Claims

What is claimed is:

1. A compound which comprises:

(i) a modified oligonucleotide consisting of 12-30 linked nucleosides, at least a 12 nucleobase sequence portion of which is complementary to nucleotides present within the region selected from nucleotides 718-751, 1388-1423, 553-611, 1394-1423, 1469-1508, 1659-1689, 2100-2129 and 1399-1423 of SEQ ID NO: 9;

(ii) a modified oligonucleotide consisting of 12-30 linked nucleosides, at least a 12 nucleobase sequence portion of which is present within the nucleobase sequences selected from SEQ ID NOs: 30, 28, 38, 39, 40, 43, 44, 45, 50, 51, 52, 54, 55, 56, and 78, optionally wherein the modified oligonucleotide consists of 20 linked nucleosides; or

(iii) a modified oligonucleotide comprising at least 12 linked nucleosides, wherein the nucleobase sequence of the at least 12 linked nucleosides is present within the nucleobase sequences selected from SEQ ID NOs: 30, 28, 38, 39, 40, 43, 44, 45, 50, 51, 52, 54, 55, 56, and 78, optionally wherein the modified oligonucleotide comprises at least 14 linked nucleosides;

wherein the modified oligonucleotide comprises:

(i) a gap segment consisting of linked deoxynucleosides;

(ii) a 5’ wing segment consisting of linked modified nucleosides; and

(iii) a 3’ wing segment consisting of linked modified nucleosides;

wherein the gap segment is positioned between the 5’ wing segment and the 3’ wing segment and wherein each modified nucleoside within each wing segment comprises a modified sugar, and

wherein the modified oligonucleotide of (i)-(iii) demonstrates at least 60% inhibition of human connective tissue growth factor mRNA levels.

2. The compound of claim 1, wherein:

(i) the modified oligonucleotide is a single-stranded oligonucleotide or a double-stranded oligonucleotide; and/or

(ii) the modified oligonucleotide has a sequence which is 100% identical over its length to a portion of one of the sequences selected from SEQ ID NOs: 30, 28, 38, 39, 40, 43, 44, 45, 50, 51, 52, 54, 55, 56, and 78.

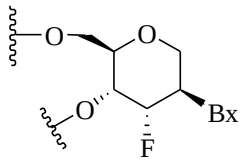
3. The compound of claims 1 or 2, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage, optionally wherein the at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage, optionally wherein all of the internucleoside linkages are phosphorothioate internucleoside linkages.

4. The compound of any of claims 1-3, wherein at least one nucleoside comprises a modified sugar, optionally wherein:

(i) the modified sugar is a bicyclic sugar; or

(ii) at least one of the modified sugar comprises a 2'-O-methoxyethyl.

5. The compound of any of claims 1-4, comprising at least one tetrahydropyran modified nucleoside wherein a tetrahydropyran ring replaces the furanose ring, optionally wherein each of the at least one tetrahydropyran modified nucleoside has the structure:



wherein Bx is an optionally protected heterocyclic base moiety.

6. The compound of any of claims 1-5, wherein at least one nucleoside comprises a modified nucleobase, optionally wherein the modified nucleobase is a 5-methylcytosine.

7. The compound of claim 1, wherein the modified oligonucleotide comprises:

(i) a gap segment consisting of thirteen linked deoxynucleosides;

(ii) a 5’ wing segment consisting of two linked modified nucleosides; and

(iii) a 3’ wing segment consisting of five linked modified nucleosides;

wherein the gap segment is positioned between the 5’ wing segment and the 3’ wing segment, wherein each modified nucleoside within each wing segment comprises a 2’-O-methoxyethyl sugar; and wherein each internucleoside linkage is a phosphorothioate linkage.

8. The compound of claim 1 or 7, wherein each cytosine nucleobase is a 5-methylcytosine.

9. The compound of any one of claims 1 to 7, wherein the modified oligonucleotide consists of 20 linked nucleosides.

10. The compound of any one of claims 1 to 8, wherein the nucleobase sequence is the sequence selected from one of SEQ ID NOs: 30, 28, 38, 39, 40, 43, 44, 45, 50, 51, 52, 54, 55, 56, and 78.

11. A composition which comprises a modified oligonucleotide comprising linked nucleosides, the nucleobase sequence of which is a sequence selected from one of SEQ ID NOs: 30, 28, 38, 39, 40, 43, 44, 45, 50, 51, 52, 54, 55, 56, and 78, or a salt thereof, and a pharmaceutically acceptable carrier or diluent, wherein the modified oligonucleotide demonstrates at least 60% inhibition of human connective tissue growth factor mRNA levels.

12. The compound of any of claims 1 to 10, wherein the nucleobase sequence is 100% complimentary within the range of nucleotides of SEQ ID NO:9 , optionally, wherein:

(i) the modified oligonucleotide is a single-stranded oligonucleotide or a double-stranded oligonucleotide; or

(ii) the modified oligonucleotide consists of 20 linked nucleosides.

13. Use of a compound of any one of claims 1 to 10 or 12 for the manufacture of a medicament for use in a method of inhibiting expression of connective tissue growth factor in a cell or a tissue, wherein the method comprises contacting the cell or tissue with the compound under conditions such that expression of connective tissue growth factor is inhibited.

14. Use of a compound of any one of claims 1 to 10 or 12 for the manufacture of a medicament for use in a method of treating an animal having a disease or condition associated with expression of connective tissue growth factor, wherein the method comprises administering to the animal an amount of the compound effective to inhibit expression of connective tissue growth factor so as to thereby treat the animal, optionally wherein:

(i) the disease or condition is a hyperproliferative disorder, optionally wherein the hyperproliferative disorder is selected from cancer and fibrotic disease e.g., hypertrophic scarring, keloids, skin scarring, liver fibrosis, pulmonary fibrosis, renal fibrosis, cardiac fibrosis, or restenosis; or

(ii) the disease or disorder is joint fibrosis (including frozen shoulder syndrome, tendon and peripheral nerve damage), spinal cord damage, coronary bypass, abdominal and peritoneal adhesions (including endometriosis, uterine leiomyomata and fibroids), radial keratotomy and photorefractive keratectomy, retinal reattachment surgery, device mediated fibrosis (in for example diabetes), tendon adhesions, Dupuytren contracture, or scleroderma.

15. Use of a compound of any one of claims 1 to 10 or 12 for the manufacture of a medicament for use in a method of reducing scarring resulting from wound healing in a subject in need thereof, wherein the method comprises administering to the subject an amount of the compound effective to inhibit expression of connective tissue growth factor in the subject so as to thereby reduce scarring resulting from wound healing in the subject, optionally, wherein wound healing is healing at a wound selected from the group consisting of skin breakage, surgical incisions, and burns.