

Claims

1. An oligonucleotide for reducing STAT3 expression, comprising an antisense strand comprising the nucleotide sequence of SEQ ID NO: 965 and a sense strand comprising the nucleotide sequence of SEQ ID NO: 875, wherein the sense strand comprises a saturated C18 hydrocarbon chain conjugated to the 5' terminal nucleotide of the sense strand, and wherein each of the antisense and sense strands comprise at least one 2'-modified nucleotide and at least one modified internucleotide linkage.
2. The oligonucleotide of claim 1 comprising an antisense strand comprising the nucleotide sequence of SEQ ID NO: 1145 and a sense strand comprising the nucleotide sequence of SEQ ID NO: 1055.
3. The oligonucleotide of claim 1 or 2, wherein the sense strand comprises at its 3' end a stem-loop set forth as: S1-L-S2, wherein S1 is complementary to S2, and wherein L forms a loop between S1 and S2 of 3 to 5 nucleotides in length.
4. The oligonucleotide of claim 3, wherein L is a tetraloop, optionally wherein L is 4 nucleotides in length.
5. The oligonucleotide of any one of the preceding claims, wherein L comprises a sequence set forth as GAAA.
6. The oligonucleotide of claim 1, wherein the 2'-modification comprises 2'-aminoethyl, 2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl, and 2'-deoxy-2'-fluoro- β -D-arabinonucleic acid.
7. The oligonucleotide of any one of claims 1 or 3-6, wherein the sense strand comprises 36 nucleotides with positions 1-36 from 5' to 3', wherein:
 - a) one or more positions 8-11 comprise 2'-fluoro modification, preferably all positions 8-11 comprises 2'-fluoro modification; and/or

b) one or more positions 1-7, 12-36 comprise 2'-O-methyl modification, preferably all positions 1-7, 12-36 comprise 2'-O-methyl modification.

8. The oligonucleotide of any one of claims 1 or 3-7, wherein the antisense strand comprises 22 nucleotides with positions 1-22 from 5' to 3', and wherein:

a) one or more positions 2, 3, 4, 5, 7, 10 and 14 comprise a 2'-fluoro modification, preferably all positions 2, 3, 4, 5, 7, 10 and 14 comprise 2'-fluoro modification; and/or

b) one or more positions 1, 6, 8, 9, 11-13, 15-22 comprise 2'-O-methyl modification, preferably all positions 1, 6, 8, 9, 11-13, 15-22 comprise 2'-O-methyl modification.

9. The oligonucleotide of any one of the preceding claims, wherein a 4'-carbon of the sugar of the 5'-nucleotide of the antisense strand comprises a phosphate analog.

10. The oligonucleotide of any one of the preceding claims, wherein at least one nucleotide of the oligonucleotide is conjugated to one or more targeting ligands, optionally, wherein the one or more targeting ligands is a saturated or unsaturated fatty acid moiety.

11. An oligonucleotide for reducing STAT3 expression, the oligonucleotide comprising an antisense of SEQ ID NO: 1145 and further comprising a sense strand of SEQ ID NO: 1055, wherein:

the antisense strand comprises

[MePhosphonate-4O-

mUs][fUs][fAs][fA][fU][mU][fU][mU][mA][fA][mG][mC][mU][fG][mA][mU][mA][m
A][mU][mUs][mGs][mG]

and the sense strand comprises

[mAs][mA][mU][mU][mA][mU][mC][fA][fG][fC][fU][mU][mA][mA][mA][mA][mU][
mU][mA][mA][mG][mC][mA][mG][mC][mC][mG][ademA-GalNAc][ademA-
GalNAc][ademA-GalNAc][mG][mG][mC][mU][mG][mC].

12. A pharmaceutical composition comprising the oligonucleotide or oligonucleotide-ligand conjugate of any one of the preceding claims and a pharmaceutically acceptable carrier, delivery agent or excipient.
13. A composition for use in treating a disorder or condition associated with STAT3 expression in a patient in need thereof, wherein the composition comprises the oligonucleotide or oligonucleotide-ligand conjugate of any one of the preceding claims.
14. The composition of claim 13 wherein the disorder or condition associated with STAT3 expression is cancer.
15. The composition of claim 14, wherein the cancer comprises a carcinoma, sarcoma, melanoma, lymphoma, and leukemia, prostate cancer, breast cancer, hepatocellular carcinoma (HCC), colorectal cancer, pancreatic cancer or a glioblastoma.