

WHAT IS CLAIMED:

1. A recombinant vector comprising a polycistronic expression cassette, wherein said polycistronic expression cassette comprises a transcriptional regulatory element operably linked to a polynucleotide that comprises, from 5' to 3':
 - a. a first polynucleotide sequence that encodes a chimeric antigen receptor (CAR) that comprises an extracellular antigen-binding domain that specifically binds to CD19, a transmembrane domain, and a cytoplasmic domain;
 - b. a second polynucleotide sequence that comprises an F2A element;
 - c. a third polynucleotide sequence that encodes a fusion protein that comprises IL-15, or a functional fragment or functional variant thereof, and IL-15R α , or a functional fragment or functional variant thereof;
 - d. a fourth polynucleotide sequence that comprises a T2A element; and
 - e. a fifth polynucleotide sequence that encodes a marker protein.
2. The recombinant vector of claim 1, wherein said F2A element comprises (a) a polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 137, or the amino acid sequence of SEQ ID NO: 137, comprising 1, 2, or 3 amino acid modifications; (b) a polynucleotide sequence at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 141; (c) a polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 138, or the amino acid sequence of SEQ ID NO: 138, comprising 1, 2, or 3 amino acid modifications; or (d) a polynucleotide sequence at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 142.
3. The recombinant vector of claim 1 or 2, wherein said T2A element comprises (a) a polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 139, or the amino acid sequence of SEQ ID NO: 139, comprising 1, 2, or 3 amino acid modifications; (b) a polynucleotide sequence at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence SEQ ID NO: 143; (c) a polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 140 or 182, or the amino acid sequence of SEQ ID NO: 140 or 182, comprising 1, 2, or 3 amino acid modifications; or (d) a polynucleotide sequence at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 144, 145, or 165.

4. The recombinant vector of any one of claims 1-3, wherein said antigen-binding domain comprises: a heavy chain variable region (VH) comprising complementarity determining regions VH CDR1, VH CDR2, and VH CDR3; and a light chain variable region (VL) comprising complementarity determining regions VL CDR1, VL CDR2, and VL CDR3.
5. The recombinant vector of any one of claims 1-4, wherein said CAR further comprises a hinge region positioned between said antigen-binding domain and said transmembrane domain of said CAR.
6. The recombinant vector of any one of claims 1-5, wherein said transmembrane domain of said CAR comprises the amino acid sequence of SEQ ID NO: 43, 44, or 45, or the amino acid sequence of SEQ ID NO: 43, 44, or 45, comprising 1, 2, or 3 amino acid modifications.
7. The recombinant vector of any one of claims 1-6, wherein said cytoplasmic domain comprises a primary signaling domain of human CD3 ζ , or a functional fragment or functional variant thereof.
8. The recombinant vector of any one of claims 1-7, wherein said cytoplasmic domain comprises a co-stimulatory domain, or functional fragment or variant thereof, of a protein selected from the group consisting of CD28, 4-1BB, OX40, CD2, CD7, CD27, CD30, CD40, CDS, ICAM-1, LFA-1, B7-H3, and ICOS.
9. The recombinant vector of any one of claims 1-8, wherein said CAR (a) comprises an amino acid sequence at least at least 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 72, 74, 76, 77, 78, 79, 80, or 81; or (b) is encoded by a polynucleotide sequence at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 82, 83, 86, 87, 90, 91, 92, 93, 94, or 95.
10. The recombinant vector of any one of claims 1-9, wherein said IL-15, or said functional fragment or functional variant thereof, is operably linked to said IL-15R α , or said functional fragment or functional variant thereof, via a second peptide linker.
11. The recombinant vector of any one of claims 1-10, wherein said fusion protein (a) comprises an amino acid sequence at least 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 119, 121, or 180; or (b) is encoded by a polynucleotide sequence at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 126, 127, 130, 131, or 181.
12. The recombinant vector of any one of claims 1-11, wherein said marker protein comprises: domain III of HER1, or a functional fragment or functional variant thereof; an N-

terminal portion of domain IV of HER1; and a transmembrane domain of CD28, or a functional fragment or functional variant thereof.

13. The recombinant vector of any one of claims 1-12, wherein said marker protein (a) comprises an amino acid sequence at least 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 96, 97, 166, or 167; or (b) is encoded by a polynucleotide sequence at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 107, 108, 109, 162, 173, or 174.

14. The recombinant vector of any one of claims 1-13, wherein said regulatory element comprises a promoter.

15. A recombinant vector comprising a polycistronic expression cassette, wherein said polycistronic expression cassette comprises (a) a transcriptional regulatory element operably linked to a polynucleotide sequence at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 149; or (b) a transcriptional regulatory element operably linked to a polynucleotide that encodes an amino acid sequence at least 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 152.

16. The recombinant vector of any one of claims 1-15, further comprising a Left inverted terminal repeat (ITR) and a Right ITR, wherein said Left ITR and said Right ITR flank said polycistronic expression cassette.

17. The recombinant vector of claim 16, wherein said Left ITR and said Right ITR are ITRs of a DNA transposon selected from the group consisting of a Sleeping Beauty transposon, a piggyBac transposon, TcBuster transposon, and a Tol2 transposon.

18. A population of cells that comprise the recombinant vector of any one of claims 1-17.

19. A method of producing a population of engineered cells, comprising:

- a. introducing into a population of cells the recombinant vector of claim 16 or 17, and a DNA transposase or a polynucleotide encoding a DNA transposase; and
- b. culturing said population of cells under conditions wherein said transposase integrates the polycistronic expression cassette into the genome of said population of cells,

thereby producing the population of engineered cells.

20. Use of (a) the population of cells of claim 18, or (b) the population of engineered cells of claim 19 in the manufacture of a medicament for treating cancer or autoimmune disease or disorder in a subject in need thereof.