

What is Claimed

1. An RNAi construct comprising a sense strand and an antisense strand, wherein the antisense strand comprises a region having at least 15 contiguous nucleotides differing by no more than 3 nucleotides from an antisense sequence listed in Table 1 or 2, and wherein the RNAi construct inhibits the expression of Patatin-Like Phospholipase Domain Containing 3 (PNPLA3).
2. The RNAi construct of claim 1, wherein the antisense strand comprises a region that is complementary to a PNPLA3 mRNA sequence.
3. The RNAi construct any of the above claims, wherein the sense strand comprises a region having at least 15 contiguous nucleotides differing by no more than 3 nucleotides from an antisense sequence listed in Table 1 or 2.
4. The RNAi construct any of the above claims, wherein the construct preferentially inhibits a PNPLA3-rs738409 minor allele.
5. The RNAi construct of claim 4, wherein the construct has at least 10% greater inhibition of a PNPLA3-rs738409 minor allele as compared to the major allele.
6. The RNAi construct of any of the above claims, wherein the construct preferentially inhibits a PNPLA3-rs738408 minor allele.
7. The RNAi construct of claim 6, wherein the construct has at least 10% greater inhibition of a PNPLA3-rs738409-rs738408 double minor allele as compared to the major allele.
8. The RNAi construct any of the above claims, wherein the sense strand comprises a sequence that is sufficiently complementary to the sequence of the antisense strand to form a duplex region of about 15 to about 30 base pairs in length.
9. The RNAi construct of claim 8, wherein the duplex region is about 17 to about 24 base pairs in length.
10. The RNAi construct of claim 8, wherein the duplex region is about 19 to about 21 base pairs in length.
11. The RNAi construct of claim 10, wherein the duplex region is 19 base pairs in length.

12. The RNAi construct of any one of claims 8 to 11, wherein the sense strand and the antisense strand are each about 15 to about 30 nucleotides in length.
13. The RNAi construct of claim 12, wherein the sense strand and the antisense strand are each about 19 to about 27 nucleotides in length.
14. The RNAi construct of claim 12, wherein the sense strand and the antisense strand are each about 21 to about 25 nucleotides in length.
15. The RNAi construct of claim 12, wherein the sense strand and the antisense strand are each about 21 to about 23 nucleotides in length.
16. The RNAi construct of any one of claims 1 to 15, wherein the RNAi construct comprises at least one blunt end.
17. The RNAi construct of any one of claims 1 to 15, wherein the RNAi construct comprises at least one nucleotide overhang of 1 to 4 unpaired nucleotides.
18. The RNAi construct of claim 17, wherein the nucleotide overhang has 2 unpaired nucleotides.
19. The RNAi construct of claim 17 or 18, wherein the RNAi construct comprises a nucleotide overhang at the 3' end of the sense strand, the 3' end of the antisense strand, or the 3' end of both the sense strand and the antisense strand.
20. The RNAi construct of any one of claims 17 to 19, wherein the nucleotide overhang comprises a 5'-UU-3' dinucleotide or a 5'-dTdT-3' dinucleotide.
21. The RNAi construct of any one of claims 1 to 20, wherein the RNAi construct comprises at least one modified nucleotide.
22. The RNAi construct of claim 21, wherein the modified nucleotide is a 2'-modified nucleotide.
23. The RNAi construct of claim 21, wherein the modified nucleotide is a 2'-fluoro modified nucleotide, a 2'-O-methyl modified nucleotide, a 2'-O-methoxyethyl modified nucleotide, a 2'-O-allyl modified nucleotide, a bicyclic nucleic acid (BNA), a glycol nucleic acid, an inverted base or combinations thereof.

24. The RNAi construct of claim 23, wherein the modified nucleotide is a 2'-O-methyl modified nucleotide, a 2'-O-methoxyethyl modified nucleotide, a 2'-fluoro modified nucleotide, or combinations thereof.
25. The RNAi construct of claim 21, wherein all of the nucleotides in the sense and antisense strands are modified nucleotides.
26. The RNAi construct of claim 25, wherein the modified nucleotides are 2'-O-methylmodified nucleotides, 2'-fluoro modified nucleotides, or combinations thereof.
27. The RNAi construct of any one of claims 1 to 26, wherein the RNAi construct comprises at least one phosphorothioate internucleotide linkage.
28. The RNAi construct of claim 27, wherein the RNAi construct comprises two consecutive phosphorothioate internucleotide linkages at the 3' end of the antisense strand.
29. The RNAi construct of claim 27, wherein the RNAi construct comprises two consecutive phosphorothioate internucleotide linkages at both the 3' and 5' ends of the antisense strand and two consecutive phosphorothioate internucleotide linkages at the 5' end of the sense strand.
30. The RNAi construct of any one of claims 1 to 29, wherein the antisense strand comprises a sequence selected from the antisense sequences listed in Table 1 or Table 2.
31. The RNAi construct of claim 30, wherein the sense strand comprises a sequence selected from the sense sequences listed in Table 1 or Table 2.
32. The RNAi construct of any one of claims 1 to 31, wherein the RNAi construct is any one of the duplex compounds listed in any one of Tables 1 to 2.
33. The RNAi construct of any one of claims 1 to 32, wherein the RNAi construct reduces the expression level of PNPLA3 in liver cells following incubation with the RNAi construct as compared to the PNPLA3 expression level in liver cells that have been incubated with a control RNAi construct.
34. The RNAi construct of claim 27, wherein the liver cells are Hep3B or HepG2 cells.
35. The RNAi construct of any one of claims 1 to 26, wherein the RNAi construct inhibits at least 10% of PNPLA3 expression at 5 nM in Hep3B cells *in vitro*.

36. The RNAi construct of any one of claims 1 to 26, wherein the RNAi construct inhibits at least 10% of PNPLA3 expression at 5 nM in HepG2 cells *in vitro*.
37. The RNAi construct of any one of claims 1 to 26, wherein the RNAi construct inhibits PNPLA3 expression in Hep3B cells with an IC₅₀ of less than about 1 nM.
38. The RNAi construct of any one of claims 1 to 26, wherein the RNAi construct inhibits PNPLA3 expression in HepG2 cells with an IC₅₀ of less than about 1 nM.
39. A pharmaceutical composition comprising the RNAi construct of any one of claims 1 to 38 and a pharmaceutically acceptable carrier, excipient, or diluent.
40. A method for reducing the expression of PNPLA3 in a patient in need thereof comprising administering to the patient the RNAi construct of any one of claims 1 to 38.
41. The method of claim 40, wherein the expression level of PNPLA3 in hepatocytes is reduced in the patient following administration of the RNAi construct as compared to the PNPLA3 expression level in a patient not receiving the RNAi construct.