What is Claimed

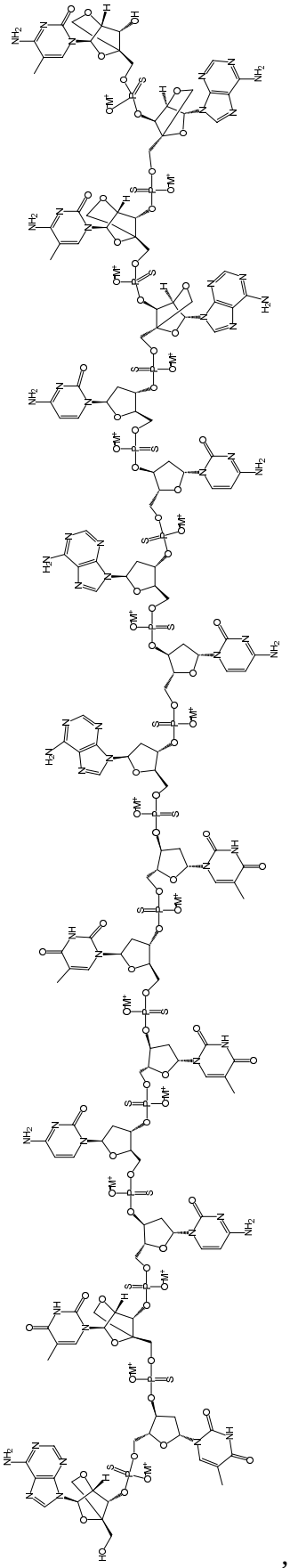
1. An antisense oligonucleotide (ASO) comprising the contiguous nucleotide sequence of AtTcctttacaccACAC (SEQ ID NO: 4), wherein the upper letter is beta-D-oxy-LNA and the lower letter is DNA.

2. The ASO of claim 1, which comprises an internucleotide linkage selected from the group consisting of a phosphodiester linkage, a phosphotriester linkage, a methylphosonate linkage, a phosphoramidate linkage, a phosphorothioate linkage, and combinations thereof.

3. The ASO of claim 2, wherein the internucleotide linkage is a phosphorothioate linkage.

4. The ASO of claim 1, wherein the contiguous nucleotide sequence is OxyAs DNAts OxyTs DNAcs DNAcs DNAts DNAts DNAts DNAas DNAcs DNAas DNAcs DNAcs OxyAs OxyMCs OxyAs OxyMC, wherein OxyA, OxyT, and Oxy MC are adenine beta D-oxy-LNA, thymine beta D-oxy-LNA, and methyl cytosine beta D-oxy-LNA, respectively, wherein DNAt, DNAc, and DNAa are thymine DNA, cytosine DNA, and adenine DNA, respectively, and wherein s is a phosphorothioate linkage between two nucleotides.

5. The ASO of claim 1, comprising the structure:



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wherein M^+ is a counterion.

6. The ASO of claim 5, wherein the counterion is selected from the group consisting of H^+, Na^+, $NH4^+$, and any combination thereof.

7. The ASO of claim 6, wherein the counterion is Na^+.

8. A conjugate comprising the ASO of claim 1, wherein the ASO is covalently attached to at least one non-nucleotide or non-polynucleotide moiety.

9. The conjugate of claim 8, wherein the non-nucleotide or non-polynucleotide moiety comprises a protein, a fatty acid chain, a sugar residue, a glycoprotein, a polymer, or any combinations thereof.

10. A pharmaceutical composition comprising the ASO of claim 1 and a pharmaceutically acceptable carrier.

11. The composition of claim 10, which further comprises a therapeutic agent.

12. The composition of claim 11, wherein the therapeutic agent is an alpha-synuclein antagonist.

13. A kit comprising the ASO of claim 1 and instructions for use.

14. Use of the ASO of claim 1 for the manufacture of a medicament for inhibiting or reducing expression of SNCA mRNA and/or SNCA protein in a cell, wherein the medicament is to be administered to the cell expressing SNCA mRNA and/or SNCA protein to inhibit or reduce the expression of SNCA mRNA and/or SCNA protein in the cell.

15. Use of the ASO of claim 1 for the manufacture of a medicament for the treatment of a synucleinopathy in a subject in need thereof, wherein an effective amount of the medicament is to be administered to the subject.

17. The ASO of claim 1 for use in therapy.

18. The ASO of claim 1 for use in therapy of inhibiting or reducing expression of SNCA mRNA and/or SNCA protein in a cell, wherein the ASO is to be administered to the cell expressing SNCA mRNA and/or SNCA protein to inhibit or reduce the expression of SNCA mRNA and/or SCNA protein in the cell.

19. The ASO of claim 1 for use in therapy of a synucleinopathy in a subject in need thereof.

20. The use of claim 15 or the ASO for use of claim 19, wherein the synucleinopathy is selected from the group consisting of Parkinson's disease, Parkinson's Disease Dementia (PDD), multiple system atrophy, dementia with Lewy bodies, and any combinations thereof.

21. A pharmaceutical composition comprising the ASO of any one claims 3 to 5 or 7 and a pharmaceutically acceptable carrier.