

## CLAIMS

1. A non-naturally occurring polynucleotide encoding: (a) a miRNA that inhibits the expression of an immune checkpoint protein; and (b) a chimeric receptor.
2. The polynucleotide of claim 1, wherein the miRNA inhibits the expression of PD-1.
3. The polynucleotide of claim 2, comprising a nucleic acid sequence having at least 80% sequence identity with SEQ ID NO: 267 or that is capable of hybridizing under stringent hybridization conditions to the complement of SEQ ID NO: 267.
4. The polynucleotide of claim 1, wherein the chimeric receptor is a T-cell receptor.
5. The polynucleotide of claim 1, wherein the chimeric receptor is a chimeric antigen receptor.
6. The polynucleotide of claim 5, wherein the chimeric antigen receptor comprises an antigen-binding domain that binds to an epitope on ROR1.
7. The polynucleotide of claim 6, wherein the chimeric antigen receptor comprises the amino acid sequence of SEQ ID NO: 465, or a functional fragment or variant thereof.
8. The polynucleotide of claim 5, wherein the chimeric antigen receptor comprises a spacer comprising a stalk region comprising the amino acid sequence of SEQ ID NO: 467, or a functional fragment or variant thereof, and a stalk extension region comprising the amino acid sequence of SEQ ID NO: 473, or a functional fragment or variant thereof.
9. The polynucleotide of claim 1, further encoding a cytokine.
10. The polynucleotide of claim 9, wherein the cytokine is IL-15, or functional fragment or variant thereof, and is membrane bound.
11. The polynucleotide of claim 10, encoding a fusion protein comprising IL-15, or a functional fragment or variant thereof, and IL-15R $\alpha$ , or a functional fragment or variant thereof.
12. The polynucleotide of claim 11, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 523 or a functional fragment or variant thereof.

13. The polynucleotide of claim 1, further encoding a cell tag.
14. The polynucleotide of claim 13, wherein the truncated HER1 comprises a HER1 Domain III, or a functional fragment or variant thereof, and a truncated HER1 Domain IV, or a functional fragment or variant thereof.
15. The polynucleotide of claim 14, wherein the cell tag further comprises a CD28 transmembrane domain or a functional fragment or variant thereof.
16. A vector comprising the polynucleotide of any one of claims 1–15.
17. The vector of claim 16, comprising a *Sleeping Beauty* transposon.
18. A modified immune effector cell comprising the polynucleotide of any one of claims 1–15.
19. A composition comprising the polynucleotide of any one of claims 1–15 or the cell of claim 18.
20. A kit comprising the polynucleotide of any one of claims 1–15 or the cell of claim 18.
21. Use of the modified immune effector cell of claim 18 in manufacture of a medicament for treatment of a disease or disorder, wherein the medicament is to be administered to a subject suffered from the disease or disorder.
22. A method for the detection of a disease or disorder associated with the overexpression of an antigen in a subject, the method comprising: a) contacting a sample from the subject with one or more of the antibodies, or antigen-binding fragments thereof; and b) detecting an increased level of binding of the antibody or fragment thereof to the sample as compared to such binding to a control sample lacking the disease, thereby detecting the disease in the subject.
23. Use of polynucleotides encoding a chimeric antigen receptor or a cell comprising the same in manufacture of a medicament to be administered to a subject in a serial manner, wherein the encoded chimeric antigen receptors are selected from a collection of chimeric antigen receptors having different structural compositions and binding specificities for an array of antigen targets.
24. Use of the medicament of claim 23 in a serial manner whereby a period of time elapses between

a first and a second administrations.