

CLAIMS

1. A polynucleotide that is complementary to IL-34, or a portion thereof, comprising a nucleotide sequence according to:
 - a. 5'-CTTTGGGCCGACCAGCTTC-3' (SEQ ID NO: 3), or
 - b. 5'-TCCATGACCCGGAAGCAGTT-3' (SEQ ID NO: 5),wherein at least one cytidine of the nucleotide sequence is chemically modified, and at least one nucleoside is a 2'-*O*-(2-methoxyethyl) (2'-MOE) nucleoside;
or a pharmaceutically acceptable salt thereof.
2. The polynucleotide of claim 1, wherein no more than 10 nucleosides are chemically modified.
3. The polynucleotide of claim 1 or 2, comprising six 2'-MOE nucleosides or eight 2'-MOE nucleosides.
4. The polynucleotide of claim 1, wherein at least one cytidine of the polynucleotide is replaced with 5-methylcytidine.
5. The polynucleotide of any one of claims 1-4, comprising a nucleotide sequence selected from the group consisting of:
 - a. 5'-CxTxTxTGGGCXGCACCAGCxTxTxCx-3' (SEQ ID NO: 40), wherein Cx is 2'-*O*-(2-methoxyethyl)cytidine, Tx is 2'-*O*-(2-methoxyethyl)thymidine, and X is 5-methylcytidine;
 - b. 5'-CxTxTxTGGGCXGCACCAGCTxTxCx-3' (SEQ ID NO: 41), wherein Cx is 2'-*O*-(2-methoxyethyl)cytidine, Tx is 2'-*O*-(2-methoxyethyl)thymidine, and X is 5-methylcytidine;
 - c. 5'-TxCxCxAxTGACCXGGAAGCAxGxTxTx-3' (SEQ ID NO: 42), wherein Cx is 2'-*O*-(2-methoxyethyl)cytidine, Ax is 2'-*O*-(2-methoxyethyl)adenosine, Tx is 2'-*O*-(2-methoxyethyl)thymidine, Gx is 2'-*O*-(2-methoxyethyl)guanosine, and X is 5-methylcytidine; and

- d. 5'-TxCxCxATGACCXGGAAGCAGxTxTx-3' (SEQ ID NO: 43), wherein Cx is 2'-*O*-(2-methoxyethyl)cytidine, Tx is 2'-*O*-(2-methoxyethyl)thymidine, Gx is 2'-*O*-(2-methoxyethyl)guanosine, and X is 5-methylcytidine;
or a pharmaceutically acceptable salt thereof.
6. The polynucleotide of any one of claims 1-5, wherein the polynucleotide is an IL-34 antisense oligonucleotide.
7. The polynucleotide of any one of claims 1-5, wherein the polynucleotide is part of an IL-34 siRNA complex.
8. The polynucleotide of any one of claims 1-7, wherein at least one internucleoside linkage of the polynucleotide is selected from the group consisting of a phosphorothioate linkage, a phosphorodithioate linkage, a phosphotriester linkage, an alkylphosphonate linkage, an aminoalkylphosphotriester linkage, an alkylene phosphonate linkage, a phosphinate linkage, a phosphoramidate linkage, and an aminoalkylphosphoramidate linkage, a thiophosphoramidate linkage, thionoalkylphosphonate linkage, a thionoalkylphosphotriester linkage, a thiophosphate linkage, a selenophosphate linkage, and a boranophosphate linkage.
9. A pharmaceutical composition, comprising (a) a polynucleotide of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, and (b) a pharmaceutically acceptable excipient.
10. Use of a polynucleotide of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 10 in the manufacture of a medicament for treating an inflammatory disease in a patient in need thereof.
11. The use of claim 10, wherein the inflammatory disease is rheumatoid arthritis or osteoarthritis.
12. The use of any one of claims 11 to 14, wherein the use (i) inhibits inflammatory cytokine production in cells of the patient; (ii) reduces or inhibits an IL-34 mediated inflammatory response in cells of the patient; and/or (iii) reduces or inhibits IL-34-mediated macrophage colony-stimulating factor receptor (M-CSFR-1) signaling in cells of the patient.

13. Use of a polynucleotide of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 10 in the manufacture of a medicament for the treatment of reducing or eliminating a fibrotic stricture in a patient suffering from an inflammatory disease.

14. The use of claim 17 or 18, wherein the inflammatory disease is selected from the group consisting of an inflammatory bowel disease, rheumatoid arthritis, psoriasis, osteoarthritis, pouchitis, (type I and II), tissue or organ rejection, multiple sclerosis, periodontal inflammation, periodontitis, pigmented villonodular synovitis, hepatitis, sinusitis, colon cancer, colorectal cancer, colitis-associated colon cancer, sporadic colorectal cancer, coronary artery disease, Sjogren's syndrome (SS), obesity, chronic inflammation, pulmonary sarcoidosis, skin lesions, a CNS inflammatory disease, and an autoimmune disease.

15. The use of claim 19, wherein the inflammatory disease is rheumatoid arthritis or osteoarthritis.

16. The use of claim 19, wherein the inflammatory disease is an inflammatory bowel disease (e.g., Crohn's disease, gastroduodenal Crohn's disease, Crohn's (granulomatous) colitis, inflammatory Crohn's disease, fibrostricturing Crohn's disease, ulcerative colitis, collagenous colitis, lymphocytic colitis, ischaemic colitis, diversion colitis, Behçet's disease, microscopic colitis, ulcerative proctitis, proctosigmoiditis, jejunoileitis, left-sided colitis, pancolitis, ileocolitis, ileitis, or indeterminate colitis), optionally wherein the inflammatory bowel disease is inflammatory Crohn's disease or fibrostricturing Crohn's disease.

17. Use of a polynucleotide of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 10 in the manufacture of a medicament for preventing or treating fibrosis in a patient in need thereof.

18. The use of claim 24, wherein the fibrosis is selected from the group consisting of renal fibrosis, cardiac fibrosis, endomyocardial fibrosis, myelofibrosis, retroperitoneal fibrosis, nephrogenic systemic fibrosis, pulmonary fibrosis, synovial fibrosis, and intestinal fibrosis.

19. The use of any one of claims 24-26, wherein the patient is suffering from rheumatoid arthritis, osteoarthritis, or Crohn's disease.
20. The use of any one of claims 11-29, wherein the polynucleotide is administered intraarticularly, rectally, topically, parenterally, orally, pulmonarily, intratracheally, intranasally, transdermally, or intraduodenally.
21. The use of any one of claims 11-30, wherein the patient is a human.
22. A polynucleotide of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 10 for use in therapy.