CLAIMS

What is claimed is:

1. A conjugate consisting of:

(1) (a) an antisense oligonucleotide (ASO), wherein the ASO is at least 5 nucleotides in length and (b) at least one G-quadruplex structure, or

(2) (a) an antisense oligonucleotide (ASO), wherein the ASO is at least 5 nucleotides in length, (b) at least one G-quadruplex structure, and (c) a linker connecting the at least one G-quadruplex structure to the ASO, or

(3) (a) an antisense oligonucleotide (ASO), wherein the ASO is at least 5 nucleotides in length, (b) at least one G-quadruplex structure, and (d) single or multiple ligands or functional moieties conjugated to the at least one G-quadruplex structure, or

(4) (a) an antisense oligonucleotide (ASO), wherein the ASO is at least 5 nucleotides in length, (b) at least one G-quadruplex structure, (c) a linker connecting the at least one G-quadruplex structure to the ASO, and (d) single or multiple ligands or functional moieties conjugated to the at least one G-quadruplex structure,

wherein the ASO and the at least one G-quadruplex structure are heterologous to each other, and wherein the conjugate has increased nuclease resistance relative to the unconjugated ASO.

2. The conjugate of claim 1, wherein the ASO is chemically modified.

3. The conjugate of claim 1, wherein the ASO adopts a gapmer design or a mixmer design.

4. The conjugate of claim 1, wherein the conjugate comprises (a) one G-quadruplex structure 5' to the ASO, (b) one G-quadruplex structure 3' to the ASO, or (c) both.

5. The conjugate of claim 1, wherein the at least one G-quadruplex structure comprises

(a) a nucleic acid molecule comprising the nucleic acid sequence $(g)_w(n)_a(g)_x(n)_b(g)_y(n)_c(g)_z$, wherein g and n are natural or chemical analogues of guanine nucleobase and any nucleobase respectively, w, x, y, z are independently of each other integers of at least 0, a, b, c are independently of each other integers of at least 0, and the sum of integers w, x, y, z is at least 8;

(b) four nucleic acid molecules wherein each of said molecules comprises a sequence of $(g)_z$, wherein z is an integer of at least 2; or

(c) two nucleic acid molecules wherein each of said molecules comprises a sequence of $(g)_y(n)_b(g)_z$, wherein b is an integer of at least 0, y and z are independently of each other integers of at least 0, and the sum of integers y and z is at least 4.

6. The conjugate according to claim 5, wherein the nucleic acid molecule comprises the nucleic acid sequence $(g)_w(n)_a(g)_x(n)_b(g)_y(n)_c(g)_z$ wherein g and n are natural or chemical analogues of guanine nucleobase and any nucleobase respectively, w, x, y, z are independently of each other integers of at least 3 and a, b, c are independently of each other integers of at least 1.

7. The conjugate of claim 1, wherein the at least one G-quadruplex structure is chemically modified.

8. The conjugate of claim 1, wherein loops of the at least one G-quadruplex structure comprise non-nucleosidic analogues without a base.

9. The conjugate of claim 1, wherein the linker is composed of unmodified nucleotides or wherein the linker is composed of chemically modified nucleotides, in part or in full.

10. The conjugate of claim 1, wherein the linker comprises a reducible linkage, an acid-labile linkage, or a protease-labile linkage.

11. The conjugate of claim 1, wherein the linker is connected to a phosphate or phosphate analogue, sugar, or base on the G-tetrad core or loop of the at least one G-quadruplex structure.

12. The conjugate of claim 1, wherein the linker is connected to a phosphate or phosphate analogue, sugar, or base on the ASO.

13. The conjugate of claim 1, wherein the at least one G-quadruplex structure and the ASO are connected across the backbone, in the form of a contiguous nucleotide sequence.

14. The conjugate of claim 1, wherein the ligand or functional moiety is selected from the group consisting of small molecules, carbohydrates, vitamins, lipids, aptamers, peptides, proteins, antibodies, fluorescent labels, and radiolabel tracers.

15. The conjugate of claim 1, wherein the ligand or functional moiety is connected to a phosphate or phosphate analogue, sugar, base or non-nucleosidic analogue on the G-tetrad core or loop of the at least one G-quadruplex structure.

16. The conjugate of claim 1, wherein the ASO is complementary to a portion of a DNA, pre-mRNA, mRNA, regulatory RNA, or non-coding RNA.

17. The conjugate of claim 1 for use in the prevention and treatment of diseases, disorders, and conditions.

18. An *in vitro* method of modulating the stability, translation, splicing, cleavage, or activity of a target nucleic acid molecule, comprising contacting the target nucleic acid molecule with a conjugate of claim 1 having an ASO complementary to a portion of the target nucleic acid molecule.

19. Use of a conjugate of claim 1 in the manufacture of a medicament for modulating the stability, translation, splicing, cleavage, or activity of a target nucleic acid molecule *in vivo*, wherein the conjugate has an ASO complementary to a portion of the target nucleic acid molecule.

20. An *in vitro* method of imaging or diagnosing, the method comprising contacting a selective probe with a target nucleic acid molecule, wherein the selective probe comprises a conjugate of claim 1.

21. Use of a conjugate of claim 1 in the manufacture of a selective probe for use in a method of imaging or diagnosing.