CLAIMS

1. A nucleic acid comprising:

(a) a 5’ end and a 3’ end;

(b) a seed region that is complementary to a region of a gene comprising an allelic polymorphism;

(c) a single nucleotide polymorphism (SNP) position nucleotide at a position within the seed region, wherein the SNP position nucleotide is complementary to the allelic polymorphism;

(d) a mismatch (MM) position nucleotide that is a mismatch with a nucleotide in the gene; and

(e) at least one modified nucleotide (X) on either side of the SNP position nucleotide, wherein each X is located within four, three, or two nucleotides from the SNP position nucleotide; and/or

(f) at least one modified nucleotide (Y) on either side of the MM position nucleotide, wherein each Y is located within four, three or two nucleotides from the MM position nucleotide; and

(g) wherein X comprises a sugar modification selected from the group consisting of 2’-ribo, 2’-deoxyribo, 2′-F-4′-thioarabino (2’-F-ANA), 2’-O-(2-methoxyethyl) (2’-MOE), 4’-S-RNA, locked nucleic acid (LNA), 4’-S-F-ANA, 2’-O-allyl, 2’-O-ethylamine, 2’-O-cyanoethyl-RNA (CNet-RNA), tricyclo-DNA, cyclohexenyl nucleic acid (CeNA), arabino nucleic acid (ANA), and hexitol nucleic acid (HNA) and/or wherein Y comprises a sugar modification selected from the group consisting of 2’-ribo, 2’-deoxyribo, 2’-F-ANA, 2’-MOE, 4’-S-RNA, LNA, 4’-S-F-ANA, 2’-O-allyl, 2’-O-ethylamine, CNet-RNA, tricyclo-DNA, CeNA, ANA, and HNA.

2. The nucleic acid of claim 1, wherein an X is positioned immediately 5’ to the SNP position nucleotide or immediately 3’ to the SNP position nucleotide.

3. The nucleic acid of claim 1, wherein an X is positioned immediately 5’ to the SNP position nucleotide and immediately 3’ to the SNP position nucleotide.

4. The nucleic acid of claim 1, wherein a Y is positioned immediately 5’ to the MM position nucleotide or immediately 3’ to the MM position nucleotide.

5. The nucleic acid of claim 1, wherein a Y is positioned immediately 5’ to the MM position nucleotide and immediately 3’ to the MM position nucleotide.

6. The nucleic acid of claim 1, wherein the SNP position nucleotide is present from position 2 to position 6 from the 5’ end.

7. The nucleic acid of claim 1, wherein the MM position nucleotide is located 2-11 nucleotides from the SNP position nucleotide.

8. An siRNA molecule comprising a sense strand and an antisense strand, wherein the antisense strand comprises a nucleic acid comprising:

(a) a 5’ end and a 3’ end;

(b) a seed region that is complementary to a region of a gene comprising an allelic polymorphism;

(c) a single nucleotide polymorphism (SNP) position nucleotide that is complementary to the allelic polymorphism;

(d) a mismatch (MM) position nucleotide that is a mismatch with a nucleotide in the gene;

(e) at least three 2’-fluoro-ribonucleotides located within four, three or two nucleotides from the SNP position nucleotide; and

(f) at least three 2’-methoxy-ribonucleotides located within four, three or two nucleotides from the MM position nucleotide; and

(g) wherein a 2’-fluoro-ribonucleotide is positioned immediately 3’ to the SNP position nucleotide.

9. The siRNA molecule of claim 8, wherein a 2’-methoxy-ribonucleotide is positioned immediately 5’ to the MM position nucleotide and/or a 2’-methoxy-ribonucleotide is positioned immediately 3’ to the MM position nucleotide.

10. The siRNA molecule of claim 8, wherein the SNP position nucleotide is present in a seed region, and wherein the MM position nucleotide is located 2-11 nucleotides from the SNP position nucleotide.

11. The siRNA molecule of claim 10, wherein the SNP position nucleotide is present from position 2 to position 6 from the 5’ end, and wherein the MM position nucleotide is located 2-6 nucleotides from the SNP position nucleotide.