

CLAIMS

1. One or more recombinant nucleic acids comprising:
 - a. a first nucleic acid sequence at least 15 nucleotides in length complementary to an mRNA encoding human TGF- β Receptor 2 (TGFB2) comprising the sequence set forth in SEQ ID NO: 2, and
 - b. a second nucleic acid sequence at least 15 nucleotides in length complementary to an mRNA encoding human TGF- β Receptor 2 (TGFB2) comprising the sequence set forth in SEQ ID NO: 2, wherein the first nucleic acid sequence and the second nucleic acid sequence are distinct.
2. The one or more recombinant nucleic acids of claim 1, wherein the first nucleic acid and/or second nucleic acids is at least 16, 17, 18, 19, 20, 21, or 22 nucleotides in length.
3. The one or more recombinant nucleic acids of claim 1 or 2, wherein the length complementary to an mRNA encoding TGFB2 of the first nucleic acid and/or second nucleic acid is 22 nucleotides.
4. The one or more recombinant nucleic acids of any one of claims 1-3, wherein the first nucleic acid and/or second nucleic acid comprises a short hairpin RNA (shRNA), a small interfering RNA (siRNA), a double stranded RNA (dsRNA), or an antisense oligonucleotide.
5. The one or more recombinant nucleic acids of claim 4, wherein the first nucleic acid and/or second nucleic acid comprises an shRNA.
6. The one or more recombinant nucleic acids of any one of claims 1-5, wherein the first nucleic acid and/or second nucleic acids each comprises a sequence selected from the group consisting of the sequences set forth in SEQ ID NOs: 81, 51, 53, 36-50, 52, 54-80, or 82-84.
7. The one or more recombinant nucleic acids of any one of claims 1-6, wherein the first nucleic acid and/or second nucleic acid comprises the sequence(s) set forth in SEQ ID NOs: 81, 51 and/or 53
8. The one or more recombinant nucleic acids of any one of claims 1-7, wherein the first nucleic acid and/or second nucleic acid reduce expression of TGFB2 in a cell by at least 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 75%, 80%, 85%, 90%, 95%, or 99% as compared to a control cell that does not comprise the respective nucleic acid(s).

- 9.** The one or more recombinant nucleic acids of any one of claims 1-8, further comprising at least a third nucleic acid sequence at least 15 nucleotides in length, wherein the third nucleic acid sequence comprises one or more of: (1) a nucleic acid sequence complementary to nucleotides 1126 to 1364 of an mRNA encoding human Fas Cell Surface Death Receptor (FAS) comprising the sequence set forth in SEQ ID NO: 3, or (2) a nucleic acid sequence complementary to nucleotides 518 to 559 of an mRNA encoding human Protein Tyrosine Phosphatase Non-Receptor Type 2 (PTPN2) comprising the sequence set forth in SEQ ID NO: 4.
- 10.** The one or more recombinant nucleic acids of claim 9, wherein the third nucleic acid comprises a sequence selected from the group consisting of the sequences set forth in SEQ ID NOs: 92, 85-91, or 93-99.
- 11.** The one or more recombinant nucleic acids of claim 9, wherein the third nucleic acid comprises a sequence selected from the group consisting of the sequences set forth in SEQ ID NOs: 110, 100-109, or 11-112.
- 12.** The one or more recombinant nucleic acids of any one of claims 1-11, further comprising at least a third and a fourth nucleic acid sequence at least 15 nucleotides in length, wherein the third nucleic acid sequence comprises a nucleic acid sequence complementary to nucleotides 1126 to 1364 of an mRNA encoding human Fas Cell Surface Death Receptor (FAS) comprising the sequence set forth in SEQ ID NO: 3, and the fourth nucleic acid sequence complementary to nucleotides 518 to 559 of an mRNA encoding human Protein Tyrosine Phosphatase Non-Receptor Type 2 (PTPN2) comprising the sequence set forth in SEQ ID NO: 4.
- 13.** The one or more recombinant nucleic acids of any one of claims 9-12, wherein the third nucleic acid reduces expression of FAS in a cell by at least 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 75%, 80%, 85%, 90%, 95%, or 99% and/or reduces expression of PTPN2 in a cell by at least 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 75%, 80%, 85%, 90%, 95%, or 99%, as compared to a control cell that does not comprise the nucleic acid.
- 14.** The one or more recombinant nucleic acids of any one of claims 1-13, wherein the one or more recombinant nucleic acids are incorporated into one or more expression cassettes.

15. The one or more recombinant nucleic acids of claim 14, wherein the expression cassette comprises the sequence set forth in any one of SEQ ID NOs: 128, 129, 130, 131, 139, 140, or 141.
16. The one or more recombinant nucleic acids of claim 14 or 15, wherein the expression cassette comprises the sequence set forth in any one of SEQ ID NOs: 134, 133, or 135-137.
17. An expression vector comprising the recombinant nucleic acids of any one of claims 1-16.
18. An immune cell comprising one or more recombinant nucleic acids comprising:
 - a. a first nucleic acid sequence at least 15 nucleotides in length complementary to an mRNA encoding human TGF- β Receptor 2 (TGFB2) comprising the sequence set forth in SEQ ID NO: 2, and
 - b. a second nucleic acid sequence at least 15 nucleotides in length complementary to an mRNA encoding human TGF- β Receptor 2 (TGFB2) comprising the sequence set forth in SEQ ID NO: 2, wherein the first nucleic acid sequence and the second nucleic acid sequence are distinct.
19. The immune cell of claim 18, wherein the immune cell is a primary immune cell.
20. The immune cell of claim 18 or 19, wherein the immune cell is a primary human T cell, a natural killer (NK) cell, a natural killer T (NKT) cell, a T cell, a $\gamma\delta$ T cell, a CD8⁺ T cell, a CD4⁺ T cell, a primary T cell, primary human T cell, a T cell progenitor, or an induced pluripotent stem cell (iPSC).
21. A population of cells comprising the immune cell of any one of claims 18-20.
22. A pharmaceutical composition comprising the immune cell of any one of claims 18-20, and a pharmaceutically acceptable excipient.
23. A pharmaceutical composition comprising the one or more recombinant nucleic acids of any one of claims 1 to 16 or the vector of claim 17, and a pharmaceutically acceptable excipient.
24. Use of the immune cell of any one of claims 18-20 in the manufacture of a medicament for treating a disease in a subject, wherein the immune cell is to be administered to the subject.

25. Use of the one or more recombinant nucleic acids of any one of claims 1 to 16 in the manufacture of a medicament for treating a disease in a subject, wherein the one or more recombinant nucleic acids is to be administered to the subject.
26. The use of claim 24 or 25, wherein the disease is cancer.
27. A method comprising contacting a cell obtained from a subject with one or more recombinant nucleic acids, wherein the one or more recombinant nucleic acids comprise:
- a. a first nucleic acid sequence at least 15 nucleotides in length complementary to an mRNA encoding human TGF- β Receptor 2 (TGFB2) comprising the sequence set forth in SEQ ID NO: 2, and
 - b. a second nucleic acid sequence at least 15 nucleotides in length complementary to an mRNA encoding human TGF- β Receptor 2 (TGFB2) comprising the sequence set forth in SEQ ID NO: 2, wherein the first nucleic acid sequence and the second nucleic acid sequence are distinct.
28. The one or more recombinant nucleic acids of any one of claims 1 to 16 or the immune cell of any one of claims 18-20, for use in therapy.