Claims

1. A polynucleotide, comprising:

    a. an immune cell survival-enhancing gene comprising a nucleic acid encoding a protein selected from:

        i. CD28, wherein the CD28 comprises one or more of the following activating mutations: D124E, D124V, T195I, or T195P; or

        ii. An inhibitor of apoptosis selected from Survivin, Bcl2, Bcl6, or Bcl-XL,

        wherein the immune cell survival-enhancing gene is operably linked to a first heterologous regulatory sequence effective for expression of the protein within an immune cell thereby enhancing survival of the immune cell; and

    b. a gene encoding a receptor capable of binding to an antigen, wherein the gene is operably linked to a second heterologous regulatory sequence effective for expression of the receptor within the immune cell.

2. A transposon comprising the polynucleotide according to claim 1.

3. An immune cell whose genome comprises the polynucleotide according to claim 1.

4. A method for preparing an immune cell according to claim 3, the method comprising the step of introducing the polynucleotide into an immune cell.

5. The method of claim 4, wherein the polynucleotide further comprises transposon ends, and wherein the method further comprises the step of introducing into the immune cell a corresponding transposase, such that the gene encoding the protein and the gene encoding the receptor are transposed into the genome of the immune cell.

6. The method of claim 5, wherein the transposase is introduced as a nucleic acid encoding the transposase.

7. The method of claim 6, wherein the nucleic acid encoding the transposase is an mRNA.

8. The method of claim 7, wherein the nucleic acid encoding the transposase is operably linked to a promoter that is active in the immune cell.

9. The method of claim 8, wherein the immune cell is a T-cell, wherein binding of the receptor to a target cell which displays the antigen on its surface causes the T-cell to kill the target cell.

10. A lentiviral vector comprising the polynucleotide according to claim 1.

11. The immune cell of claim 3, wherein the immune cell is a T-cell.

12. The immune cell of claim 11, wherein the survival upon repeated antigen challenge of the T-cell is increased by at least 25% relative to the survival of an immune cell whose genome does not comprise the polynucleotide.

13. The polynucleotide of claim 1, wherein the gene encoding the receptor encodes a CD 19-binding chimeric antigen receptor, a polypeptide with sequence given by SEQ ID NO: 229, and is operably linked to either a PGK promoter or a GAPDH promoter; and the immune cell survival-enhancing gene has a sequence given by SEQ ID NO: 226 encoding Survivin and is operably linked to a PGK promoter.

14. The polynucleotide of claim 1, wherein the gene encoding the receptor encodes a CD 19-binding chimeric antigen receptor, a polypeptide with sequence given by SEQ ID NO: 229, and is operably linked to either a PGK promoter or a GAPDH promoter; and the immune cell survival-enhancing gene has a sequence given by SEQ ID NO: 227 encoding CD28-D124E-T195P and is operably linked to a PGK promoter.

15. The polynucleotide of claim 1, wherein the gene encoding the receptor encodes a CD 19 binding chimeric antigen receptor, a polypeptide with sequence given by SEQ ID NO: 229, and is operably linked to either a PGK promoter or a GAPDH promoter; and the immune cell survival-enhancing gene encodes a polypeptide with sequence given by SEQ ID NO: 238 and is operably linked to a PGK promoter.