1481-1547	Artificial Sequence	36 mer sense strand	GAUGC UAAUGAAACUGGUGAGC AGCCGGGCUGC	839
NR1H3-1485-1551	Artificial Sequence	36 mer sense strand	C UAAUGAAACUGGUGAGCCAGCA GCCGGGCUGC	840
NR1H3-1515-1581	Artificial Sequence	36 mer sense strand	AGCAGCGUCCACUCAGAGCAGCA GCCGGGCUGC	841
NR1H3-1517-1583	Artificial Sequence	36 mer sense strand	CAGCGUCCACUCAGAGCAAAGCA GCCGGGCUGC	842
NR1H3-1518-1584	Artificial Sequence	36 mer sense strand	AGCGUCCACUCAGAGCAAGAGCA GCCGGGCUGC	843
NR1H3-1533-1599	Artificial Sequence	36 mer sense strand	CAAGUGUUUGCACUGCGUCAGCA GCCGGGCUGC	844
NR1H3-1535-1601	Artificial Sequence	36 mer sense strand	AGUGUUUGCACUGCGUCUGAGCA GCCGGGCUGC	845
NR1H3-1545-1611	Artificial Sequence	36 mer sense strand	CUGCGUCUGCAGGACAAAAAGCA GCCGGGCUGC	846
NR1H3-1554-1620	Artificial Sequence	36 mer sense strand	CAGGACAAAAAGCUCCACAGCA GCCGGGCUGC	847
NR1H3-1581-1647	Artificial Sequence	36 mer sense strand	UCUGAGAUCUGGGAUGUGCAGC AGCCGGGCUGC	848
NR1H3-1586-1652	Artificial Sequence	36 mer sense strand	GAUCUGGGAUGUGCACGAAAGC AGCCGGGCUGC	849
NR1H3-1587-1653	Artificial Sequence	36 mer sense strand	AUCUGGGAUGUGCACGAAUAGC AGCCGGGCUGC	850
NR1H3-1588-1654	Artificial Sequence	36 mer sense strand	UCUGGGAUGUGCACGAAUGAGC AGCCGGGCUGC	851
NR1H3-1663-1727	Artificial Sequence	36 mer sense strand	UGCCUCCUAGAAGUGGAACAGCA GCCGGGCUGC	852
NR1H3-1671-1735	Artificial Sequence	36 mer sense strand	AGAAGUGGAACAGACUGAGAGC AGCCGGGCUGC	853
NR1H3-1684-1748	Artificial Sequence	36 mer sense strand	ACUGAGAAGGGCAAACAUUAGC AGCCGGGCUGC	854
NR1H3-1731-1795	Artificial Sequence	36 mer sense strand	GUGGCAU UAAAAGAGAGUCAGC AGCCGGGCUGC	855
NR1H3-1732-1796	Artificial Sequence	36 mer sense strand	UGGCAU UAAAAGAGAGUCAAGC AGCCGGGCUGC	856

NR1H3-763-783-860	Artificial Sequence	22 mer antisense strand	UUGUUCUUCUGACAGGACACGG	857
NR1H3-765-785-862	Artificial Sequence	22 mer antisense strand	UUCUGUUCUUCUGACAGGACGG	858
NR1H3-767-787-864	Artificial Sequence	22 mer antisense strand	UGAUCUGUUCUUCUGACAGGGG	859
NR1H3-768-788-865	Artificial Sequence	22 mer antisense strand	UGGAUCUGUUCUUCUGACAGGG	860
NR1H3-769-789-866	Artificial Sequence	22 mer antisense strand	UCGGAUCUGUUCUUCUGACAGG	861
NR1H3-794-814-891	Artificial Sequence	22 mer antisense strand	UCUCUUGCCGCUUCAGUUUCGG	862
NR1H3-1152-1172-1249	Artificial Sequence	22 mer antisense strand	UAUGUCUCCAGAAGCAUCACGG	863
NR1H3-1189-1209-1286	Artificial Sequence	22 mer antisense strand	UAAGGUGAUACUCUCACUCCGG	864
NR1H3-1195-1215-1292	Artificial Sequence	22 mer antisense strand	UUUGAGGAAGGUGAUACUCUGG	865
NR1H3-1200-1220-1297	Artificial Sequence	22 mer antisense strand	UAAUCCUUGAGGAAGGUGAUGG	866
NR1H3-1201-1221-1298	Artificial Sequence	22 mer antisense strand	UAAAUCCUUGAGGAAGGUGAGG	867
NR1H3-1202-1222-1299	Artificial Sequence	22 mer antisense strand	UGAAAUCCUUGAGGAAGGUGGG	868
NR1H3-1203-1223-1300	Artificial Sequence	22 mer antisense strand	UUGAAAUCCUUGAGGAAGGUGG	869
NR1H3-1204-1224-1301	Artificial Sequence	22 mer antisense strand	UCUGAAAUCCUUGAGGAAGGGG	870

NR1H3-1205-1225-1302	Artificial Sequence	22 mer antisense strand	UACUGAAAUCCUUGAGGAAGGG	871
NR1H3-1206-1226-1303	Artificial Sequence	22 mer antisense strand	U AACUGAAAUCCUUGAGGAAGG	872
NR1H3-1208-1228-1305	Artificial Sequence	22 mer antisense strand	UAUAACUGAAAUCCUUGAGGGG	873
NR1H3-1209-1229-1306	Artificial Sequence	22 mer antisense strand	UUUAUAACUGAAAUCCUUGAGGG	874
NR1H3-1210-1230-1307	Artificial Sequence	22 mer antisense strand	UUUAUAACUGAAAUCCUUGAGG	875
NR1H3-1211-1231-1308	Artificial Sequence	22 mer antisense strand	UGUUAUAACUGAAAUCCUUGGG	876
NR1H3-1212-1232-1309	Artificial Sequence	22 mer antisense strand	UGGUUAUAACUGAAAUCCUUGG	877
NR1H3-1213-1233-1310	Artificial Sequence	22 mer antisense strand	UCGGUUAUAACUGAAAUCCUGG	878
NR1H3-1214-1234-1311	Artificial Sequence	22 mer antisense strand	UCCGGUUAUAACUGAAAUCCGG	879
NR1H3-1221-1241-1318	Artificial Sequence	22 mer antisense strand	UAGUCUUCCCGGUUAUAACUGG	880
NR1H3-1249-1269-1346	Artificial Sequence	22 mer antisense strand	UAAUUCCACUUGCAGCCCUGGG	881
NR1H3-1254-1274-1351	Artificial Sequence	22 mer antisense strand	UUGAUGAAUUCCACUUGCAGGG	882
NR1H3-1255-1275-1352	Artificial Sequence	22 mer antisense strand	UUUGAUGAAUUCCACUUGCAGG	883
NR1H3-1256-1276-1353	Artificial Sequence	22 mer antisense strand	UGUUGAUGAAUUCCACUUGC GG	884

NR1H3-1257-1277-1354	Artificial Sequence	22 mer antisense strand	UGGUUGAUGAAUUCCACUUGGG	885
NR1H3-1260-1280-1357	Artificial Sequence	22 mer antisense strand	UUGGGGUUGAUGAAUUCCACGG	886
NR1H3-1261-1281-1358	Artificial Sequence	22 mer antisense strand	UAUGGGGUUGAUGAAUUCCAGG	887
NR1H3-1263-1283-1360	Artificial Sequence	22 mer antisense strand	UAGAUGGGGUUGAUGAAUUCGG	888
NR1H3-1264-1284-1361	Artificial Sequence	22 mer antisense strand	UAAGAUGGGGUUGAUGAAUUGG	889
NR1H3-1405-1471-1502	Artificial Sequence	22 mer antisense strand	UUCCACAUAUGUGUGCUGCAGG	890
NR1H3-1409-1475-1506	Artificial Sequence	22 mer antisense strand	UGGCUUCCACAUAUGUGUGCGG	891
NR1H3-1458-1524-1555	Artificial Sequence	22 mer antisense strand	UGGAACAUCAGUCGGUCAUGGG	892
NR1H3-1464-1530-1561	Artificial Sequence	22 mer antisense strand	UUCCGUGGGAACAUCAGUCGGG	893
NR1H3-1465-1531-1562	Artificial Sequence	22 mer antisense strand	UAUCCGUGGGAACAUCAGUCGG	894
NR1H3-1467-1533-1564	Artificial Sequence	22 mer antisense strand	UGCAUCCGUGGGAACAUCAGGG	895
NR1H3-1469-1535-1566	Artificial Sequence	22 mer antisense strand	UUAGCAUCCGUGGGAACAUCGG	896
NR1H3-1470-1536-1567	Artificial Sequence	22 mer antisense strand	UUUAGCAUCCGUGGGAACAUGG	897
NR1H3-1480-1546-1577	Artificial Sequence	22 mer antisense strand	UACCAGUUUCAUUAGCAUCCGG	898

NR1H3-1482-1548-1579	Artificial Sequence	22 mer antisense strand	UUCACCAGUUUCAUUAGCAUGG	899
NR1H3-1524-1590-1621	Artificial Sequence	22 mer antisense strand	UCAAACACUUGCUCUGAGUGGG	900
NR1H3-1594-1660-1691	Artificial Sequence	22 mer antisense strand	UAACAGUCAUUCGUGCACAUGG	901
NR1H3-1595-1661-1692	Artificial Sequence	22 mer antisense strand	UGAACAGUCAUUCGUGCACAGG	902
NR1H3-1596-1662	Artificial Sequence	22 mer antisense strand	UAGAACAGUCAUUCGUGCACGG	903
NR1H3-1670-1734	Artificial Sequence	22 mer antisense strand	UUCAGUCUGUUCCACUUCUAGG	904
NR1H3-1672-1736	Artificial Sequence	22 mer antisense strand	UUCUCAGUCUGUUCCACUUCGG	905
NR1H3-1673-1737	Artificial Sequence	22 mer antisense strand	UUUCUCAGUCUGUUCCACUUGG	906
NR1H3-1674-1738	Artificial Sequence	22 mer antisense strand	UCUUCUCAGUCUGUUCCACUGG	907
NR1H3-1675-1739-1766	Artificial Sequence	22 mer antisense strand	UCCUUCUCAGUCUGUUCCACGG	908
NR1H3-1676-1740-1767	Artificial Sequence	22 mer antisense strand	UCCCUUCUCAGUCUGUUCCAGG	909
NR1H3-1678-1742-1769	Artificial Sequence	22 mer antisense strand	UUGCCCUUCUCAGUCUGUUCGG	910
NR1H3-1207-1227	Artificial Sequence	22 mer antisense strand	UUAACUGAAAUCCUUGAGGAGG	911
NR1H3-1220-1240	Artificial Sequence	22 mer antisense strand	UGUCUUCCCGGUUAUAACUGGG	912

NR1H3-1224-1244	Artificial Sequence	22 mer antisense strand	UCAAAGUCUUCCCGGUUAUAGG	913
NR1H3-1244-1264	Artificial Sequence	22 mer antisense strand	UCACUUGCAGCCCUGCUUUGGG	914
NR1H3-1252-1272	Artificial Sequence	22 mer antisense strand	UAUGAAUUCCACUUGCAGCCGG	915
NR1H3-1259-1279	Artificial Sequence	22 mer antisense strand	UGGGGUUGAUGAAUCCACUGG	916
NR1H3-1265-1285	Artificial Sequence	22 mer antisense strand	UGAAGAUGGGGUUGAUGAAUGG	917
NR1H3-1266-1286	Artificial Sequence	22 mer antisense strand	UCGAAGAUGGGGUUGAUGAAGG	918
NR1H3-1429-1495	Artificial Sequence	22 mer antisense strand	UAUGGAGACGUAGGCAUGCAGG	919
NR1H3-1433-1499	Artificial Sequence	22 mer antisense strand	UGUGGAUGGAGACGUAGGCAGG	920
NR1H3-1437-1503	Artificial Sequence	22 mer antisense strand	UGAUGGUGGAUGGAGACGUAGG	921
NR1H3-1439-1505	Artificial Sequence	22 mer antisense strand	UGGGAUGGUGGAUGGAGACGGG	922
NR1H3-1446-1512	Artificial Sequence	22 mer antisense strand	UGGUCAUGGGGAUGGUGGAUGG	923
NR1H3-1463-1529	Artificial Sequence	22 mer antisense strand	UCCGUGGGAACAUCAGUCGGGG	924
NR1H3-1475-1541	Artificial Sequence	22 mer antisense strand	UUUUCAUUAGCAUCCGUGGGGG	925
NR1H3-1479-1545	Artificial Sequence	22 mer antisense strand	UCCAGUUUCAUUAGCAUCCGGG	926

NR1H3-1481-1547	Artificial Sequence	22 mer antisense strand	UCACCAGUUUCAUUAGCAUCGG	927
NR1H3-1485-1551	Artificial Sequence	22 mer antisense strand	UGGCUCACCAGUUUCAUUAGGG	928
NR1H3-1515-1581	Artificial Sequence	22 mer antisense strand	UGCUCUGAGUGGACGCUGCUGG	929
NR1H3-1517-1583	Artificial Sequence	22 mer antisense strand	UUUGCUCUGAGUGGACGCUGGG	930
NR1H3-1518-1584	Artificial Sequence	22 mer antisense strand	UCUUGCUCUGAGUGGACGCUGG	931
NR1H3-1533-1599	Artificial Sequence	22 mer antisense strand	UGACGCAGUGCAAACACUUGGG	932
NR1H3-1535-1601	Artificial Sequence	22 mer antisense strand	UCAGACGCAGUGCAAACACUGG	933
NR1H3-1545-1611	Artificial Sequence	22 mer antisense strand	UUUUUGUCCUGCAGACGCAGGG	934
NR1H3-1554-1620	Artificial Sequence	22 mer antisense strand	UGUGGGAGCUUUUUGUCCUGGG	935
NR1H3-1581-1647	Artificial Sequence	22 mer antisense strand	UGCACAUCCCAGAUCUCAGAGG	936
NR1H3-1586-1652	Artificial Sequence	22 mer antisense strand	UUUCGUGCACAUCCCAGAUCGG	937
NR1H3-1587-1653	Artificial Sequence	22 mer antisense strand	UAUUCGUGCACAUCCCAGAUGG	938
NR1H3-1588-1654	Artificial Sequence	22 mer antisense strand	UCAUUCGUGCACAUCCCAGAGG	939
NR1H3-1663-1727	Artificial Sequence	22 mer antisense strand	UGUUCCACUUCUAGGAGGCAGG	940

NR1H3-1671-1735	Artificial Sequence	22 mer antisense strand	UCUCAGUCUGUCCACUUCUGG	941
NR1H3-1684-1748	Artificial Sequence	22 mer antisense strand	UAAUGUUUGCCCUUCUCAGUGG	942
NR1H3-1731-1795	Artificial Sequence	22 mer antisense strand	UGACUCUCUUUAAUGCCACGG	943
NR1H3-1732-1796	Artificial Sequence	22 mer antisense strand	UUGACUCUCUUUAAUGCCAGG	944
NR1H3-763-783-860	Artificial Sequence	Modified sense strand	[mGs][mU][mG][mU][mC][mC][mU][fG][fU][fC][fA][mG][mA][mA][mG][mA][mA][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	945
NR1H3-765-785-862	Artificial Sequence	Modified sense strand	[mGs][mU][mC][mC][mU][mG][mU][fC][fA][fG][fA][mA][mG][mA][mA][mC][mA][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	946
NR1H3-767-787-864	Artificial Sequence	Modified sense strand	[mCs][mC][mU][mG][mU][mC][mA][fG][fA][fA][fG][mA][mA][mC][mA][mG][mA][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	947
NR1H3-768-788-865	Artificial Sequence	Modified sense strand	[mCs][mU][mG][mU][mC][mA][mG][fA][fA][fG][fA][mA][mC][mA][mG][mA][mU][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	948
NR1H3-769-789-866	Artificial Sequence	Modified sense strand	[mUs][mG][mU][mC][mA][mG][mA][fA][fG][fA][fA][mC][mA][mG][mA][mU][mC][mC][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-	949

			GalNAc][mG][mG][mC][mU][mG][mC]	
NR1H3-794-814-891	Artificial Sequence	Modified sense strand	[mGs][mA][mA][mA][mC][mU][mG][fA][fA][fG][fC][mG][mG][mC][mA][mA][mG][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	950
NR1H3-1152-1172-1249	Artificial Sequence	Modified sense strand	[mGs][mU][mG][mA][mU][mG][mC][fU][fU][fC][fU][mG][mG][mA][mG][mA][mC][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	951
NR1H3-1189-1209-1286	Artificial Sequence	Modified sense strand	[mGs][mG][mA][mG][mU][mG][mA][fG][fA][fG][fU][mA][mU][mC][mA][mC][mC][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	952
NR1H3-1195-1215-1292	Artificial Sequence	Modified sense strand	[mAs][mG][mA][mG][mU][mA][mU][fC][fA][fC][fC][mU][mU][mC][mC][mU][mC][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	953
NR1H3-1200-1220-1297	Artificial Sequence	Modified sense strand	[mAs][mU][mC][mA][mC][mC][mU][fU][fC][fC][fU][mC][mA][mA][mG][mG][mA][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	954
NR1H3-1201-1221-1298	Artificial Sequence	Modified sense strand	[mUs][mC][mA][mC][mC][mU][mU][fC][fC][fU][fC][mA][mA][mG][mG][mA][mU][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	955

NR1H3-1202-1222-1299	Artificial Sequence	Modified sense strand	[mCs][mA][mC][mC][mU][mU][mC][fC][fU][fC][fA][mA][mG][mG][mA][mU][mU][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	956
NR1H3-1203-1223-1300	Artificial Sequence	Modified sense strand	[mAs][mC][mC][mU][mU][mC][mC][fU][fC][fA][fA][mG][mG][mA][mU][mU][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	957
NR1H3-1204-1224-1301	Artificial Sequence	Modified sense strand	[mCs][mC][mU][mU][mC][mC][mU][fC][fA][fA][fG][mG][mA][mU][mU][mU][mC][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	958
NR1H3-1205-1225-1302	Artificial Sequence	Modified sense strand	[mCs][mU][mU][mC][mC][mU][mC][fA][fA][fG][fG][mA][mU][mU][mU][mC][mA][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	959
NR1H3-1206-1226-1303	Artificial Sequence	Modified sense strand	[mUs][mU][mC][mC][mU][mC][mA][fA][fG][fG][fA][mU][mU][mU][mC][mA][mG][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	960
NR1H3-1207-1227	Artificial Sequence	Modified sense strand	[mUs][mC][mC][mU][mC][mA][mA][fG][fG][fA][fU][mU][mU][mC][mA][mG][mU][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	961
NR1H3-1208-1228-1305	Artificial Sequence	Modified sense strand	[mCs][mC][mU][mC][mA][mA][mG][fG][fA][fU][fU][mU][mC][mA][mG][mU][mU][mA][mU][mA][mG][mC][mA]	962

			[mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	
NR1H3-1209-1229-1306	Artificial Sequence	Modified sense strand	[mCs][mU][mC][mA][mA][mG][mG][fA][fU][fU][fU][mC][mA][mG][mU][mU][mA][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	963
NR1H3-1210-1230-1307	Artificial Sequence	Modified sense strand	[mUs][mC][mA][mA][mG][mG][mA][fU][fU][fU][fC][mA][mG][mU][mU][mA][mU][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	964
NR1H3-1211-1231-1308	Artificial Sequence	Modified sense strand	[mCs][mA][mA][mG][mG][mA][mU][fU][fU][fC][fA][mG][mU][mU][mA][mU][mA][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	965
NR1H3-1212-1232-1309	Artificial Sequence	Modified sense strand	[mAs][mA][mG][mG][mA][mU][mU][fU][fC][fA][fG][mU][mU][mA][mU][mA][mA][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	966
NR1H3-1213-1233-1310	Artificial Sequence	Modified sense strand	[mAs][mG][mG][mA][mU][mU][mU][fC][fA][fG][fU][mU][mA][mU][mA][mA][mC][mC][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	967
NR1H3-1214-1234-1311	Artificial Sequence	Modified sense strand	[mGs][mG][mA][mU][mU][mU][mC][fA][fG][fU][fU][mA][mU][mA][mA][mC][mC][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-	968

			GalNAc][mG][mG][mC][mU][mG][mC]	
NR1H3-1220	Artificial Sequence	Modified sense strand	[mCs][mA][mG][mU][mU][mA][mU][fA][fA][fC][fC][mG][mG][mG][mA][mA][mG][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	969
NR1H3-1221-1241-1318	Artificial Sequence	Modified sense strand	[mAs][mG][mU][mU][mA][mU][mA][fA][fC][fC][fG][mG][mG][mA][mA][mG][mA][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	970
NR1H3-1224-1244	Artificial Sequence	Modified sense strand	[mUs][mA][mU][mA][mA][mC][mC][fG][fG][fG][fA][mA][mG][mA][mC][mU][mU][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	971
NR1H3-1244-1264	Artificial Sequence	Modified sense strand	[mCs][mA][mA][mA][mG][mC][mA][fG][fG][fG][fC][mU][mG][mC][mA][mA][mG][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	972
NR1H3-1249-1269-1346	Artificial Sequence	Modified sense strand	[mCs][mA][mG][mG][mG][mC][mU][fG][fC][fA][fA][mG][mU][mG][mG][mA][mA][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	973
NR1H3-1252-1272	Artificial Sequence	Modified sense strand	[mGs][mG][mC][mU][mG][mC][mA][fA][fG][fU][fG][mG][mA][mA][mU][mU][mC][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	974

NR1H3-1254-1274-1351	Artificial Sequence	Modified sense strand	[mCs][mU][mG][mC][mA][mA][mG][fU][fG][fG][fA][mA][mU][mU][mC][mA][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	975
NR1H3-1255-1275-1352	Artificial Sequence	Modified sense strand	[mUs][mG][mC][mA][mA][mG][mU][fG][fG][fA][fA][mU][mU][mC][mA][mU][mC][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	976
NR1H3-1256-1276-1353	Artificial Sequence	Modified sense strand	[mGs][mC][mA][mA][mG][mU][mG][fG][fA][fA][fU][mU][mC][mA][mU][mC][mA][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	977
NR1H3-1257-1277-1354	Artificial Sequence	Modified sense strand	[mCs][mA][mA][mG][mU][mG][mG][fA][fA][fU][fU][mC][mA][mU][mC][mA][mA][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	978
NR1H3-1259	Artificial Sequence	Modified sense strand	[mAs][mG][mU][mG][mG][mA][mA][fU][fU][fC][fA][mU][mC][mA][mA][mC][mC][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	979
NR1H3-1260-1280-1357	Artificial Sequence	Modified sense strand	[mGs][mU][mG][mG][mA][mA][mU][fU][fC][fA][fU][mC][mA][mA][mC][mC][mC][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	980
NR1H3-1261-1281-1358	Artificial Sequence	Modified sense strand	[mUs][mG][mG][mA][mA][mU][mU][fC][fA][fU][fC][mA][mA][mC][mC][mC][mC][mA][mU][mA][mG][mC][mA]	981

			[mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	
NR1H3-1263-1283-1360	Artificial Sequence	Modified sense strand	[mGs][mA][mA][mU][mU][mC][mA][fU][fC][fA][fA][mC][mC][mC][mC][mA][mU][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	982
NR1H3-1264-1284-1361	Artificial Sequence	Modified sense strand	[mAs][mA][mU][mU][mC][mA][mU][fC][fA][fA][fC][mC][mC][mC][mA][mU][mC][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	983
NR1H3-1265-1285	Artificial Sequence	Modified sense strand	[mAs][mU][mU][mC][mA][mU][mC][fA][fA][fC][fC][mC][mC][mA][mU][mC][mU][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	984
NR1H3-1266-1286	Artificial Sequence	Modified sense strand	[mUs][mU][mC][mA][mU][mC][mA][fA][fC][fC][fC][mC][mA][mU][mC][mU][mU][mC][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	985
NR1H3-1405-1471-1502	Artificial Sequence	Modified sense strand	[mUs][mG][mC][mA][mG][mC][mA][fC][fA][fC][fA][mU][mA][mU][mG][mU][mG][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	986
NR1H3-1409-1475-1506	Artificial Sequence	Modified sense strand	[mGs][mC][mA][mC][mA][mC][mA][fU][fA][fU][fG][mU][mG][mG][mA][mA][mG][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-	987

			GalNAc][mG][mG][mC][mU][mG][mC]	
NR1H3-1429-1495	Artificial Sequence	Modified sense strand	[mUs][mG][mC][mA][mU][mG][mC][fC][fU][fA][fC][mG][mU][mC][mU][mC][mC][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	988
NR1H3-1433-1499	Artificial Sequence	Modified sense strand	[mUs][mG][mC][mC][mU][mA][mC][fG][fU][fC][fU][mC][mC][mA][mU][mC][mC][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	989
NR1H3-1437-1503	Artificial Sequence	Modified sense strand	[mUs][mA][mC][mG][mU][mC][mU][fC][fC][fA][fU][mC][mC][mA][mC][mC][mA][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	990
NR1H3-1439-1505	Artificial Sequence	Modified sense strand	[mCs][mG][mU][mC][mU][mC][mC][fA][fU][fC][fC][mA][mC][mC][mA][mU][mC][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	991
NR1H3-1446-1512	Artificial Sequence	Modified sense strand	[mAs][mU][mC][mC][mA][mC][mC][fA][fU][fC][fC][mC][mC][mA][mU][mG][mA][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	992
NR1H3-1458-1524-1555	Artificial Sequence	Modified sense strand	[mCs][mA][mU][mG][mA][mC][mC][fG][fA][fC][fU][mG][mA][mU][mG][mU][mU][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	993

NR1H3-1463-1529	Artificial Sequence	Modified sense strand	[mCs][mC][mG][mA][mC][mU][mG][fA][fU][fG][fU][mU][mC][mC][mC][mA][mC][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	994
NR1H3-1464-1530-1561	Artificial Sequence	Modified sense strand	[mCs][mG][mA][mC][mU][mG][mA][fU][fG][fU][fU][mC][mC][mC][mA][mC][mG][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	995
NR1H3-1465-1531-1562	Artificial Sequence	Modified sense strand	[mGs][mA][mC][mU][mG][mA][mU][fG][fU][fU][fC][mC][mC][mA][mC][mG][mG][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	996
NR1H3-1467-1533-1564	Artificial Sequence	Modified sense strand	[mCs][mU][mG][mA][mU][mG][mU][fU][fC][fC][fC][mA][mC][mG][mG][mA][mU][mG][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	997
NR1H3-1469-1535-1566	Artificial Sequence	Modified sense strand	[mGs][mA][mU][mG][mU][mU][mC][fC][fC][fA][fC][mG][mG][mA][mU][mG][mC][mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	998
NR1H3-1470-1536-1567	Artificial Sequence	Modified sense strand	[mAs][mU][mG][mU][mU][mC][mC][fC][fA][fC][fG][mG][mA][mU][mG][mC][mU][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	999
NR1H3-1475-1541	Artificial Sequence	Modified sense strand	[mCs][mC][mC][mA][mC][mG][mG][fA][fU][fG][fC][mU][mA][mA][mU][mG][mA][mA][mA][mA][mG][mC][mA]	1000

			[mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	
NR1H3-1479-1545	Artificial Sequence	Modified sense strand	[mCs][mG][mG][mA][mU][mG][mC][fU][fA][fA][fU][mG][mA][mA][mA][mC][mU][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1001
NR1H3-1480-1546-1577	Artificial Sequence	Modified sense strand	[mGs][mG][mA][mU][mG][mC][mU][fA][fA][fU][fG][mA][mA][mA][mC][mU][mG][mG][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1002
NR1H3-1481-1547	Artificial Sequence	Modified sense strand	[mGs][mA][mU][mG][mC][mU][mA][fA][fU][fG][fA][mA][mA][mC][mU][mG][mG][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1003
NR1H3-1482-1548-1579	Artificial Sequence	Modified sense strand	[mAs][mU][mG][mC][mU][mA][mA][fU][fG][fA][fA][mA][mC][mU][mG][mG][mU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1004
NR1H3-1485-1551	Artificial Sequence	Modified sense strand	[mCs][mU][mA][mA][mU][mG][mA][fA][fA][fC][fU][mG][mG][mU][mG][mA][mG][mC][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1005
NR1H3-1515-1581	Artificial Sequence	Modified sense strand	[mAs][mG][mC][mA][mG][mC][mG][fU][fC][fC][fA][mC][mU][mC][mA][mG][mA][mG][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-	1006

			GalNAc][mG][mG][mC][mU][mG][mC]	
NR1H3-1517-1583	Artificial Sequence	Modified sense strand	[mCs][mA][mG][mC][mG][mU][mC][fC][fA][fC][fU][mC][mA][mG][mA][mG][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1007
NR1H3-1518-1584	Artificial Sequence	Modified sense strand	[mAs][mG][mC][mG][mU][mC][mC][fA][fC][fU][fC][mA][mG][mA][mG][mC][mA][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1008
NR1H3-1524-1590-1621	Artificial Sequence	Modified sense strand	[mCs][mA][mC][mU][mC][mA][mG][fA][fG][fC][fA][mA][mG][mU][mG][mU][mU][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1009
NR1H3-1533-1599	Artificial Sequence	Modified sense strand	[mCs][mA][mA][mG][mU][mG][mU][fU][fU][fG][fC][mA][mC][mU][mG][mC][mG][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1010
NR1H3-1535-1601	Artificial Sequence	Modified sense strand	[mAs][mG][mU][mG][mU][mU][mU][fG][fC][fA][fC][mU][mG][mC][mG][mU][mC][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1011
NR1H3-1545-1611	Artificial Sequence	Modified sense strand	[mCs][mU][mG][mC][mG][mU][mC][fU][fG][fC][fA][mG][mG][mA][mC][mA][mA][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1012

NR1H3-1554-1620	Artificial Sequence	Modified sense strand	[mCs][mA][mG][mG][mA][mC][mA][fA][fA][fA][fA][mG][mC][mU][mC][mC][mC][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1013
NR1H3-1581-1647	Artificial Sequence	Modified sense strand	[mUs][mC][mU][mG][mA][mG][mA][fU][fC][fU][fG][mG][mG][mA][mU][mG][mU][mG][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1014
NR1H3-1586-1652	Artificial Sequence	Modified sense strand	[mGs][mA][mU][mC][mU][mG][mG][fG][fA][fU][fG][mU][mG][mC][mA][mC][mG][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1015
NR1H3-1587-1653	Artificial Sequence	Modified sense strand	[mAs][mU][mC][mU][mG][mG][mG][fA][fU][fG][fU][mG][mC][mA][mC][mG][mA][mA][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1016
NR1H3-1588-1654	Artificial Sequence	Modified sense strand	[mUs][mC][mU][mG][mG][mG][mA][fU][fG][fU][fG][mC][mA][mC][mG][mA][mA][mU][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1017
NR1H3-1594-1660-1691	Artificial Sequence	Modified sense strand	[mAs][mU][mG][mU][mG][mC][mA][fC][fG][fA][fA][mU][mG][mA][mC][mU][mG][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1018
NR1H3-1595-1661-1692	Artificial Sequence	Modified sense strand	[mUs][mG][mU][mG][mC][mA][mC][fG][fA][fA][fU][mG][mA][mC][mU][mG][mU][mU][mC][mA][mG][mC][mA]	1019

			[mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	
NR1H3-1596-1662	Artificial Sequence	Modified sense strand	[mGs][mU][mG][mC][mA][mC][mG][fA][fA][fU][fG][mA][mC][mU][mG][mU][mU][mC][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1020
NR1H3-1663-1727	Artificial Sequence	Modified sense strand	[mUs][mG][mC][mC][mU][mC][mC][fU][fA][fG][fA][mA][mG][mU][mG][mG][mA][mA][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1021
NR1H3-1670-1734	Artificial Sequence	Modified sense strand	[mUs][mA][mG][mA][mA][mG][mU][fG][fG][fA][fA][mC][mA][mG][mA][mC][mU][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1022
NR1H3-1671-1735	Artificial Sequence	Modified sense strand	[mAs][mG][mA][mA][mG][mU][mG][fG][fA][fA][fC][mA][mG][mA][mC][mU][mG][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1023
NR1H3-1672-1736	Artificial Sequence	Modified sense strand	[mGs][mA][mA][mG][mU][mG][mG][fA][fA][fC][fA][mG][mA][mC][mU][mG][mA][mG][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1024
NR1H3-1673-1737	Artificial Sequence	Modified sense strand	[mAs][mA][mG][mU][mG][mG][mA][fA][fC][fA][fG][mA][mC][mU][mG][mA][mG][mA][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-	1025

			GalNAc][mG][mG][mC][mU][mG][mC]	
NR1H3-1674-1738	Artificial Sequence	Modified sense strand	[mAs][mG][mU][mG][mG][mA][mA][fC][fA][fG][fA][mC][mU][mG][mA][mG][mA][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1026
NR1H3-1675-1739-1766	Artificial Sequence	Modified sense strand	[mGs][mU][mG][mG][mA][mA][mC][fA][fG][fA][fC][mU][mG][mA][mG][mA][mA][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1027
NR1H3-1676-1740-1767	Artificial Sequence	Modified sense strand	[mUs][mG][mG][mA][mA][mC][mA][fG][fA][fC][fU][mG][mA][mG][mA][mA][mG][mG][mG][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1028
NR1H3-1678-1742-1769	Artificial Sequence	Modified sense strand	[mGs][mA][mA][mC][mA][mG][mA][fC][fU][fG][fA][mG][mA][mA][mG][mG][mG][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1029
NR1H3-1684-1748	Artificial Sequence	Modified sense strand	[mAs][mC][mU][mG][mA][mG][mA][fA][fG][fG][fG][mC][mA][mA][mA][mC][mA][mU][mU][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1030
NR1H3-1731-1795	Artificial Sequence	Modified sense strand	[mGs][mU][mG][mG][mC][mA][mU][fU][fA][fA][fA][mA][mG][mA][mG][mA][mG][mU][mC][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1031

NR1H3-1732-1796	Artificial Sequence	Modified sense strand	[mUs][mG][mG][mC][mA][mU][mU][fA][fA][fA][fA][mG][mA][mG][mA][mG][mU][mC][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC]	1032
NR1H3-763-783-860	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fGs][fU][fU][mC][fU][mU][mC][fU][mG][mA][mC][fA][mG][mG][mA][mC][mA][mCs][mGs][mG]	1033
NR1H3-765-785-862	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fCs][fU][fG][mU][fU][mC][mU][fU][mC][mU][mG][fA][mC][mA][mG][mG][mA][mCs][mGs][mG]	1034
NR1H3-767-787-864	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fAs][fU][fC][mU][fG][mU][mU][fC][mU][mU][mC][fU][mG][mA][mC][mA][mG][mGs][mGs][mG]	1035
NR1H3-768-788-865	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fGs][fA][fU][mC][fU][mG][mU][fU][mC][mU][mU][fC][mU][mG][mA][mC][mA][mGs][mGs][mG]	1036
NR1H3-769-789-866	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fG][mG][fA][mU][fC][mU][mG][fU][mU][mC][mU][fU][mC][mU][mG][mA][mC][mAs][mGs][mG]	1037
NR1H3-794-814-891	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fUs][fC][fU][mU][fG][mC][mC][fG][mC][mU][mU][fC][mA][mG][mU][mU][mU][mCs][mGs][mG]	1038
NR1H3-1152-1172-1249	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fUs][fG][fU][mC][fU][mC][mC][fA][mG][mA][mA][fG][mC][mA][mU][mC][mA][mCs][mGs][mG]	1039
NR1H3-1189-1209-1286	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fAs][fG][fG][mU][fG][mA][mU][fA][mC][mU][mC][fU][mC][mA][mC][mU][mC][mCs][mGs][mG]	1040
NR1H3-1195-1215-1292	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fUs][fG][fA][mG][fG][mA][mA][fG][mG][mU][mG][fA][mU][mA][mC][mU][mC][mUs][mGs][mG]	1041

NR1H3-1200-1220-1297	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fAs][fU][fC][mC][fU][mU][mG][fA][mG][mG][mA][fA][mG][mG][mU][mG][mA][mUs][mGs][mG]	1042
NR1H3-1201-1221-1298	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fAs][fA][fU][mC][fC][mU][mU][fG][mA][mG][mG][fA][mA][mG][mG][mU][mG][mAs][mGs][mG]	1043
NR1H3-1202-1222-1299	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fAs][fA][fA][mU][fC][mC][mU][fU][mG][mA][mG][fG][mA][mA][mG][mG][mU][mGs][mGs][mG]	1044
NR1H3-1203-1223-1300	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fGs][fA][fA][mA][fU][mC][mC][fU][mU][mG][mA][fG][mG][mA][mA][mG][mG][mUs][mGs][mG]	1045
NR1H3-1204-1224-1301	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fUs][fG][fA][mA][fA][mU][mC][fC][mU][mU][mG][fA][mG][mG][mA][mA][mG][mGs][mGs][mG]	1046
NR1H3-1205-1225-1302	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fCs][fU][fG][mA][fA][mA][mU][fC][mC][mU][mU][fG][mA][mG][mG][mA][mA][mGs][mGs][mG]	1047
NR1H3-1206-1226-1303	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fAs][fC][fU][mG][fA][mA][mA][fU][mC][mC][mU][fU][mG][mA][mG][mG][mA][mAs][mGs][mG]	1048
NR1H3-1207-1227	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fAs][fA][fC][mU][fG][mA][mA][fA][mU][mC][mC][fU][mU][mG][mA][mG][mG][mAs][mGs][mG]	1049
NR1H3-1208-1228-1305	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fUs][fA][fA][mC][fU][mG][mA][fA][mA][mU][mC][fC][mU][mU][mG][mA][mG][mGs][mGs][mG]	1050
NR1H3-1209-1229-1306	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fAs][fU][fA][mA][fC][mU][mG][fA][mA][mA][mU][fC][mC][mU][mU][mG][mA][mGs][mGs][mG]	1051
NR1H3-1210-1230-1307	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fUs][fA][fU][mA][fA][mC][mU][fG][mA][mA][mA][fU][mC][mC][mU][mU][mG][mA][mGs][mGs][mG]	1052

NR1H3-1211-1231-1308	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fUs][fU][fA][mU][fA][mA][mC][fU][mG][mA][mA][fA][mU][mC][mC][mU][mU][mGs][mGs][mG]	1053
NR1H3-1212-1232-1309	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fGs][fU][fU][mA][fU][mA][mA][fC][mU][mG][mA][fA][mA][mU][mC][mC][mU][mUs][mGs][mG]	1054
NR1H3-1213-1233-1310	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fGs][fG][fU][mU][fA][mU][mA][fA][mC][mU][mG][fA][mA][mA][mU][mC][mC][mUs][mGs][mG]	1055
NR1H3-1214-1234-1311	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fCs][fG][fG][mU][fU][mA][mU][fA][mA][mC][mU][fG][mA][mA][mA][mU][mC][mCs][mGs][mG]	1056
NR1H3-1220	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fUs][fC][fU][mU][fC][mC][mC][fG][mG][mU][mU][fA][mU][mA][mA][mC][mU][mGs][mGs][mG]	1057
NR1H3-1221-1241-1318	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fGs][fU][fC][mU][fU][mC][mC][fC][mG][mG][mU][fU][mA][mU][mA][mA][mC][mUs][mGs][mG]	1058
NR1H3-1224-1244	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fAs][fA][fA][mG][fU][mC][mU][fU][mC][mC][mC][fG][mG][mU][mU][mA][mU][mAs][mGs][mG]	1059
NR1H3-1244-1264	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fAs][fC][fU][mU][fG][mC][mA][fG][mC][mC][mC][fU][mG][mC][mU][mU][mU][mGs][mGs][mG]	1060
NR1H3-1249-1269-1346	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fAs][fU][fU][mC][fC][mA][mC][fU][mU][mG][mC][fA][mG][mC][mC][mC][mU][mGs][mGs][mG]	1061
NR1H3-1252-1272	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fUs][fG][fA][mA][fU][mU][mC][fC][mA][mC][mU][fU][mG][mC][mA][mG][mC][mCs][mGs][mG]	1062
NR1H3-1254-1274-1351	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fGs][fA][fU][mG][fA][mA][mU][fU][mC][mC][mA][fC][mU][mU][mG][mC][mA][mGs][mGs][mG]	1063

NR1H3-1255-1275-1352	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fUs][fG][fA][mU][fG][mA][mA][fU][mU][mC][mC][fA][mC][mU][mU][mG][mC][mAs][mGs][mG]	1064
NR1H3-1256-1276-1353	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fUs][fU][fG][mA][fU][mG][mA][fA][mU][mU][mC][fC][mA][mC][mU][mU][mG][mCs][mGs][mG]	1065
NR1H3-1257-1277-1354	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fGs][fU][fU][mG][fA][mU][mG][fA][mA][mU][mU][fC][mC][mA][mC][mU][mU][mGs][mGs][mG]	1066
NR1H3-1259	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fGs][fG][fG][mU][fU][mG][mA][fU][mG][mA][mA][fU][mU][mC][mC][mA][mC][mUs][mGs][mG]	1067
NR1H3-1260-1280-1357	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fGs][fG][fG][mG][fU][mU][mG][fA][mU][mG][mA][fA][mU][mU][mC][mC][mA][mCs][mGs][mG]	1068
NR1H3-1261-1281-1358	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fUs][fG][fG][mG][fG][mU][mU][fG][mA][mU][mG][fA][mA][mU][mU][mC][mC][mAs][mGs][mG]	1069
NR1H3-1263-1283-1360	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fGs][fA][fU][mG][fG][mG][mG][fU][mU][mG][mA][fU][mG][mA][mA][mU][mU][mCs][mGs][mG]	1070
NR1H3-1264-1284-1361	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fAs][fG][fA][mU][fG][mG][mG][fG][mU][mU][mG][fA][mU][mG][mA][mA][mU][mUs][mGs][mG]	1071
NR1H3-1265-1285	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fAs][fA][fG][mA][fU][mG][mG][fG][mG][mU][mU][fG][mA][mU][mG][mA][mA][mUs][mGs][mG]	1072
NR1H3-1266-1286	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fGs][fA][fA][mG][fA][mU][mG][fG][mG][mG][mU][fU][mG][mA][mU][mG][mA][mAs][mGs][mG]	1073
NR1H3-1405-1471-1502	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fCs][fC][fA][mC][fA][mU][mA][fU][mG][mU][mG][fU][mG][mC][mU][mG][mC][mAs][mGs][mG]	1074

NR1H3-1409-1475-1506	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fGs][fC][fU][mU][fC][mC][mA][fC][mA][mU][mA][fU][mG][mU][mG][mU][mG][mCs][mGs][mG]	1075
NR1H3-1429-1495	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fUs][fG][fG][mA][fG][mA][mC][fG][mU][mA][mG][fG][mC][mA][mU][mG][mC][mAs][mGs][mG]	1076
NR1H3-1433-1499	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fUs][fG][fG][mA][fU][mG][mG][fA][mG][mA][mC][fG][mU][mA][mG][mG][mC][mAs][mGs][mG]	1077
NR1H3-1437-1503	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fAs][fU][fG][mG][fU][mG][mG][fA][mU][mG][mG][fA][mG][mA][mC][mG][mU][mAs][mGs][mG]	1078
NR1H3-1439-1505	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fGs][fG][fA][mU][fG][mG][mU][fG][mG][mA][mU][fG][mG][mA][mG][mA][mC][mGs][mGs][mG]	1079
NR1H3-1446-1512	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fGs][fU][fC][mA][fU][mG][mG][fG][mG][mA][mU][fG][mG][mU][mG][mG][mA][mUs][mGs][mG]	1080
NR1H3-1458-1524-1555	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fGs][fA][fA][mC][fA][mU][mC][fA][mG][mU][mC][fG][mG][mU][mC][mA][mU][mGs][mGs][mG]	1081
NR1H3-1463-1529	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fCs][fG][fU][mG][fG][mG][mA][fA][mC][mA][mU][fC][mA][mG][mU][mC][mG][mGs][mGs][mG]	1082
NR1H3-1464-1530-1561	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fCs][fC][fG][mU][fG][mG][mG][fA][mA][mC][mA][fU][mC][mA][mG][mU][mC][mGs][mGs][mG]	1083
NR1H3-1465-1531-1562	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fUs][fC][fC][mG][fU][mG][mG][fG][mA][mA][mC][fA][mU][mC][mA][mG][mU][mCs][mGs][mG]	1084
NR1H3-1467-1533-1564	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fCs][fA][fU][mC][fC][mG][mU][fG][mG][mG][mA][fA][mC][mA][mU][mC][mA][mGs][mGs][mG]	1085

NR1H3-1469-1535-1566	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fA][mG][fC][mA][fU][mC][mC][fG][mU][mG][mG][fG][mA][mA][mC][mA][mU][mCs][mGs][mG]	1086
NR1H3-1470-1536-1567	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fUs][fA][fG][mC][fA][mU][mC][fC][mG][mU][mG][fG][mG][mA][mA][mC][mA][mUs][mGs][mG]	1087
NR1H3-1475-1541	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fUs][fU][fC][mA][fU][mU][mA][fG][mC][mA][mU][fC][mC][mG][mU][mG][mG][mGs][mGs][mG]	1088
NR1H3-1479-1545	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fCs][fA][fG][mU][fU][mU][mC][fA][mU][mU][mA][fG][mC][mA][mU][mC][mC][mGs][mGs][mG]	1089
NR1H3-1480-1546-1577	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fCs][fC][fA][mG][fU][mU][mU][fC][mA][mU][mU][fA][mG][mC][mA][mU][mC][mCs][mGs][mG]	1090
NR1H3-1481-1547	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fAs][fC][fC][mA][fG][mU][mU][fU][mC][mA][mU][fU][mA][mG][mC][mA][mU][mCs][mGs][mG]	1091
NR1H3-1482-1548-1579	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fCs][fA][fC][mC][fA][mG][mU][fU][mU][mC][mA][fU][mU][mA][mG][mC][mA][mUs][mGs][mG]	1092
NR1H3-1485-1551	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fGs][fC][fU][mC][fA][mC][mC][fA][mG][mU][mU][fU][mC][mA][mU][mU][mA][mGs][mGs][mG]	1093
NR1H3-1515-1581	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fCs][fU][fC][mU][fG][mA][mG][fU][mG][mG][mA][fC][mG][mC][mU][mG][mC][mUs][mGs][mG]	1094
NR1H3-1517-1583	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fUs][fG][fC][mU][fC][mU][mG][fA][mG][mU][mG][fG][mA][mC][mG][mC][mU][mGs][mGs][mG]	1095
NR1H3-1518-1584	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fUs][fU][fG][mC][fU][mC][mU][fG][mA][mG][mU][fG][mG][mA][mC][mG][mC][mUs][mGs][mG]	1096

NR1H3-1524-1590-1621	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fAs][fA][fA][mC][fA][mC][mU][fU][mG][mC][mU][fC][mU][mG][mA][mG][mU][mGs][mGs][mG]	1097
NR1H3-1533-1599	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fAs][fC][fG][mC][fA][mG][mU][fG][mC][mA][mA][fA][mC][mA][mC][mU][mU][mGs][mGs][mG]	1098
NR1H3-1535-1601	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fAs][fG][fA][mC][fG][mC][mA][fG][mU][mG][mC][fA][mA][mA][mC][mA][mC][mUs][mGs][mG]	1099
NR1H3-1545-1611	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fUs][fU][fU][mG][fU][mC][mC][fU][mG][mC][mA][fG][mA][mC][mG][mC][mA][mGs][mGs][mG]	1100
NR1H3-1554-1620	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fUs][fG][fG][mG][fA][mG][mC][fU][mU][mU][mU][fU][mG][mU][mC][mC][mU][mGs][mGs][mG]	1101
NR1H3-1581-1647	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fCs][fA][fC][mA][fU][mC][mC][fC][mA][mG][mA][fU][mC][mU][mC][mA][mG][mAs][mGs][mG]	1102
NR1H3-1586-1652	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fUs][fC][fG][mU][fG][mC][mA][fC][mA][mU][mC][fC][mC][mA][mG][mA][mU][mCs][mGs][mG]	1103
NR1H3-1587-1653	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fUs][fU][fC][mG][fU][mG][mC][fA][mC][mA][mU][fC][mC][mC][mA][mG][mA][mUs][mGs][mG]	1104
NR1H3-1588-1654	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fAs][fU][fU][mC][fG][mU][mG][fC][mA][mC][mA][fU][mC][mC][mC][mA][mG][mAs][mGs][mG]	1105
NR1H3-1594-1660-1691	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fAs][fC][fA][mG][fU][mC][mA][fU][mU][mC][mG][fU][mG][mC][mA][mC][mA][mUs][mGs][mG]	1106
NR1H3-1595-1661-1692	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fAs][fA][fC][mA][fG][mU][mC][fA][mU][mU][mC][fG][mU][mG][mC][mA][mC][mAs][mGs][mG]	1107

NR1H3-1596-1662	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fGs][fA][fA][mC][fA][mG][mU][fC][mA][mU][mU][fC][mG][mU][mG][mC][mA][mCs][mGs][mG]	1108
NR1H3-1663-1727	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fUs][fU][fC][mC][fA][mC][mU][fU][mC][mU][mA][fG][mG][mA][mG][mG][mC][mAs][mGs][mG]	1109
NR1H3-1670-1734	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fCs][fA][fG][mU][fC][mU][mG][fU][mU][mC][mC][fA][mC][mU][mU][mC][mU][mAs][mGs][mG]	1110
NR1H3-1671-1735	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fUs][fC][fA][mG][fU][mC][mU][fG][mU][mU][mC][fC][mA][mC][mU][mU][mC][mUs][mGs][mG]	1111
NR1H3-1672-1736	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fCs][fU][fC][mA][fG][mU][mC][fU][mG][mU][mU][fC][mC][mA][mC][mU][mU][mCs][mGs][mG]	1112
NR1H3-1673-1737	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fUs][fC][fU][mC][fA][mG][mU][fC][mU][mG][mU][fU][mC][mC][mA][mC][mU][mUs][mGs][mG]	1113
NR1H3-1674-1738	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fUs][fU][fC][mU][fC][mA][mG][fU][mC][mU][mG][fU][mU][mC][mC][mA][mC][mUs][mGs][mG]	1114
NR1H3-1675-1739-1766	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fCs][fU][fU][mC][fU][mC][mA][fG][mU][mC][mU][fG][mU][mU][mC][mC][mA][mCs][mGs][mG]	1115
NR1H3-1676-1740-1767	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fCs][fCs][fC][fU][mU][fC][mU][mC][fA][mG][mU][mC][fU][mG][mU][mU][mC][mC][mAs][mGs][mG]	1116
NR1H3-1678-1742-1769	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fGs][fC][fC][mC][fU][mU][mC][fU][mC][mA][mG][fU][mC][mU][mG][mU][mU][mCs][mGs][mG]	1117
NR1H3-1684-1748	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fAs][fAs][fU][fG][mU][fU][mU][mG][fC][mC][mC][mU][fU][mC][mU][mC][mA][mG][mUs][mGs][mG]	1118

NR1H3-1731-1795	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fGs][fAs][fC][fU][mC][fU][mC][mU][fU][mU][mU][mA][fA][mU][mG][mC][mC][mA][mCs][mGs][mG]	1119
NR1H3-1732-1796	Artificial Sequence	Modified antisense strand	[MePhosphonate-4O-mUs][fUs][fGs][fA][fC][mU][fC][mU][mC][fU][mU][mU][mU][fA][mA][mU][mG][mC][mC][mAs][mGs][mG]	1120
Stem-loop	Artificial Sequence		GCAGCCGAAAGGCUGC	1121
Forward-1198	Artificial Sequence		GTTATAACCGGGAAGACTTTGC	1122
Reverse-1326	Artificial Sequence		TGATAGCAATGAGCAAGGCA	1123
Probe-1253	Artificial Sequence		ATGGCCCTGGAGAACTCGAAGAT G	1124
NR1H3-764-784-861	Hs-Mf-Mm	19 mer sense strand	UGUCCUGUCAGAAGAACAG	1125
NR1H3-766-786-863	Hs-Mf-Mm	19 mer sense strand	UCCUGUCAGAAGAACAGAU	1126
NR1H3-789-809-886	Hs-Mf-Mm	19 mer sense strand	CUGAAGAAACUGAAGCGGC	1127
NR1H3-790-810-887	Hs-Mf-Mm	19 mer sense strand	UGAAGAAACUGAAGCGGCA	1128
NR1H3-791-811-888	Hs-Mf-Mm	19 mer sense strand	GAAGAAACUGAAGCGGCAA	1129
NR1H3-792-812-889	Hs-Mf-Mm	19 mer sense strand	AAGAAACUGAAGCGGCAAG	1130
NR1H3-793-813-890	Hs-Mf-Mm	19 mer sense strand	AGAAACUGAAGCGGCAAGA	1131
NR1H3-795-815-892	Hs-Mf-Mm	19 mer sense strand	AAACUGAAGCGGCAAGAGG	1132
NR1H3-796-816-893	Hs-Mf-Mm	19 mer sense strand	AACUGAAGCGGCAAGAGGA	1133
NR1H3-797-817-894	Hs-Mf-Mm	19 mer sense strand	ACUGAAGCGGCAAGAGGAG	1134
NR1H3-798-818-895	Hs-Mf-Mm	19 mer sense strand	CUGAAGCGGCAAGAGGAGG	1135
NR1H3-799-819-896	Hs-Mf-Mm	19 mer sense strand	UGAAGCGGCAAGAGGAGGA	1136
NR1H3-802-822-899	Hs-Mf-Mm	19 mer sense strand	AGCGGCAAGAGGAGGAACA	1137
NR1H3-803-823-900	Hs-Mf-Mm	19 mer sense strand	GCGGCAAGAGGAGGAACAG	1138

NR1H3-804-824-901	Hs-Mf-Mm	19 mer sense strand	CGGCAAGAGGAGGAACAGG	1139
NR1H3-806-826-903	Hs-Mf-Mm	19 mer sense strand	GCAAGAGGAGGAACAGGCU	1140
NR1H3-808-828-905	Hs-Mf-Mm	19 mer sense strand	AAGAGGAGGAACAGGCUCA	1141
NR1H3-809-829-906	Hs-Mf-Mm	19 mer sense strand	AGAGGAGGAACAGGCUCAU	1142
NR1H3-810-830-907	Hs-Mf-Mm	19 mer sense strand	GAGGAGGAACAGGCUCAUG	1143
NR1H3-811-831-908	Hs-Mf-Mm	19 mer sense strand	AGGAGGAACAGGCUCAUGC	1144
NR1H3-813-833-910	Hs-Mf-Mm	19 mer sense strand	GAGGAACAGGCUCAUGCCA	1145
NR1H3-844-864	Hs-Mf	19 mer sense strand	CCAGGGCUUCCUCACCCCC	1146
NR1H3-895-915-992	Hs-Mf-Mm	19 mer sense strand	UGGGCAUGAUCGAGAAGCU	1147
NR1H3-898-918-995	Hs-Mf-Mm	19 mer sense strand	GCAUGAUCGAGAAGCUCGU	1148
NR1H3-915-935-1012	Hs-Mf-Mm	19 mer sense strand	GUCGCUGCCCAGCAACAGU	1149
NR1H3-917-937-1014	Hs-Mf-Mm	19 mer sense strand	CGCUGCCCAGCAACAGUGU	1150
NR1H3-922-942-1019	Hs-Mf-Mm	19 mer sense strand	CCCAGCAACAGUGUAACCG	1151
NR1H3-924-944-1021	Hs-Mf-Mm	19 mer sense strand	CAGCAACAGUGUAACCGGC	1152
NR1H3-925-945-1022	Hs-Mf-Mm	19 mer sense strand	AGCAACAGUGUAACCGGCG	1153
NR1H3-927-947-1024	Hs-Mf-Mm	19 mer sense strand	CAACAGUGUAACCGGCGCU	1154
NR1H3-928-948-1025	Hs-Mf-Mm	19 mer sense strand	AACAGUGUAACCGGCGCUC	1155
NR1H3-929-949-1026	Hs-Mf-Mm	19 mer sense strand	ACAGUGUAACCGGCGCUCC	1156
NR1H3-930-950-1027	Hs-Mf-Mm	19 mer sense strand	CAGUGUAACCGGCGCUCCU	1157
NR1H3-931-951-1028	Hs-Mf-Mm	19 mer sense strand	AGUGUAACCGGCGCUCCUU	1158
NR1H3-932-952-1029	Hs-Mf-Mm	19 mer sense strand	GUGUAACCGGCGCUCCUUU	1159
NR1H3-933-953-1030	Hs-Mf-Mm	19 mer sense strand	UGUAACCGGCGCUCCUUUU	1160

NR1H3-941-961	Hs-Mf	19 mer sense strand	GCGCUCCUUUUCUGACCGG	1161
NR1H3-944-964	Hs-Mf	19 mer sense strand	CUCCUUUUCUGACCGGCUU	1162
NR1H3-945-965	Hs-Mf	19 mer sense strand	UCCUUUUCUGACCGGCUUC	1163
NR1H3-946-966	Hs-Mf	19 mer sense strand	CCUUUUCUGACCGGCUUCG	1164
NR1H3-947-967	Hs-Mf	19 mer sense strand	CUUUUCUGACCGGCUUCGA	1165
NR1H3-949-969	Hs-Mf	19 mer sense strand	UUUCUGACCGGCUUCGAGU	1166
NR1H3-951-971	Hs-Mf	19 mer sense strand	UCUGACCGGCUUCGAGUCA	1167
NR1H3-952-972	Hs-Mf	19 mer sense strand	CUGACCGGCUUCGAGUCAC	1168
NR1H3-953-973	Hs-Mf	19 mer sense strand	UGACCGGCUUCGAGUCACG	1169
NR1H3-1151-1171-1248	Hs-Mf-Mm	19 mer sense strand	GGUGAUGCUUCUGGAGACA	1170
NR1H3-1153-1173-1250	Hs-Mf-Mm	19 mer sense strand	UGAUGCUUCUGGAGACAUC	1171
NR1H3-1154-1174-1251	Hs-Mf-Mm	19 mer sense strand	GAUGCUUCUGGAGACAUCU	1172
NR1H3-1155-1175-1252	Hs-Mf-Mm	19 mer sense strand	AUGCUUCUGGAGACAUCUC	1173
NR1H3-1156-1176-1253	Hs-Mf-Mm	19 mer sense strand	UGCUUCUGGAGACAUCUCG	1174
NR1H3-1157-1177-1254	Hs-Mf-Mm	19 mer sense strand	GCUUCUGGAGACAUCUCGG	1175
NR1H3-1158-1178-1255	Hs-Mf-Mm	19 mer sense strand	CUUCUGGAGACAUCUCGGA	1176
NR1H3-1159-1179-1256	Hs-Mf-Mm	19 mer sense strand	UUCUGGAGACAUCUCGGAG	1177
NR1H3-1160-1180-1257	Hs-Mf-Mm	19 mer sense strand	UCUGGAGACAUCUCGGAGG	1178
NR1H3-1161-1181-1258	Hs-Mf-Mm	19 mer sense strand	CUGGAGACAUCUCGGAGGU	1179
NR1H3-1162-1182-1259	Hs-Mf-Mm	19 mer sense strand	UGGAGACAUCUCGGAGGUA	1180
NR1H3-1163-1183-1260	Hs-Mf-Mm	19 mer sense strand	GGAGACAUCUCGGAGGUAC	1181
NR1H3-1164-1184-1261	Hs-Mf-Mm	19 mer sense strand	GAGACAUCUCGGAGGUACA	1182

NR1H3-1165-1185-1262	Hs-Mf-Mm	19 mer sense strand	AGACAUCUCGGAGGUACAA	1183
NR1H3-1166-1186-1263	Hs-Mf-Mm	19 mer sense strand	GACAUCUCGGAGGUACAAC	1184
NR1H3-1167-1187-1264	Hs-Mf-Mm	19 mer sense strand	ACAUCUCGGAGGUACAACC	1185
NR1H3-1169-1189-1266	Hs-Mf-Mm	19 mer sense strand	AUCUCGGAGGUACAACCCU	1186
NR1H3-1170-1190-1267	Hs-Mf-Mm	19 mer sense strand	UCUCGGAGGUACAACCCUG	1187
NR1H3-1171-1191-1268	Hs-Mf-Mm	19 mer sense strand	CUCGGAGGUACAACCCUGG	1188
NR1H3-1173-1193-1270	Hs-Mf-Mm	19 mer sense strand	CGGAGGUACAACCCUGGGA	1189
NR1H3-1175-1195-1272	Hs-Mf-Mm	19 mer sense strand	GAGGUACAACCCUGGGAGU	1190
NR1H3-1176-1196-1273	Hs-Mf-Mm	19 mer sense strand	AGGUACAACCCUGGGAGUG	1191
NR1H3-1177-1197-1274	Hs-Mf-Mm	19 mer sense strand	GGUACAACCCUGGGAGUGA	1192
NR1H3-1178-1198-1275	Hs-Mf-Mm	19 mer sense strand	GUACAACCCUGGGAGUGAG	1193
NR1H3-1179-1199-1276	Hs-Mf-Mm	19 mer sense strand	UACAACCCUGGGAGUGAGA	1194
NR1H3-1180-1200-1277	Hs-Mf-Mm	19 mer sense strand	ACAACCCUGGGAGUGAGAG	1195
NR1H3-1181-1201-1278	Hs-Mf-Mm	19 mer sense strand	CAACCCUGGGAGUGAGAGU	1196
NR1H3-1182-1202-1279	Hs-Mf-Mm	19 mer sense strand	AACCCUGGGAGUGAGAGUA	1197
NR1H3-1183-1203-1280	Hs-Mf-Mm	19 mer sense strand	ACCCUGGGAGUGAGAGUAU	1198
NR1H3-1184-1204-1281	Hs-Mf-Mm	19 mer sense strand	CCCUGGGAGUGAGAGUAUC	1199
NR1H3-1185-1205-1282	Hs-Mf-Mm	19 mer sense strand	CCUGGGAGUGAGAGUAUCA	1200
NR1H3-1186-1206-1283	Hs-Mf-Mm	19 mer sense strand	CUGGGAGUGAGAGUAUCAC	1201
NR1H3-1187-1207-1284	Hs-Mf-Mm	19 mer sense strand	UGGGAGUGAGAGUAUCACC	1202
NR1H3-1188-1208-1285	Hs-Mf-Mm	19 mer sense strand	GGGAGUGAGAGUAUCACCU	1203
NR1H3-1190-1210-1287	Hs-Mf-Mm	19 mer sense strand	GAGUGAGAGUAUCACCUUC	1204

NR1H3-1191-1211-1288	Hs-Mf-Mm	19 mer sense strand	AGUGAGAGUAUCACCUUCC	1205
NR1H3-1192-1212-1289	Hs-Mf-Mm	19 mer sense strand	GUGAGAGUAUCACCUUCCU	1206
NR1H3-1193-1213-1290	Hs-Mf-Mm	19 mer sense strand	UGAGAGUAUCACCUUCCUC	1207
NR1H3-1194-1214-1291	Hs-Mf-Mm	19 mer sense strand	GAGAGUAUCACCUUCCUCA	1208
NR1H3-1196-1216-1293	Hs-Mf-Mm	19 mer sense strand	GAGUAUCACCUUCCUCAAG	1209
NR1H3-1197-1217-1294	Hs-Mf-Mm	19 mer sense strand	AGUAUCACCUUCCUCAAGG	1210
NR1H3-1198-1218-1295	Hs-Mf-Mm	19 mer sense strand	GUAUCACCUUCCUCAAGGA	1211
NR1H3-1199-1219-1296	Hs-Mf-Mm	19 mer sense strand	UAUCACCUUCCUCAAGGAU	1212
NR1H3-1200-1220-1297	Hs-Mf-Mm	19 mer sense strand	AUCACCUUCCUCAAGGAUU	1213
NR1H3-1203-1223-1300	Hs-Mf-Mm	19 mer sense strand	ACCUUCCUCAAGGAUUUCA	1214
NR1H3-1204-1224-1301	Hs-Mf-Mm	19 mer sense strand	CCUUCCUCAAGGAUUUCAG	1215
NR1H3-1207-1227-1304	Hs-Mf-Mm	19 mer sense strand	UCCUCAAGGAUUUCAGUUA	1216
NR1H3-1211-1231-1308	Hs-Mf-Mm	19 mer sense strand	CAAGGAUUUCAGUUAUAAC	1217
NR1H3-1212-1232-1309	Hs-Mf-Mm	19 mer sense strand	AAGGAUUUCAGUUAUAACC	1218
NR1H3-1213-1233-1310	Hs-Mf-Mm	19 mer sense strand	AGGAUUUCAGUUAUAACCG	1219
NR1H3-1214-1234-1311	Hs-Mf-Mm	19 mer sense strand	GGAUUUCAGUUAUAACCGG	1220
NR1H3-1215-1235-1312	Hs-Mf-Mm	19 mer sense strand	GAUUUCAGUUAUAACCGGG	1221
NR1H3-1216-1236-1313	Hs-Mf-Mm	19 mer sense strand	AUUUCAGUUAUAACCGGGA	1222
NR1H3-1217-1237-1314	Hs-Mf-Mm	19 mer sense strand	UUUCAGUUAUAACCGGGAA	1223
NR1H3-1218-1238-1315	Hs-Mf-Mm	19 mer sense strand	UUCAGUUAUAACCGGGAAG	1224
NR1H3-1219-1239-1316	Hs-Mf-Mm	19 mer sense strand	UCAGUUAUAACCGGGAAGA	1225
NR1H3-1220-1240-1317	Hs-Mf-Mm	19 mer sense strand	CAGUUAUAACCGGGAAGAC	1226

NR1H3-1222-1242-1319	Hs-Mf-Mm	19 mer sense strand	GUUAUAACCGGGAAGACUU	1227
NR1H3-1223-1243-1320	Hs-Mf-Mm	19 mer sense strand	UUAUAACCGGGAAGACUUU	1228
NR1H3-1224-1244-1321	Hs-Mf-Mm	19 mer sense strand	UAUAACCGGGAAGACUUUG	1229
NR1H3-1225-1245-1322	Hs-Mf-Mm	19 mer sense strand	AUAACCGGGAAGACUUUGC	1230
NR1H3-1226-1246-1323	Hs-Mf-Mm	19 mer sense strand	UAACCGGGAAGACUUUGCC	1231
NR1H3-1227-1247-1324	Hs-Mf-Mm	19 mer sense strand	AACCGGGAAGACUUUGCCA	1232
NR1H3-1228-1248-1325	Hs-Mf-Mm	19 mer sense strand	ACCGGGAAGACUUUGCCAA	1233
NR1H3-1229-1249-1326	Hs-Mf-Mm	19 mer sense strand	CCGGGAAGACUUUGCCAAA	1234
NR1H3-1232-1252-1329	Hs-Mf-Mm	19 mer sense strand	GGAAGACUUUGCCAAAGCA	1235
NR1H3-1233-1253-1330	Hs-Mf-Mm	19 mer sense strand	GAAGACUUUGCCAAAGCAG	1236
NR1H3-1234-1254-1331	Hs-Mf-Mm	19 mer sense strand	AAGACUUUGCCAAAGCAGG	1237
NR1H3-1235-1255-1332	Hs-Mf-Mm	19 mer sense strand	AGACUUUGCCAAAGCAGGG	1238
NR1H3-1236-1256-1333	Hs-Mf-Mm	19 mer sense strand	GACUUUGCCAAAGCAGGGC	1239
NR1H3-1237-1257-1334	Hs-Mf-Mm	19 mer sense strand	ACUUUGCCAAAGCAGGGCU	1240
NR1H3-1238-1258-1335	Hs-Mf-Mm	19 mer sense strand	CUUUGCCAAAGCAGGGCUG	1241
NR1H3-1241-1261-1338	Hs-Mf-Mm	19 mer sense strand	UGCCAAAGCAGGGCUGCAA	1242
NR1H3-1242-1262-1339	Hs-Mf-Mm	19 mer sense strand	GCCAAAGCAGGGCUGCAAG	1243
NR1H3-1243-1263-1340	Hs-Mf-Mm	19 mer sense strand	CCAAAGCAGGGCUGCAAGU	1244
NR1H3-1244-1264-1341	Hs-Mf-Mm	19 mer sense strand	CAAAGCAGGGCUGCAAGUG	1245
NR1H3-1245-1265-1342	Hs-Mf-Mm	19 mer sense strand	AAAGCAGGGCUGCAAGUGG	1246
NR1H3-1246-1266-1343	Hs-Mf-Mm	19 mer sense strand	AAGCAGGGCUGCAAGUGGA	1247
NR1H3-1247-1267-1344	Hs-Mf-Mm	19 mer sense strand	AGCAGGGCUGCAAGUGGAA	1248

NR1H3-1248-1268-1345	Hs-Mf-Mm	19 mer sense strand	GCAGGGCUGCAAGUGGAAU	1249
NR1H3-1250-1270-1347	Hs-Mf-Mm	19 mer sense strand	AGGGCUGCAAGUGGAAUUC	1250
NR1H3-1251-1271-1348	Hs-Mf-Mm	19 mer sense strand	GGGCUGCAAGUGGAAUUCA	1251
NR1H3-1252-1272-1349	Hs-Mf-Mm	19 mer sense strand	GGCUGCAAGUGGAAUUCAU	1252
NR1H3-1253-1273-1350	Hs-Mf-Mm	19 mer sense strand	GCUGCAAGUGGAAUUCAUC	1253
NR1H3-1256-1276-1353	Hs-Mf-Mm	19 mer sense strand	GCAAGUGGAAUUCAUCAAC	1254
NR1H3-1258-1278-1355	Hs-Mf-Mm	19 mer sense strand	AAGUGGAAUUCAUCAACCC	1255
NR1H3-1259-1279-1356	Hs-Mf-Mm	19 mer sense strand	AGUGGAAUUCAUCAACCCC	1256
NR1H3-1261-1281-1358	Hs-Mf-Mm	19 mer sense strand	UGGAAUUCAUCAACCCCAU	1257
NR1H3-1262-1282-1359	Hs-Mf-Mm	19 mer sense strand	GGAAUUCAUCAACCCCAUC	1258
NR1H3-1265-1285-1362	Hs-Mf-Mm	19 mer sense strand	AUUCAUCAACCCCAUCUUC	1259
NR1H3-1266-1286-1363	Hs-Mf-Mm	19 mer sense strand	UUCAUCAACCCCAUCUUCG	1260
NR1H3-1267-1287-1364	Hs-Mf-Mm	19 mer sense strand	UCAUCAACCCCAUCUUCGA	1261
NR1H3-1268-1288-1365	Hs-Mf-Mm	19 mer sense strand	CAUCAACCCCAUCUUCGAG	1262
NR1H3-1269-1289-1366	Hs-Mf-Mm	19 mer sense strand	AUCAACCCCAUCUUCGAGU	1263
NR1H3-1270-1290-1367	Hs-Mf-Mm	19 mer sense strand	UCAACCCCAUCUUCGAGUU	1264
NR1H3-1271-1291-1368	Hs-Mf-Mm	19 mer sense strand	CAACCCCAUCUUCGAGUUC	1265
NR1H3-1272-1292-1369	Hs-Mf-Mm	19 mer sense strand	AACCCCAUCUUCGAGUUCU	1266
NR1H3-1273-1293-1370	Hs-Mf-Mm	19 mer sense strand	ACCCCAUCUUCGAGUUCUC	1267
NR1H3-1275-1295-1372	Hs-Mf-Mm	19 mer sense strand	CCCAUCUUCGAGUUCUCCA	1268
NR1H3-1276-1296-1373	Hs-Mf-Mm	19 mer sense strand	CCAUCUUCGAGUUCUCCAG	1269
NR1H3-1277-1297-1374	Hs-Mf-Mm	19 mer sense strand	CAUCUUCGAGUUCUCCAGG	1270

NR1H3-1278-1298-1375	Hs-Mf-Mm	19 mer sense strand	AUCUUCGAGUUCUCCAGGG	1271
NR1H3-1279-1299-1376	Hs-Mf-Mm	19 mer sense strand	UCUUCGAGUUCUCCAGGGC	1272
NR1H3-1280-1300-1377	Hs-Mf-Mm	19 mer sense strand	CUUCGAGUUCUCCAGGGCC	1273
NR1H3-1281-1301-1378	Hs-Mf-Mm	19 mer sense strand	UUCGAGUUCUCCAGGGCCA	1274
NR1H3-1282-1302-1379	Hs-Mf-Mm	19 mer sense strand	UCGAGUUCUCCAGGGCCA	1275
NR1H3-1283-1303-1380	Hs-Mf-Mm	19 mer sense strand	CGAGUUCUCCAGGGCCAUG	1276
NR1H3-1284-1304-1381	Hs-Mf-Mm	19 mer sense strand	GAGUUCUCCAGGGCCAUGA	1277
NR1H3-1285-1305-1382	Hs-Mf-Mm	19 mer sense strand	AGUUCUCCAGGGCCAUGAA	1278
NR1H3-1286-1306-1383	Hs-Mf-Mm	19 mer sense strand	GUUCUCCAGGGCCAUGAAU	1279
NR1H3-1288-1308-1385	Hs-Mf-Mm	19 mer sense strand	UCUCCAGGGCCAUGAAUGA	1280
NR1H3-1289-1309-1386	Hs-Mf-Mm	19 mer sense strand	CUCCAGGGCCAUGAAUGAG	1281
NR1H3-1290-1310-1387	Hs-Mf-Mm	19 mer sense strand	UCCAGGGCCAUGAAUGAGC	1282
NR1H3-1291-1311-1388	Hs-Mf-Mm	19 mer sense strand	CCAGGGCCAUGAAUGAGCU	1283
NR1H3-1292-1312-1389	Hs-Mf-Mm	19 mer sense strand	CAGGGCCAUGAAUGAGCUG	1284
NR1H3-1293-1313-1390	Hs-Mf-Mm	19 mer sense strand	AGGGCCAUGAAUGAGCUGC	1285
NR1H3-1294-1314-1391	Hs-Mf-Mm	19 mer sense strand	GGGCCAUGAAUGAGCUGCA	1286
NR1H3-1295-1315-1392	Hs-Mf-Mm	19 mer sense strand	GGCCAUGAAUGAGCUGCAA	1287
NR1H3-1296-1316-1393	Hs-Mf-Mm	19 mer sense strand	GCCAUGAAUGAGCUGCAAC	1288
NR1H3-1297-1317-1394	Hs-Mf-Mm	19 mer sense strand	CCAUGAAUGAGCUGCAACU	1289
NR1H3-1338-1358-1435	Hs-Mf-Mm	19 mer sense strand	CUCAUUGCUAUCAGCAUCU	1290
NR1H3-1339-1359-1436	Hs-Mf-Mm	19 mer sense strand	UCAUUGCUAUCAGCAUCUU	1291
NR1H3-1340-1360-1437	Hs-Mf-Mm	19 mer sense strand	CAUUGCUAUCAGCAUCUUC	1292

NR1H3-1341-1361-1438	Hs-Mf-Mm	19 mer sense strand	AUUGCUAUCAGCAUCUUCU	1293
NR1H3-1342-1362-1439	Hs-Mf-Mm	19 mer sense strand	UUGCUAUCAGCAUCUUCUC	1294
NR1H3-1343-1363-1440	Hs-Mf-Mm	19 mer sense strand	UGCUAUCAGCAUCUUCUCU	1295
NR1H3-1344-1364-1441	Hs-Mf-Mm	19 mer sense strand	GCUAUCAGCAUCUUCUCUG	1296
NR1H3-1345-1365-1442	Hs-Mf-Mm	19 mer sense strand	CUAUCAGCAUCUUCUCUGC	1297
NR1H3-1346-1366-1443	Hs-Mf-Mm	19 mer sense strand	UAUCAGCAUCUUCUCUGCA	1298
NR1H3-1347-1367-1444	Hs-Mf-Mm	19 mer sense strand	AUCAGCAUCUUCUCUGCAG	1299
NR1H3-1377-1443-1474	Hs-Mf-Mm	19 mer sense strand	GUGCAGGACCAGCUCCAGG	1300
NR1H3-1379-1445-1476	Hs-Mf-Mm	19 mer sense strand	GCAGGACCAGCUCCAGGUA	1301
NR1H3-1383-1449-1480	Hs-Mf-Mm	19 mer sense strand	GACCAGCUCCAGGUAGAGA	1302
NR1H3-1384-1450-1481	Hs-Mf-Mm	19 mer sense strand	ACCAGCUCCAGGUAGAGAG	1303
NR1H3-1385-1451-1482	Hs-Mf-Mm	19 mer sense strand	CCAGCUCCAGGUAGAGAGG	1304
NR1H3-1387-1453-1484	Hs-Mf-Mm	19 mer sense strand	AGCUCCAGGUAGAGAGGCU	1305
NR1H3-1388-1454-1485	Hs-Mf-Mm	19 mer sense strand	GCUCCAGGUAGAGAGGCUG	1306
NR1H3-1391-1457-1488	Hs-Mf-Mm	19 mer sense strand	CCAGGUAGAGAGGCUGCAG	1307
NR1H3-1393-1459-1490	Hs-Mf-Mm	19 mer sense strand	AGGUAGAGAGGCUGCAGCA	1308
NR1H3-1394-1460-1491	Hs-Mf-Mm	19 mer sense strand	GGUAGAGAGGCUGCAGCAC	1309
NR1H3-1395-1461-1492	Hs-Mf-Mm	19 mer sense strand	GUAGAGAGGCUGCAGCACA	1310
NR1H3-1396-1462-1493	Hs-Mf-Mm	19 mer sense strand	UAGAGAGGCUGCAGCACAC	1311
NR1H3-1397-1463-1494	Hs-Mf-Mm	19 mer sense strand	AGAGAGGCUGCAGCACACA	1312
NR1H3-1398-1464-1495	Hs-Mf-Mm	19 mer sense strand	GAGAGGCUGCAGCACACAU	1313
NR1H3-1399-1465-1496	Hs-Mf-Mm	19 mer sense strand	AGAGGCUGCAGCACACAUA	1314

NR1H3-1400-1466-1497	Hs-Mf-Mm	19 mer sense strand	GAGGCUGCAGCACACAUAU	1315
NR1H3-1401-1467-1498	Hs-Mf-Mm	19 mer sense strand	AGGCUGCAGCACACAUAUG	1316
NR1H3-1402-1468-1499	Hs-Mf-Mm	19 mer sense strand	GGCUGCAGCACACAUAUGU	1317
NR1H3-1403-1469-1500	Hs-Mf-Mm	19 mer sense strand	GCUGCAGCACACAUAUGUG	1318
NR1H3-1404-1470-1501	Hs-Mf-Mm	19 mer sense strand	CUGCAGCACACAUAUGUGG	1319
NR1H3-1406-1472-1503	Hs-Mf-Mm	19 mer sense strand	GCAGCACACAUAUGUGGAA	1320
NR1H3-1407-1473-1504	Hs-Mf-Mm	19 mer sense strand	CAGCACACAUAUGUGGAAG	1321
NR1H3-1408-1474-1505	Hs-Mf-Mm	19 mer sense strand	AGCACACAUAUGUGGAAGC	1322
NR1H3-1410-1476-1507	Hs-Mf-Mm	19 mer sense strand	CACACAUAUGUGGAAGCCC	1323
NR1H3-1411-1477-1508	Hs-Mf-Mm	19 mer sense strand	ACACAUAUGUGGAAGCCCU	1324
NR1H3-1412-1478-1509	Hs-Mf-Mm	19 mer sense strand	CACAUAUGUGGAAGCCCUG	1325
NR1H3-1413-1479-1510	Hs-Mf-Mm	19 mer sense strand	ACAUAUGUGGAAGCCCUGC	1326
NR1H3-1414-1480-1511	Hs-Mf-Mm	19 mer sense strand	CAUAUGUGGAAGCCCUGCA	1327
NR1H3-1415-1481-1512	Hs-Mf-Mm	19 mer sense strand	AUAUGUGGAAGCCCUGCAU	1328
NR1H3-1416-1482-1513	Hs-Mf-Mm	19 mer sense strand	UAUGUGGAAGCCCUGCAUG	1329
NR1H3-1417-1483-1514	Hs-Mf-Mm	19 mer sense strand	AUGUGGAAGCCCUGCAUGC	1330
NR1H3-1418-1484-1515	Hs-Mf-Mm	19 mer sense strand	UGUGGAAGCCCUGCAUGCC	1331
NR1H3-1419-1485-1516	Hs-Mf-Mm	19 mer sense strand	GUGGAAGCCCUGCAUGCCU	1332
NR1H3-1420-1486-1517	Hs-Mf-Mm	19 mer sense strand	UGGAAGCCCUGCAUGCCUA	1333
NR1H3-1421-1487-1518	Hs-Mf-Mm	19 mer sense strand	GGAAGCCCUGCAUGCCUAC	1334
NR1H3-1422-1488-1519	Hs-Mf-Mm	19 mer sense strand	GAAGCCCUGCAUGCCUACG	1335
NR1H3-1423-1489-1520	Hs-Mf-Mm	19 mer sense strand	AAGCCCUGCAUGCCUACGU	1336

NR1H3-1424-1490-1521	Hs-Mf-Mm	19 mer sense strand	AGCCCUGCAUGCCUACGUC	1337
NR1H3-1425-1491-1522	Hs-Mf-Mm	19 mer sense strand	GCCCUGCAUGCCUACGUCU	1338
NR1H3-1426-1492-1523	Hs-Mf-Mm	19 mer sense strand	CCCUGCAUGCCUACGUCUC	1339
NR1H3-1427-1493-1524	Hs-Mf-Mm	19 mer sense strand	CCUGCAUGCCUACGUCUCC	1340
NR1H3-1428-1494-1525	Hs-Mf-Mm	19 mer sense strand	CUGCAUGCCUACGUCUCCA	1341
NR1H3-1429-1495-1526	Hs-Mf-Mm	19 mer sense strand	UGCAUGCCUACGUCUCCAU	1342
NR1H3-1430-1496-1527	Hs-Mf-Mm	19 mer sense strand	GCAUGCCUACGUCUCCAUC	1343
NR1H3-1431-1497-1528	Hs-Mf-Mm	19 mer sense strand	CAUGCCUACGUCUCCAUCC	1344
NR1H3-1432-1498-1529	Hs-Mf-Mm	19 mer sense strand	AUGCCUACGUCUCCAUCCA	1345
NR1H3-1433-1499-1530	Hs-Mf-Mm	19 mer sense strand	UGCCUACGUCUCCAUCCAC	1346
NR1H3-1434-1500-1531	Hs-Mf-Mm	19 mer sense strand	GCCUACGUCUCCAUCCACC	1347
NR1H3-1435-1501-1532	Hs-Mf-Mm	19 mer sense strand	CCUACGUCUCCAUCCACCA	1348
NR1H3-1436-1502-1533	Hs-Mf-Mm	19 mer sense strand	CUACGUCUCCAUCCACCAU	1349
NR1H3-1437-1503-1534	Hs-Mf-Mm	19 mer sense strand	UACGUCUCCAUCCACCAUC	1350
NR1H3-1438-1504-1535	Hs-Mf-Mm	19 mer sense strand	ACGUCUCCAUCCACCAUCC	1351
NR1H3-1439-1505-1536	Hs-Mf-Mm	19 mer sense strand	CGUCUCCAUCCACCAUCCC	1352
NR1H3-1440-1506-1537	Hs-Mf-Mm	19 mer sense strand	GUCUCCAUCCACCAUCCCC	1353
NR1H3-1442-1508-1539	Hs-Mf-Mm	19 mer sense strand	CUCCAUCCACCAUCCCCAU	1354
NR1H3-1443-1509-1540	Hs-Mf-Mm	19 mer sense strand	UCCAUCCACCAUCCCCAUG	1355
NR1H3-1444-1510-1541	Hs-Mf-Mm	19 mer sense strand	CCAUCCACCAUCCCCAUGA	1356
NR1H3-1445-1511-1542	Hs-Mf-Mm	19 mer sense strand	CAUCCACCAUCCCCAUGAC	1357
NR1H3-1446-1512-1543	Hs-Mf-Mm	19 mer sense strand	AUCCACCAUCCCCAUGACC	1358

NR1H3-1447-1513	Hs-Mf	19 mer sense strand	UCCACCAUCCCCAUGACCG	1359
NR1H3-1448-1514	Hs-Mf	19 mer sense strand	CCACCAUCCCCAUGACCGA	1360
NR1H3-1449-1515	Hs-Mf	19 mer sense strand	CACCAUCCCCAUGACCGAC	1361
NR1H3-1450-1516	Hs-Mf	19 mer sense strand	ACCAUCCCCAUGACCGACU	1362
NR1H3-1451-1517	Hs-Mf	19 mer sense strand	CCAUCCCCAUGACCGACUG	1363
NR1H3-1452-1518-1549	Hs-Mf-Mm	19 mer sense strand	CAUCCCCAUGACCGACUGA	1364
NR1H3-1453-1519-1550	Hs-Mf-Mm	19 mer sense strand	AUCCCCAUGACCGACUGAU	1365
NR1H3-1454-1520-1551	Hs-Mf-Mm	19 mer sense strand	UCCCCAUGACCGACUGAUG	1366
NR1H3-1455-1521-1552	Hs-Mf-Mm	19 mer sense strand	CCCCAUGACCGACUGAUGU	1367
NR1H3-1456-1522-1553	Hs-Mf-Mm	19 mer sense strand	CCCAUGACCGACUGAUGUU	1368
NR1H3-1457-1523-1554	Hs-Mf-Mm	19 mer sense strand	CCAUGACCGACUGAUGUUC	1369
NR1H3-1459-1525-1556	Hs-Mf-Mm	19 mer sense strand	AUGACCGACUGAUGUUCCC	1370
NR1H3-1460-1526-1557	Hs-Mf-Mm	19 mer sense strand	UGACCGACUGAUGUUCCCA	1371
NR1H3-1461-1527-1558	Hs-Mf-Mm	19 mer sense strand	GACCGACUGAUGUUCCCAC	1372
NR1H3-1462-1528-1559	Hs-Mf-Mm	19 mer sense strand	ACCGACUGAUGUUCCCACG	1373
NR1H3-1463-1529-1560	Hs-Mf-Mm	19 mer sense strand	CCGACUGAUGUUCCCACGG	1374
NR1H3-1465-1531-1562	Hs-Mf-Mm	19 mer sense strand	GACUGAUGUUCCCACGGAU	1375
NR1H3-1466-1532-1563	Hs-Mf-Mm	19 mer sense strand	ACUGAUGUUCCCACGGAUG	1376
NR1H3-1468-1534-1565	Hs-Mf-Mm	19 mer sense strand	UGAUGUUCCCACGGAUGCU	1377
NR1H3-1469-1535-1566	Hs-Mf-Mm	19 mer sense strand	GAUGUUCCCACGGAUGCUA	1378
NR1H3-1471-1537-1568	Hs-Mf-Mm	19 mer sense strand	UGUUCCCACGGAUGCUAAU	1379
NR1H3-1472-1538-1569	Hs-Mf-Mm	19 mer sense strand	GUUCCCACGGAUGCUAAUG	1380

NR1H3-1473-1539-1570	Hs-Mf-Mm	19 mer sense strand	UUCCCACGGAUGCUGAAUGA	1381
NR1H3-1474-1540-1571	Hs-Mf-Mm	19 mer sense strand	UCCCACGGAUGCUGAAUGAA	1382
NR1H3-1475-1541-1572	Hs-Mf-Mm	19 mer sense strand	CCCACGGAUGCUGAAUGAAA	1383
NR1H3-1476-1542-1573	Hs-Mf-Mm	19 mer sense strand	CCACGGAUGCUGAAUGAAAC	1384
NR1H3-1477-1543-1574	Hs-Mf-Mm	19 mer sense strand	CACGGAUGCUGAAUGAAACU	1385
NR1H3-1478-1544-1575	Hs-Mf-Mm	19 mer sense strand	ACGGAUGCUGAAUGAAACUG	1386
NR1H3-1479-1545-1576	Hs-Mf-Mm	19 mer sense strand	CGGAUGCUGAAUGAAACUGG	1387
NR1H3-1480-1546-1577	Hs-Mf-Mm	19 mer sense strand	GGAUGCUGAAUGAAACUGGU	1388
NR1H3-1481-1547-1578	Hs-Mf-Mm	19 mer sense strand	GAUGCUGAAUGAAACUGGUG	1389
NR1H3-1483-1549-1580	Hs-Mf-Mm	19 mer sense strand	UGCUGAAUGAAACUGGUGAG	1390
NR1H3-1484-1550-1581	Hs-Mf-Mm	19 mer sense strand	GCUAAUGAAACUGGUGAGC	1391
NR1H3-1485-1551-1582	Hs-Mf-Mm	19 mer sense strand	CUAAUGAAACUGGUGAGCC	1392
NR1H3-1486-1552-1583	Hs-Mf-Mm	19 mer sense strand	UAAUGAAACUGGUGAGCCU	1393
NR1H3-1487-1553-1584	Hs-Mf-Mm	19 mer sense strand	AAUGAAACUGGUGAGCCUC	1394
NR1H3-1488-1554-1585	Hs-Mf-Mm	19 mer sense strand	AUGAAACUGGUGAGCCUCC	1395
NR1H3-1489-1555-1586	Hs-Mf-Mm	19 mer sense strand	UGAAACUGGUGAGCCUCCG	1396
NR1H3-1491-1557-1588	Hs-Mf-Mm	19 mer sense strand	AAACUGGUGAGCCUCCGGA	1397
NR1H3-1492-1558-1589	Hs-Mf-Mm	19 mer sense strand	AACUGGUGAGCCUCCGGAC	1398
NR1H3-1494-1560	Hs-Mf	19 mer sense strand	CUGGUGAGCCUCCGGACCC	1399
NR1H3-1505-1571-1602	Hs-Mf-Mm	19 mer sense strand	CCGGACCCUGAGCAGCGUC	1400
NR1H3-1507-1573-1604	Hs-Mf-Mm	19 mer sense strand	GGACCCUGAGCAGCGUCCA	1401
NR1H3-1508-1574	Hs-Mf	19 mer sense strand	GACCCUGAGCAGCGUCCAC	1402

NR1H3-1509-1575	Hs-Mf	19 mer sense strand	ACCCUGAGCAGCGUCCACU	1403
NR1H3-1510-1576	Hs-Mf	19 mer sense strand	CCCUGAGCAGCGUCCACUC	1404
NR1H3-1511-1577-1608	Hs-Mf-Mm	19 mer sense strand	CCUGAGCAGCGUCCACUCA	1405
NR1H3-1512-1578-1609	Hs-Mf-Mm	19 mer sense strand	CUGAGCAGCGUCCACUCAG	1406
NR1H3-1513-1579-1610	Hs-Mf-Mm	19 mer sense strand	UGAGCAGCGUCCACUCAGA	1407
NR1H3-1514-1580-1611	Hs-Mf-Mm	19 mer sense strand	GAGCAGCGUCCACUCAGAG	1408
NR1H3-1515-1581-1612	Hs-Mf-Mm	19 mer sense strand	AGCAGCGUCCACUCAGAGC	1409
NR1H3-1516-1582-1613	Hs-Mf-Mm	19 mer sense strand	GCAGCGUCCACUCAGAGCA	1410
NR1H3-1517-1583-1614	Hs-Mf-Mm	19 mer sense strand	CAGCGUCCACUCAGAGCAA	1411
NR1H3-1518-1584-1615	Hs-Mf-Mm	19 mer sense strand	AGCGUCCACUCAGAGCAAG	1412
NR1H3-1519-1585-1616	Hs-Mf-Mm	19 mer sense strand	GCGUCCACUCAGAGCAAGU	1413
NR1H3-1520-1586-1617	Hs-Mf-Mm	19 mer sense strand	CGUCCACUCAGAGCAAGUG	1414
NR1H3-1521-1587-1618	Hs-Mf-Mm	19 mer sense strand	GUCCACUCAGAGCAAGUGU	1415
NR1H3-1522-1588-1619	Hs-Mf-Mm	19 mer sense strand	UCCACUCAGAGCAAGUGUU	1416
NR1H3-1523-1589-1620	Hs-Mf-Mm	19 mer sense strand	CCACUCAGAGCAAGUGUUU	1417
NR1H3-1525-1591-1622	Hs-Mf-Mm	19 mer sense strand	ACUCAGAGCAAGUGUUUGC	1418
NR1H3-1526-1592-1623	Hs-Mf-Mm	19 mer sense strand	CUCAGAGCAAGUGUUUGCA	1419
NR1H3-1527-1593-1624	Hs-Mf-Mm	19 mer sense strand	UCAGAGCAAGUGUUUGCAC	1420
NR1H3-1528-1594-1625	Hs-Mf-Mm	19 mer sense strand	CAGAGCAAGUGUUUGCACU	1421
NR1H3-1529-1595-1626	Hs-Mf-Mm	19 mer sense strand	AGAGCAAGUGUUUGCACUG	1422
NR1H3-1530-1596-1627	Hs-Mf-Mm	19 mer sense strand	GAGCAAGUGUUUGCACUGC	1423
NR1H3-1531-1597-1628	Hs-Mf-Mm	19 mer sense strand	AGCAAGUGUUUGCACUGCG	1424

NR1H3-1532-1598-1629	Hs-Mf-Mm	19 mer sense strand	GCAAGUGUUUGCACUGCGU	1425
NR1H3-1533-1599-1630	Hs-Mf-Mm	19 mer sense strand	CAAGUGUUUGCACUGCGUC	1426
NR1H3-1534-1600-1631	Hs-Mf-Mm	19 mer sense strand	AAGUGUUUGCACUGCGUCU	1427
NR1H3-1535-1601-1632	Hs-Mf-Mm	19 mer sense strand	AGUGUUUGCACUGCGUCUG	1428
NR1H3-1536-1602-1633	Hs-Mf-Mm	19 mer sense strand	GUGUUUGCACUGCGUCUGC	1429
NR1H3-1537-1603-1634	Hs-Mf-Mm	19 mer sense strand	UGUUUGCACUGCGUCUGCA	1430
NR1H3-1538-1604-1635	Hs-Mf-Mm	19 mer sense strand	GUUUGCACUGCGUCUGCAG	1431
NR1H3-1539-1605-1636	Hs-Mf-Mm	19 mer sense strand	UUUGCACUGCGUCUGCAGG	1432
NR1H3-1540-1606-1637	Hs-Mf-Mm	19 mer sense strand	UUGCACUGCGUCUGCAGGA	1433
NR1H3-1541-1607-1638	Hs-Mf-Mm	19 mer sense strand	UGCACUGCGUCUGCAGGAC	1434
NR1H3-1542-1608-1639	Hs-Mf-Mm	19 mer sense strand	GCACUGCGUCUGCAGGACA	1435
NR1H3-1543-1609-1640	Hs-Mf-Mm	19 mer sense strand	CACUGCGUCUGCAGGACAA	1436
NR1H3-1544-1610-1641	Hs-Mf-Mm	19 mer sense strand	ACUGCGUCUGCAGGACAAA	1437
NR1H3-1545-1611-1642	Hs-Mf-Mm	19 mer sense strand	CUGCGUCUGCAGGACAAAA	1438
NR1H3-1546-1612-1643	Hs-Mf-Mm	19 mer sense strand	UGCGUCUGCAGGACAAAAA	1439
NR1H3-1547-1613-1644	Hs-Mf-Mm	19 mer sense strand	GCGUCUGCAGGACAAAAAG	1440
NR1H3-1548-1614-1645	Hs-Mf-Mm	19 mer sense strand	CGUCUGCAGGACAAAAAGC	1441
NR1H3-1549-1615-1646	Hs-Mf-Mm	19 mer sense strand	GUCUGCAGGACAAAAAGCU	1442
NR1H3-1550-1616-1647	Hs-Mf-Mm	19 mer sense strand	UCUGCAGGACAAAAAGCUC	1443
NR1H3-1551-1617-1648	Hs-Mf-Mm	19 mer sense strand	CUGCAGGACAAAAAGCUCC	1444
NR1H3-1553-1619-1650	Hs-Mf-Mm	19 mer sense strand	GCAGGACAAAAAGCUCCCA	1445
NR1H3-1554-1620-1651	Hs-Mf-Mm	19 mer sense strand	CAGGACAAAAAGCUCCCAC	1446

NR1H3-1555-1621-1652	Hs-Mf-Mm	19 mer sense strand	AGGACAAAAAGCUCCCACC	1447
NR1H3-1556-1622-1653	Hs-Mf-Mm	19 mer sense strand	GGACAAAAAGCUCCCACCG	1448
NR1H3-1558-1624-1655	Hs-Mf-Mm	19 mer sense strand	ACAAAAAGCUCCCACCGCU	1449
NR1H3-1559-1625-1656	Hs-Mf-Mm	19 mer sense strand	CAAAAAGCUCCCACCGCUG	1450
NR1H3-1560-1626-1657	Hs-Mf-Mm	19 mer sense strand	AAAAAGCUCCCACCGCUGC	1451
NR1H3-1561-1627-1658	Hs-Mf-Mm	19 mer sense strand	AAAAGCUCCCACCGCUGCU	1452
NR1H3-1562-1628	Hs-Mf	19 mer sense strand	AAAGCUCCCACCGCUGCUC	1453
NR1H3-1563-1629	Hs-Mf	19 mer sense strand	AAGCUCCCACCGCUGCUCU	1454
NR1H3-1564-1630	Hs-Mf	19 mer sense strand	AGCUCCCACCGCUGCUCUC	1455
NR1H3-1565-1631	Hs-Mf	19 mer sense strand	GCUCCCACCGCUGCUCUCU	1456
NR1H3-1567-1633	Hs-Mf	19 mer sense strand	UCCCACCGCUGCUCUCUGA	1457
NR1H3-1569-1635	Hs-Mf	19 mer sense strand	CCACCGCUGCUCUCUGAGA	1458
NR1H3-1570-1636	Hs-Mf	19 mer sense strand	CACCGCUGCUCUCUGAGAU	1459
NR1H3-1572-1638-1669	Hs-Mf-Mm	19 mer sense strand	CCGCUGCUCUCUGAGAUCU	1460
NR1H3-1573-1639-1670	Hs-Mf-Mm	19 mer sense strand	CGCUGCUCUCUGAGAUCUG	1461
NR1H3-1574-1640-1671	Hs-Mf-Mm	19 mer sense strand	GCUGCUCUCUGAGAUCUGG	1462
NR1H3-1577-1643-1674	Hs-Mf-Mm	19 mer sense strand	GCUCUCUGAGAUCUGGGAU	1463
NR1H3-1579-1645-1676	Hs-Mf-Mm	19 mer sense strand	UCUCUGAGAUCUGGGAUGU	1464
NR1H3-1580-1646-1677	Hs-Mf-Mm	19 mer sense strand	CUCUGAGAUCUGGGAUGUG	1465
NR1H3-1581-1647-1678	Hs-Mf-Mm	19 mer sense strand	UCUGAGAUCUGGGAUGUGC	1466
NR1H3-1582-1648-1679	Hs-Mf-Mm	19 mer sense strand	CUGAGAUCUGGGAUGUGCA	1467
NR1H3-1583-1649-1680	Hs-Mf-Mm	19 mer sense strand	UGAGAUCUGGGAUGUGCAC	1468

NR1H3-1584-1650-1681	Hs-Mf-Mm	19 mer sense strand	GAGAUCUGGGAUGUGCACG	1469
NR1H3-1585-1651-1682	Hs-Mf-Mm	19 mer sense strand	AGAUCUGGGAUGUGCACGA	1470
NR1H3-1586-1652-1683	Hs-Mf-Mm	19 mer sense strand	GAUCUGGGAUGUGCACGAA	1471
NR1H3-1587-1653-1684	Hs-Mf-Mm	19 mer sense strand	AUCUGGGAUGUGCACGAAU	1472
NR1H3-1588-1654-1685	Hs-Mf-Mm	19 mer sense strand	UCUGGGAUGUGCACGAAUG	1473
NR1H3-1589-1655-1686	Hs-Mf-Mm	19 mer sense strand	CUGGGAUGUGCACGAAUGA	1474
NR1H3-1590-1656-1687	Hs-Mf-Mm	19 mer sense strand	UGGGAUGUGCACGAAUGAC	1475
NR1H3-1591-1657-1688	Hs-Mf-Mm	19 mer sense strand	GGGAUGUGCACGAAUGACU	1476
NR1H3-1592-1658-1689	Hs-Mf-Mm	19 mer sense strand	GGAUGUGCACGAAUGACUG	1477
NR1H3-1593-1659-1690	Hs-Mf-Mm	19 mer sense strand	GAUGUGCACGAAUGACUGU	1478
NR1H3-1656-1720	Hs-Mf	19 mer sense strand	UGGUGGCUGCCUCCUAGAA	1479
NR1H3-1657-1721	Hs-Mf	19 mer sense strand	GGUGGCUGCCUCCUAGAAG	1480
NR1H3-1658-1722	Hs-Mf	19 mer sense strand	GUGGCUGCCUCCUAGAAGU	1481
NR1H3-1659-1723	Hs-Mf	19 mer sense strand	UGGCUGCCUCCUAGAAGUG	1482
NR1H3-1660-1724	Hs-Mf	19 mer sense strand	GGCUGCCUCCUAGAAGUGG	1483
NR1H3-1661-1725	Hs-Mf	19 mer sense strand	GCUGCCUCCUAGAAGUGGA	1484
NR1H3-1662-1726	Hs-Mf	19 mer sense strand	CUGCCUCCUAGAAGUGGAA	1485
NR1H3-1663-1727	Hs-Mf	19 mer sense strand	UGCCUCCUAGAAGUGGAAC	1486
NR1H3-1664-1728	Hs-Mf	19 mer sense strand	GCCUCCUAGAAGUGGAACA	1487
NR1H3-1665-1729	Hs-Mf	19 mer sense strand	CCUCCUAGAAGUGGAACAG	1488
NR1H3-1666-1730	Hs-Mf	19 mer sense strand	CUCCUAGAAGUGGAACAGA	1489
NR1H3-1667-1731	Hs-Mf	19 mer sense strand	UCCUAGAAGUGGAACAGAC	1490

NR1H3-1668-1732	Hs-Mf	19 mer sense strand	CCUAGAAGUGGAACAGACU	1491
NR1H3-1669-1733	Hs-Mf	19 mer sense strand	CUAGAAGUGGAACAGACUG	1492
NR1H3-1671-1735	Hs-Mf	19 mer sense strand	AGAAGUGGAACAGACUGAG	1493
NR1H3-1677-1741-1768	Hs-Mf-Mm	19 mer sense strand	GGAACAGACUGAGAAGGGC	1494
NR1H3-1679-1743-1770	Hs-Mf-Mm	19 mer sense strand	AACAGACUGAGAAGGGCAA	1495
NR1H3-1680-1744-1771	Hs-Mf-Mm	19 mer sense strand	ACAGACUGAGAAGGGCAAA	1496
NR1H3-1681-1745-1772	Hs-Mf-Mm	19 mer sense strand	CAGACUGAGAAGGGCAAAC	1497
NR1H3-1682-1746-1773	Hs-Mf-Mm	19 mer sense strand	AGACUGAGAAGGGCAAACA	1498
NR1H3-1683-1747-1774	Hs-Mf-Mm	19 mer sense strand	GACUGAGAAGGGCAAACAU	1499
NR1H3-1684-1748-1775	Hs-Mf-Mm	19 mer sense strand	ACUGAGAAGGGCAAACAUU	1500
NR1H3-1685-1749-1776	Hs-Mf-Mm	19 mer sense strand	CUGAGAAGGGCAAACAUUC	1501
NR1H3-1686-1750-1777	Hs-Mf-Mm	19 mer sense strand	UGAGAAGGGCAAACAUUCC	1502
NR1H3-1687-1751-1778	Hs-Mf-Mm	19 mer sense strand	GAGAAGGGCAAACAUUCCU	1503
NR1H3-1728-1792	Hs-Mf	19 mer sense strand	CCCGUGGCAUUAAGAGA	1504
NR1H3-1729-1793	Hs-Mf	19 mer sense strand	CCGUGGCAUUAAGAGAG	1505
NR1H3-1730-1794	Hs-Mf	19 mer sense strand	CGUGGCAUUAAGAGAGU	1506
NR1H3-1731-1795	Hs-Mf	19 mer sense strand	GUGGCAUUAAGAGAGUC	1507
NR1H3-1732-1796-1826	Hs-Mf-Mm	19 mer sense strand	UGGCAUUAAGAGAGUCA	1508
NR1H3-1209-1229-1306	Hs-Mf-Mm	19 mer sense strand	CUCAAGGAUUUCAGUUAUA	1509
NR1H3-1210-1230-1307	Hs-Mf-Mm	19 mer sense strand	UCAAGGAUUUCAGUUAUAA	1510
NR1H3-1594-1660-1691	Hs-Mf-Mm	19 mer sense strand	AUGUGCACGAAUGACUGUU	1511

NR1H3-1209-1229-1306	Hs-Mf-Mm	19 mer antisense strand	UAUAACUGAAAUCCUUGAG	1512
NR1H3-1210-1230-1307	Hs-Mf-Mm	19 mer antisense strand	UUAUAACUGAAAUCCUUGA	1513
NR1H3-1515-1581-1612	Hs-Mf-Mm	19 mer antisense strand	GCUCUGAGUGGACGCUGCU	1514
NR1H3-1594-1660-1691	Hs-Mf-Mm	19 mer antisense strand	AACAGUCAUUCGUGCACAU	1515
DNA	Homo sapiens		ATGGAATTCC CCATTGGATC CCTCGAACT AACAACTTCC GTCGCTTTAC TCCGGAGTCA CTGGTGGAGA TAGAGAAGCA AATTGCTGCC AAGCAGGGAA CAAAGAAAGC CAGAGAGAAG CATAGGGAGC AGAAGGACCA AGAAGAGAAG CCTCGGCCCC AGCTGGACTT GAAAGCCTGC AACCAGCTGC CCAAGTTCTA TGGTGAGCTC CCAGCAGAAC TGATCGGGGA GCCCCTGGAG GATCTAGATC CGTTCTACAG CACACACCGG ACATTTATGG TGCTGAACAA AGGGAGGACC ATTTCCCGGT TTAGTGCCAC TCGGGCCCTG TGGCTATTCA GTCCTTTCAA CCTGATCAGA AGAACGGCCA TCAAAGTGTC TGTCCACTCG TGGTTCAGTT TATTTATTAC GGTCATTATT TTGGTTAATT GTGTGTGCAT GACCCGAACT GACCTTCCAG AGAAAATTGA ATATGTCTTC ACTGTCATTT ACACCTTTGA AGCCTTGATA AAGATACTGG CAAGAGGATT TTGTCTAAAT GAGTTCACGT ACCTGAGAGA TCCTTGGAAC TGGCTGGATT TTAGCGTCAT TACCCTGGCA TATGTTGGCA CAGCAATAGA TCTCCGTGGG ATCTCAGGCC TGCGGACATT CAGAGTTCTT	1516

			AGAGCATTAA AAACAGTTTC TGTGATCCCA GGCCTGAAGG TCATTGTGGG GGCCCTGATT CACTCAGTGA AGAAACTGGC TGATGTGACC ATCCTCACCA TCTTCTGCCT AAGTGTTTTT GCCTTGGTGG GGCTGCAACT CTTCAAGGGC AACCTCAAAA ATAAATGTGT CAAGAATGAC ATGGCTGTCA ATGAGACAAC CAACTACTCA TCTCACAGAA AACCAGATAT CTACATAAAT AAGCGAGGCA CTTCTGACCC CTTACTGTGT GGCAATGGAT CTGACTCAGG CCACTGCCCT GATGGTTATA TCTGCCTTAA AACTTCTGAC AACCCGGATT TTAACTACAC CAGCTTTGAT TCCTTTGCTT GGGCTTTCCT CTCACTGTTC CGCCTCATGA CACAGGATTC CTGGGAACGCCTCTACCAGC AGACCCTGAG GACTTCTGGG AAAATCTATA TGATCTTTTT TGTGCTCGTA ATCTTCCTGG GATCTTTCTA CCTGGTCAAC TTGATCTTGG CTGTAGTCAC CATGGCGTAT GAGGAGCAGA ACCAGGCAAC CACTGATGAA ATTGAAGCAA AGGAGAAGAA GTTCCAGGAG GCCCTCGAGA TGCTCCGGAA GGAGCAGGAG GTGCTAGCAG CACTAGGGAT TGACACAACC TCTCTCCACT CCCACAATGG ATCACCTTTA ACCTCCAAAA ATGCCAGTGA GAGAAGGCAT AGAATAAAGC CAAGAGTGTC AGAGGGCTCC ACAGAAGACA ACAAATCACC CCGCTCTGAT CCTTACAACC AGCGCAGGAT GTCTTTTCTA GGCCTCGCCT CTGGAAAACG CCGGGCTAGT CATGGCAGTG TGTTCCATTT CCGGTCCCCT GGCCGAGATA TCTCACTCCC	
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			TGAGGGAGTC ACAGATGATG GAGTCTTTCC TGGAGACCAC GAAAGCCATC GGGGCTCTCT GCTGCTGGGT GGGGGTGCTG GCCAGCAAGG CCCCCTCCCT AGAAGCCCTC TTCCTCAACC CAGCAACCCT GACTCCAGGC ATGGAGAAGA TGAACACCAA CCGCCGCCA CTAGTGAGCT TGCCCCTGGA GCTGTCGATG TCTCGGCATT CGATGCAGGA CAAAGAAGA CTTTCTTGTC AGCAGAATAC TTAGATGAAC CTTTCCGGGC CCAAAGGGCA ATGAGTGTTG TCAGTATCAT AACCTCCGTC CTTGAGGAAC TCGAGGAGTC TGAACAGAAG TGCCCACCCT GCTTGACCAG CTTGTCTCAG AAGTATCTGA TCTGGGATTG CTGCCCCATG TGGGTGAAGC TCAAGACAAT TCTCTTTGGG CTTGTGACGG ATCCCTTTGC AGAGCTCACC ATCACCTTGT GCATCGTGGT GAACACCATC TTCATGGCCA TGGAGCACCA TGGCATGAGC CCTACCTTCG AAGCCATGCT CCAGATAGGC AACATCGTCT TTACCATATT TTTTACTGCT GAAATGGTCT TCAAATCAT TGCCTTCGAC CCATACTATT ATTTCCAGAA GAAGTGGAAT ATCTTTGACT GCATCATCGT CACTGTGAGT CTGCTAGAGC TGGGCGTGGC CAAGAAGGGA AGCCTGTCTG TGCTGCGGAG CTTCCGCTTG CTGCGCGTAT TCAAGCTGGC CAAATCCTGG CCCACCTTAA ACACACTCAT CAAGATCATC GGAAACTCAG TGGGGGCACT GGGGAACCTC ACCATCATCC TGGCCATCAT TGTCTTTGTC TTTGCTCTGG TTGGCAAGCA GCTCCTAGGG GAAAACTACC	
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			GTAACAACCG AAAAAATATC TCCGCGCCCC ATGAAGACTG GCCCCGCTGG CACATGCACG ACTTCTTCCA CTCTTTCCTC ATTGTCTTCC GTATCCTCTG TGGAGAGTGG ATTGAGAACA TGTGGGCCTG CATGGAAGTT GGCCAAAAAT CCATATGCCT CATCCTTTTC TTGACGGTGA TGGTGCTAGG GAACCTGGTG GTGCTTAACC TGTTTCATCGC CCTGCTATTG AACTCTTTCA GTGCTGACAA CCTCACAGCC CCGGAGGACG ATGGGGAGGT GAACAACCTG CAGGTGGCCC TGGCACGGAT CCAGGTCTTT GGCCATCGTA CCAAACAGGC TCTTTGCAGC TTCTTCAGCA GGTCCTGCCC ATTCCCCCAG CCCAAGGCAG AGCCTGAGCT GGTGGTGAAA CTCCCCTCT CCAGCTCCAA GGCTGAGAAC CACATTGCTG CCAACACTGC CAGGGGGAGC TCTGGAGGGC TCCAAGCTCC CAGAGGCCCC AGGGATGAGC ACAGTGACTT CATCGCTAAT CCGACTGTGT GGGTCTCTGT GCCCATTGCT GAGGGTGAAT CTGATCTTGA TGACTTGGAG GATGATGGTG GGGAAGATGC TCAGAGCTTC CAGCAGGAAG TGATCCCCAA AGGACAGCAG GAGCAGCTGC AGCAAGTCGA GAGGTGTGGG GACCACCTGA CACCCAGGAG CCCAGGCACT GGAACATCTT CTGAGGACCT GGCTCCATCC CTGGGTGAGA CGTGGAAGA TGAGTCTGTT CCTCAGGTCC CTGCTGAGGG AGTGGACGAC ACAAGCTCCT CTGAGGGCAG CACGGTGGAC TGCCTAGATC CTGAGGAAAT CCTGAGGAAG ATCCCTGAGC TGGCAGATGA CCTGGAAGAA CCAGATGACT	
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			GCTTCACAGA AGGATGCATT CGCCACTGTC CCTGCTGCAA ACTGGATACC ACCAAGAGTC CATGGGATGT GGGCTGGCAG GTGCGCAAGA CTTGCTACCG TATCGTGGAG CACAGCTGGT TTGAGAGCTT CATCATCTTC ATGATCCTGC TCAGCAGTGG ATCTCTGGCC TTTGAAGACT ATTACCTGGA CCAGAAGCCC ACGGTGAAAG CTTTGCTGGA GTACACTGAC AGGGTCTTCA CCTTTATCTT TGTGTTCGAG ATGCTGCTTA AGTGGGTGGC CTATGGCTTC AAAAAGTACT TCACCAATGC CTGGTGCTGG CTGGACTTCC TCATTGTGAA TATCTCACTG ATAAGTCTCA CAGCGAAGAT TCTGGAATAT TCTGAAGTGG CTCCCATCAA AGCCCTTCGA ACCCTTCGCG CTCTGCGGCC ACTGCGGGCT CTTTCTCGAT TTGAAGGCAT GCGGGTGGTG GTGGATGCCC TGGTGGGCGC CATCCCATCC ATCATGAATG TCCTCCTCGT CTGCCTCATC TTCTGGCTCA TCTTCAGCAT CATGGGTGTG AACCTCTTCG CAGGGAAGTT TTGGAGGTGC ATCAACTATA CCGATGGAGA GTTTTCCCTT GTACCTTTGT CGATTGTGAA TAACAAGTCT GACTGCAAGA TTCAAACTC CACTGGCAGC TTCTTCTGGG TCAATGTGAA AGTCAACTTT GATAATGTTG CAATGGGTTA CCTTGCACTT CTGCAGGTGG CAACCTTTAA AGGCTGGATG GACATTATGT ATGCAGCTGT TGATTCCCGG GAGGTCAACA TGCAACCCAA GTGGGAGGAC AACGTGTACA TGTATTTGTA CTTTGTTCATC TTCATCATTT TTGGAGGCTT CTTCACACTG AATCTCTTTG	
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			TTGGGGTCAT AATTGACAAC TTCAATCAAC AGAAAAAAAAA GTTAGGGGGC CAGGACATCT TCATGACAGA GGAGCAGAAG AAATACTACA ATGCCATGAA GAAGTTGGGC TCCAAGAAGC CCCAGAAGCC CATCCCACGG CCCCTGAACA AGTTCCAGGG TTTTGTCTTT GACATCGTGA CCAGACAAGC TTTTGACATC ACCATCATGG TCCTCATCTG CCTCAACATG ATCACCATGA TGGTGGAGAC TGATGACCAA AGTGAAGAAA AGACGAAAAT TCTGGGCAAA ATCAACCAGT TCTTTGTGGC CGTCTTCACA GGCGAATGTG TCATGAAGAT GTTCGCTTTG AGGCAGTACT ACTTCACAAA TGGCTGGAAT GTGTTTGAAT TCATTGTGGT GGTTCTCTCC ATTGCGAGCC TGATTTTTTC TGCAATTCTT AAGTCACTTC AAAGTTACTT CTCCCCAACG CTCTTCAGAG TCATCCGCCT GGCCCGAATT GGCCGCATCC TCAGACTGAT CCGAGCGGCC AAGGGGATCC GCACACTGCT CTTTGCCCTC ATGATGTCCC TGCCTGCCCT CTTCAACATC GGGCTGTTGC TATTCCTTGT CATGTTTCATC TACTCTATCT TCGGTATGTC CAGCTTTCCC CATGTGAGGT GGGAGGCTGG CATCGACGAC ATGTTCAACT TCCAGACCTT CGCCAACAGC ATGCTGTGCC TCTTCCAGAT TACCACGTCG GCCGGCTGGG ATGGCCTCCT CAGCCCCATC CTCAACACAG GGCCCCCTA CTGTGACCCC AATCTGCCCA ACAGCAATGG CACCAGAGGG GACTGTGGGA GCCCAGCCGT AGGCATCATC TTCTTCACCA CCTACATCAT CATCTCCTTC CTCATCGTGG	
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			TCAACATGTA CATTGCAGTG ATTCTGGAGA ACTTCAATGT GGCCACGGAG GAGAGCACTG AGCCCCTGAG TGAGGACGAC TTTGACATGT TCTATGAGAC CTGGGAGAAG TTTGACCCAG AGGCCACTCA GTTTATTACC TTTTCTGCTC TCTCGGACTT TGCAGACACT CTCTCTGGTC CCCTGAGAAT CCCAAAACCC AATCGAAATA TACTGATCCA GATGGACCTG CCTTTGGTCC CTGGAGATAA GATCCACTGC TTGGACATCC TTTTGTCTT CACCAAGAAT GTCCTAGGAG AATCCGGGGA GTTGGATTCT CTGAAGGCAA ATATGGAGGA GAAGTTTATG GCAACTAATC TTTCAAAATC ATCCTATGAA CCAATAGCAA CCACTCTCCG ATGGAAGCAA GAAGACATT CAGCCACTGT CATTCAAAG GCCTATCGGA GCTATGTGCT GCACCGCTCC ATGGCACTCT CTAACACCCC ATGTGTGCCC AGAGCTGAGG AGGAGGCTGC ATCACTCCCA GATGAAGGTT TTGTTGCATT CACAGCAAAT GAAAATTGTG TACTCCCAGA CAAATCTGAA ACTGCTTCTG CCACATCATT CCCACCGTCC TATGAGAGTG TCACTAGAGG CCTTAGTGAT AGAGTCAACA TGAGGACATC TAGCTCAATA CAAAATGAAG ATGAAGCCAC CAGTATGGAG CTGATTGCCC CTGGGCCCTA GTGA	
Forward-942	Artificial Sequence		GTCTCTGTGCAGGAGATAGTTG	1517
Reverse-1399	Artificial Sequence		GGAGGCTCACCAGTTTCATTA	1518
NR1H3-1207-1227-1304	Hs-Mf-Mm	36 mer sense strand	UCCUCAAGGAUUUCAGUUAAGCA GCCGAAAGGCUGC	1519
NR1H3-1220-1240-1317	Hs-Mf-Mm	36 mer sense strand	CAGUUAUAACCGGGAAGACAGCA GCCGAAAGGCUGC	1520

NR1H3-1224-1244-1321	Hs-Mf-Mm	36 mer sense strand	UAUAACCGGGAAGACUUUGAGC AGCCGAAAGGCUGC	1521
NR1H3-1244-1264-1341	Hs-Mf-Mm	36 mer sense strand	CAAAGCAGGGCUGCAAGUGAGCA GCCGAAAGGCUGC	1522
NR1H3-1252-1272-1349	Hs-Mf-Mm	36 mer sense strand	GGCUGCAAGUGGAAUUCAUAGC AGCCGAAAGGCUGC	1523
NR1H3-1259-1279-1356	Hs-Mf-Mm	36 mer sense strand	AGUGGAAUUCAUCAACCCCAGCA GCCGAAAGGCUGC	1524
NR1H3-1265-1285-1362	Hs-Mf-Mm	36 mer sense strand	AUUCAUCAACCCCAUCUUCAGCA GCCGAAAGGCUGC	1525
NR1H3-1266-1286-1363	Hs-Mf-Mm	36 mer sense strand	UUCAUCAACCCCAUCUUCGAGCA GCCGAAAGGCUGC	1526
NR1H3-1429-1495-1526	Hs-Mf-Mm	36 mer sense strand	UGCAUGCCUACGUCUCCAUAAGCA GCCGAAAGGCUGC	1527
NR1H3-1433-1499-1530	Hs-Mf-Mm	36 mer sense strand	UGCCUACGUCUCCAUCCACAGCA GCCGAAAGGCUGC	1528
NR1H3-1437-1503-1534	Hs-Mf-Mm	36 mer sense strand	UACGUCUCCAUCCACCAUCAGCA GCCGAAAGGCUGC	1529
NR1H3-1439-1505-1536	Hs-Mf-Mm	36 mer sense strand	CGUCUCCAUCCACCAUCCCAGCA GCCGAAAGGCUGC	1530
NR1H3-1446-1512-1543	Hs-Mf-Mm	36 mer sense strand	AUCCACCAUCCCCAUGACCAGCA GCCGAAAGGCUGC	1531
NR1H3-1463-1529-1560	Hs-Mf-Mm	36 mer sense strand	CCGACUGAUGUUCCCACGGAGCA GCCGAAAGGCUGC	1532
NR1H3-1475-1541-1572	Hs-Mf-Mm	36 mer sense strand	CCCACGGAUGC UAAUGAAAAGCA GCCGAAAGGCUGC	1533
NR1H3-1479-1545-1576	Hs-Mf-Mm	36 mer sense strand	CGGAUGC UAAUGAAACUGGAGC AGCCGAAAGGCUGC	1534
NR1H3-1481-1547-1578	Hs-Mf-Mm	36 mer sense strand	GAUGC UAAUGAAACUGGUGAGC AGCCGAAAGGCUGC	1535
NR1H3-1485-1551-1582	Hs-Mf-Mm	36 mer sense strand	C UAAUGAAACUGGUGAGCCAGCA GCCGAAAGGCUGC	1536
NR1H3-1515-1581-1612	Hs-Mf-Mm	36 mer sense strand	AGCAGCGUCCACUCAGAGCAGCA GCCGAAAGGCUGC	1537
NR1H3-1517-1583-1614	Hs-Mf-Mm	36 mer sense strand	CAGCGUCCACUCAGAGCAAAGCA GCCGAAAGGCUGC	1538
NR1H3-1518-1584-1615	Hs-Mf-Mm	36 mer sense strand	AGCGUCCACUCAGAGCAAGAGCA GCCGAAAGGCUGC	1539
NR1H3-1533-1599-1630	Hs-Mf-Mm	36 mer sense strand	CAAGUGUUUGCACUGCGUCAGCA GCCGAAAGGCUGC	1540
NR1H3-1535-1601-1632	Hs-Mf-Mm	36 mer sense strand	AGUGUUUGCACUGCGUCUGAGCA GCCGAAAGGCUGC	1541
NR1H3-1545-1611-1642	Hs-Mf-Mm	36 mer sense strand	CUGCGUCUGCAGGACAAAAAGCA GCCGAAAGGCUGC	1542

NR1H3-1554-1620-1651	Hs-Mf-Mm	36 mer sense strand	CAGGACAAAAAGCUCCCACAGCA GCCGAAAGGCUGC	1543
NR1H3-1581-1647-1678	Hs-Mf-Mm	36 mer sense strand	UCUGAGAUCUGGGAUGUGCAGC AGCCGAAAGGCUGC	1544
NR1H3-1586-1652-1683	Hs-Mf-Mm	36 mer sense strand	GAUCUGGGAUGUGCACGAAAGC AGCCGAAAGGCUGC	1545
NR1H3-1587-1653-1684	Hs-Mf-Mm	36 mer sense strand	AUCUGGGAUGUGCACGAAUAGC AGCCGAAAGGCUGC	1546
NR1H3-1588-1654-1685	Hs-Mf-Mm	36 mer sense strand	UCUGGGAUGUGCACGAAUGAGC AGCCGAAAGGCUGC	1547
NR1H3-1663-1727	Hs-Mf	36 mer sense strand	UGCCUCCUAGAAGUGGAACAGCA GCCGAAAGGCUGC	1548
NR1H3-1671-1735	Hs-Mf	36 mer sense strand	AGAAGUGGAACAGACUGAGAGC AGCCGAAAGGCUGC	1549
NR1H3-1684-1748-1775	Hs-Mf-Mm	36 mer sense strand	ACUGAGAAGGGCAAACAUUAGC AGCCGAAAGGCUGC	1550
NR1H3-1731-1795	Hs-Mf	36 mer sense strand	GUGGCAUUA AAAAGAGAGUCAGC AGCCGAAAGGCUGC	1551
NR1H3-1732-1796-1826	Hs-Mf-Mm	36 mer sense strand	UGGCAUUA AAAAGAGAGUCAAGC AGCCGAAAGGCUGC	1552

CLAIMS

1. A double stranded RNAi oligonucleotide (dsRNAi) for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein

(i) the sense strand comprises a nucleotide sequence comprising at least 19 contiguous nucleotides, with 0 or 1 mismatches, of a portion of a nucleotide sequence of any one of SEQ ID NOs 787 and 786; and

(ii) the antisense strand comprises a nucleotide sequence comprising at least 19 contiguous nucleotides, with 0 or 1 mismatches, of a portion of a nucleotide sequence of any one of SEQ ID NOs 875 and 874.

2. The double stranded RNAi oligonucleotide (dsRNAi) of claim 1, wherein

i) the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 787, and the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 875; or

ii) the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 786, and the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 874.

3. The double stranded RNAi oligonucleotide (dsRNAi) of claim 1 or 2, wherein the sense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 787, and the antisense strand comprises a nucleotide sequence as set forth in SEQ ID NO: 875.

4. The double stranded RNAi oligonucleotide (dsRNAi) of any one of the preceding claims, wherein the 3' end of the sense strand comprises a stem-loop set forth as S1-L-S2, wherein

(i) S1 is complementary to S2, wherein S1 and S2 are each 1-10 nucleotides in length and have the same length; and

(ii) L forms a loop between S1 and S2 of 3-5 nucleotides in length, wherein L is a triloop or a tetraloop, optionally wherein the tetraloop comprises the sequence 5'-GAAA-3'.

5. The double stranded RNAi oligonucleotide (dsRNAi) of claim 4, wherein the stem-loop comprises the sequence 5'-GCAGCCGAAAGGCUGC-3' (SEQ ID NO: 1121).
6. The double stranded 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, wherein the targeting ligand is a hepatocyte targeting ligand, and wherein each hepatocyte targeting ligand comprises a N-acetylgalactosamine (GalNAc) moiety, optionally wherein the GalNAc moiety is a monovalent GalNAc moiety, a bivalent GalNAc moiety, a trivalent GalNAc moiety or a tetravalent GalNAc moiety.
7. The double stranded RNAi oligonucleotide of claim 6, wherein the one or more targeting ligands is conjugated to one or more nucleotides of the loop, optionally 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, wherein the targeting ligands are the same or different.
8. The double stranded RNAi oligonucleotide of any one of the preceding claims, wherein
 - (i) the oligonucleotide comprises at least one modified nucleotide, wherein the modified nucleotide comprises a 2'-modification;
 - (ii) the sense strand comprises 36 nucleotides with positions 1-36 from 5' to 3', wherein positions 8-11 comprise a 2'-fluoro modification;
 - (iii) the antisense strand comprises 22 nucleotides with positions 1-22 from 5' to 3', and wherein positions 2, 3, 4, 5, 7, 10, and 14 comprise a 2'-fluoro modification; and
 - (iv) the remaining nucleotides comprise a 2'-O-methyl modification.
9. The double stranded RNAi oligonucleotide of any one of the preceding claims, wherein the oligonucleotide comprises at least one modified internucleotide linkage, wherein the at least one modified internucleotide linkage is a phosphorothioate linkage, wherein:
 - (i) the antisense strand comprises a phosphorothioate linkage (a) between positions 1 and 2, and between positions 2 and 3; or (b) 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';

(ii) 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'; and

(iii) the sense strand comprises a phosphorothioate linkage between positions 1 and 2, wherein positions are numbered from 5' to 3'.

10. The double stranded RNAi oligonucleotide of any one of the preceding claims, wherein

(i) the 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog, wherein the phosphate analog is a 4'-phosphate analog comprising 5'-methoxyphosphonate-4'-oxy; and

(ii) wherein the antisense strand comprises an overhang sequence of one or more nucleotides in length at the 3' terminus, wherein the overhang sequence is 2 nucleotides in length, and wherein the overhang is selected from AA, GG, AG, and GA, optionally wherein the overhang is GG.

11. The double stranded RNAi oligonucleotide (dsRNAi) according to any one of the preceding claims, wherein

(i) the sense and antisense strands comprise the nucleotide sequences set forth in SEQ ID NOs: 964 and 1052, respectively; or

(ii) the sense and antisense strands comprise the nucleotide sequences set forth in SEQ ID NOs: 963 and 1051, respectively.

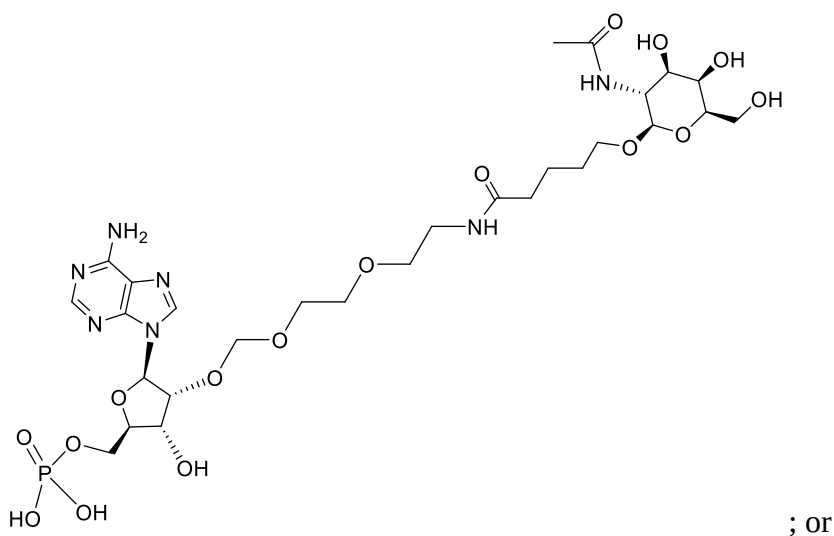
12. The double stranded RNAi oligonucleotide (dsRNAi) according to any one of the preceding claims, wherein the sense and antisense strands comprise the nucleotide sequences set forth in SEQ ID NOs: 964 and 1052, respectively.

13. An RNAi oligonucleotide for reducing (NR1H3) 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

NR1H3 mRNA target sequence of any one of SEQ ID NOs: 1510 and 1509, and wherein the region of complementarity is at least 19 contiguous nucleotides in length.

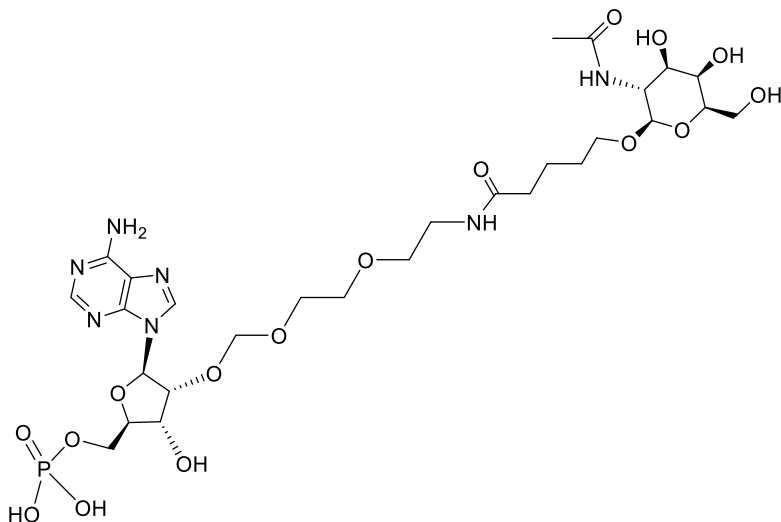
14. A double stranded RNAi oligonucleotide (dsRNAi) for reducing *NR1H3* expression, the oligonucleotide comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a duplex region, wherein

(i) the sense strand comprises the sequence and all of the modifications of 5'-mCs-mU-mC-mA-mA-mG-mG-fA-fU-fU-fU-mC-mA-mG-mU-mU-mA-mU-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: 963), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs]-fUs-fAs-fU-fA-mA-fC-mU-mG-fA-mA-mA-mU-fC-mC-mU-mU-mG-mA-mGs-mGs-mG-3' (SEQ ID NO: 1051), wherein mC, mA, mG, and mU = 2'-OMe ribonucleosides; fA, fC, fG, and fU=2'-F ribonucleosides; s = phosphorothioate, and wherein ademA-GalNAc =



(ii) the sense strand comprises the sequence and all of the modifications of 5'-mUs-mC-mA-mA-mG-mG-mA-fU-fU-fU-fC-mA-mG-mU-mU-mA-mU-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: 964), and wherein the antisense strand comprises the sequence and all of the modifications of 5'-[MePhosphonate-4O-mUs]-fUs-fUs-fA-fU-mA-fA-mC-mU-fG-mA-mA-mA-fU-mC-mC-mU-mU-mG-mAs-mGs-mG-3' (SEQ ID NO: 1052), wherein mC, mA, mG, and

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



15. A pharmaceutical composition comprising the RNAi oligonucleotide of any one of claims 1-14, and a pharmaceutically acceptable carrier, delivery agent or excipient.
16. Use of a RNAi oligonucleotide of any one of claims 1-14, or the pharmaceutical composition of claim 15, in the manufacture of a medicament for treatment of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), multiple sclerosis, or systemic lupus erythematosus.