

chain variable (V β) region and a beta chain constant (C β) region; a fourth polynucleotide sequence that comprises a second 2A element; and a fifth 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.

[0005a] In one aspect, the present disclosure refers to a recombinant vector comprising a polycistronic expression cassette, wherein the polycistronic expression cassette comprises a transcriptional regulatory element operably linked to a polycistronic polynucleotide that comprises: a. a first polynucleotide sequence that encodes a T cell receptor (TCR) alpha chain comprising an alpha chain variable (V α) region and an alpha chain constant (C α) region; b. a second polynucleotide sequence that comprises a first 2A element; c. a third polynucleotide sequence that encodes a TCR beta chain comprising a beta chain variable (V β) region and a beta chain constant (C β) region; d. a fourth polynucleotide sequence that comprises a second 2A element; and e. a fifth 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.

[0006] In some embodimentexamples, either or both of the first 2A element and the second 2A element, independently, is a P2A element, a T2A element, an F2A element, or an E2A element.

[0007] In some embodimentexamples, the first 2A element is a P2A element.

[0008] In some embodimentexamples, the P2A element comprises a polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 18 or 20, or the amino acid sequence of SEQ ID NO: 18 or 20 comprising 1, 2, or 3 amino acid modifications.

[0009] In some embodimentexamples, the P2A element comprises a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 19 or 21.

[0010] In some embodimentexamples, the second 2A element is a T2A element.

[0011] In some embodimentexamples, the T2A element comprises a polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 22 or 24, or the amino acid sequence of SEQ ID NO: 22 or 24 comprising 1, 2, or 3 amino acid modifications.

[0012] In some embodimentexamples, the T2A element comprises a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 23 or 25.

[0013] In some embodimentexamples, either or both of the second polynucleotide sequence and the fourth polynucleotide sequence, independently, encode a furin recognition site.

[0014] In some embodimentexamples, the furin recognition site comprises the amino acid sequence of SEQ ID NO: 2 or 4, or the amino acid sequence of SEQ ID NO: 2 or 4 comprising 1, 2, or 3 amino acid modifications.

[0015] In some embodimentexamples, the furin recognition site is encoded by the polynucleotide sequence of SEQ ID NO: 3 or 5 or the polynucleotide sequence of SEQ ID NO: 3 or 5 comprising 1, 2, or 3 nucleotide modifications.

[0016] In some embodimentexamples, the second polynucleotide sequence comprises a polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 10, or the amino acid sequence of SEQ ID NO: 10 comprising 1, 2, or 3 amino acid modifications.

[0017] In some embodimentexamples, the second polynucleotide sequence comprises a polynucleotide

sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 11.

[0018] In some [embodimentexamples](#), the fourth polynucleotide sequence comprises a polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 12, or the amino acid sequence of SEQ ID NO: 12 comprising 1, 2, or 3 amino acid modifications.

[0019] In some [embodimentexamples](#), the fourth polynucleotide sequence comprises a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 13.

[0020] In some [embodimentexamples](#), the IL-15, or functional fragment or functional variant thereof, comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 76.

[0021] In some [embodimentexamples](#), the IL-15, or functional fragment or functional variant thereof, is encoded by a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 77.

[0022] In some [embodimentexamples](#), the IL-15R α , or functional fragment or functional variant thereof, comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 78.

[0023] In some [embodimentexamples](#), the IL-15R α , or functional fragment or functional variant thereof, is encoded by a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 79.

[0024] In some [embodimentexamples](#), the IL-15, or functional fragment or functional variant thereof, is operably linked to the IL-15R α , or functional fragment or functional variant thereof, via a peptide linker.

[0025] In some [embodimentexamples](#), the peptide linker comprises the amino acid sequence of SEQ ID NO: 81, or the amino acid sequence of SEQ ID NO: 81 comprising 1, 2, or 3 amino acid modifications.

[0026] In some [embodimentexamples](#), the peptide linker is encoded by a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 82.

[0027] In some [embodimentexamples](#), the fusion protein is membrane bound.

[0028] In some [embodimentexamples](#), the fusion protein comprises an amino acid sequence at least

90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 70 or 73.

[0029] In some [embodimentexamples](#), the fusion protein is encoded by a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 71 or 74.

[0030] In some [embodimentexamples](#), the C α region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 40-49.

[0031] In some [embodimentexamples](#), the C α region is encoded by a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 55, 57, or 58.

[0032] In some [embodimentexamples](#), the C β region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 50-54 or 60.

[0033] In some [embodimentexamples](#), the C β region is encoded by a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 56 or 59.

[0034] In some [embodimentexamples](#), the polycistronic polynucleotide comprises, in order from 5' to 3': the first polynucleotide sequence, the second polynucleotide sequence, the third polynucleotide sequence, the fourth polynucleotide sequence, and the fifth polynucleotide sequence.

[0035] In some [embodimentexamples](#), the first polynucleotide sequence and the second polynucleotide sequence together comprise a first combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 160; the third polynucleotide sequence and the fourth polynucleotide sequence together comprise a second combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 168; or the third polynucleotide sequence, the fourth polynucleotide sequence, and the fifth polynucleotide sequence together comprise a third combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 161.

[0036] In some [embodimentexamples](#), the first combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 230; the second combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 231; or the third combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 232.

[0037] In some [embodimentexamples](#), the first polynucleotide sequence and the second polynucleotide

sequence together comprise a first combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 160; and the third polynucleotide sequence, the fourth polynucleotide sequence, and the fifth polynucleotide sequence together comprise a third combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 161.

[0038] In some [embodimentexamples](#), the first polynucleotide sequence and the second polynucleotide sequence together comprise a first combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 180 or 210; and the third polynucleotide sequence, the fourth polynucleotide sequence, and the fifth polynucleotide sequence together comprise a third combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 181.

[0039] In some [embodimentexamples](#), the first combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 230; and the third combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 232.

[0040] In some [embodimentexamples](#), the first combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 250 or 270; and the third combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 252.

[0041] In some [embodimentexamples](#), the polycistronic polynucleotide comprises, in order from 5' to 3': the first polynucleotide sequence, the fourth polynucleotide sequence, the third polynucleotide sequence, the second polynucleotide sequence, and the fifth polynucleotide sequence.

[0042] In some [embodimentexamples](#), the first polynucleotide sequence and the fourth polynucleotide sequence together comprise a fourth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 162; the third polynucleotide sequence and the second polynucleotide sequence together comprise a fifth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 166; or the third polynucleotide sequence, the second polynucleotide sequence, and the fifth polynucleotide sequence together comprise a sixth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 163.

[0043] In some [embodimentexamples](#), the fourth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 233; the fifth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 234; or the sixth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 235.

[0044] In some [embodimentexamples](#), the first polynucleotide sequence and the fourth polynucleotide sequence together comprise a fourth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 162; and the third polynucleotide sequence, the second

polynucleotide sequence, and the fifth polynucleotide sequence together comprise a sixth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 163.

[0045] In some [embodimentexamples](#), the first polynucleotide sequence and the fourth polynucleotide sequence together comprise a fourth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 182 or 212; and the third polynucleotide sequence, the second polynucleotide sequence, and the fifth polynucleotide sequence together comprise a sixth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 183.

[0046] In some [embodimentexamples](#), the fourth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 233; and the sixth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 235.

[0047] In some [embodimentexamples](#), the fourth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 253 or 273; and the sixth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 255.

[0048] In some [embodimentexamples](#), the polycistronic polynucleotide comprises, in order from 5' to 3': the first polynucleotide sequence, the second polynucleotide sequence, the fifth polynucleotide sequence, the fourth polynucleotide sequence, and the third polynucleotide sequence.

[0049] In some [embodimentexamples](#), the first polynucleotide sequence and the second polynucleotide sequence together comprise a first combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 160; the first polynucleotide sequence, the second polynucleotide sequence, and the fifth polynucleotide sequence together comprise a seventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 169; the fifth polynucleotide sequence and the fourth polynucleotide sequence together comprise an eighth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 173; or the first polynucleotide sequence, the second polynucleotide sequence, the fifth polynucleotide sequence, and the fourth polynucleotide sequence together comprise a ninth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 164.

[0050] In some [embodimentexamples](#), the first combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 230; the seventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 236; the eighth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 237; or the ninth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 238.

[0051] In some [embodimentexamples](#), the first polynucleotide sequence, the second polynucleotide

sequence, the fifth polynucleotide sequence, and the fourth polynucleotide sequence together comprise a ninth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 164; and the third polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 50.

[0052] In some [embodimentexamples](#), the first polynucleotide sequence, the second polynucleotide sequence, the fifth polynucleotide sequence, and the fourth polynucleotide sequence together comprise a ninth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 184 or 214; and the third polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 51.

[0053] In some [embodimentexamples](#), the ninth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 238; and the third polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 59.

[0054] In some [embodimentexamples](#), the ninth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 258 or 278; and the third polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 56.

[0055] In some [embodimentexamples](#), the polycistronic polynucleotide comprises, in order from 5' to 3': the first polynucleotide sequence, the fourth polynucleotide sequence, the fifth polynucleotide sequence, the second polynucleotide sequence, and the third polynucleotide sequence.

[0056] In some [embodimentexamples](#), the first polynucleotide sequence and the fourth polynucleotide sequence together comprise a fourth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 162; the first polynucleotide sequence, the fourth polynucleotide sequence, and the fifth polynucleotide sequence together comprise a tenth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 167; the fifth polynucleotide sequence and the second polynucleotide sequence together comprise an eleventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 172; or the first polynucleotide sequence, the fourth polynucleotide sequence, the fifth polynucleotide sequence, and the second polynucleotide sequence together comprise a twelfth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 165.

[0057] In some [embodimentexamples](#), the fourth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 233; the tenth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 239; the eleventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 240; or the

twelfth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 241.

[0058] In some embodiment examples, the first polynucleotide sequence, the fourth polynucleotide sequence, the fifth polynucleotide sequence, and the second polynucleotide sequence together comprise a twelfth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 165; and the third polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 50.

[0059] In some embodiment examples, the first polynucleotide sequence, the fourth polynucleotide sequence, the fifth polynucleotide sequence, and the second polynucleotide sequence together comprise a twelfth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 185 or 215; and the third polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 51.

[0060] In some embodiment examples, the twelfth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 241; and the third polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 59.

[0061] In some embodiment examples, the twelfth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 261 or 281; and the third polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 56.

[0062] In some embodiment examples, the polycistronic polynucleotide comprises, in order from 5' to 3': the third polynucleotide sequence, the second polynucleotide sequence, the first polynucleotide sequence, the fourth polynucleotide sequence, and the fifth polynucleotide sequence.

[0063] In some embodiment examples, the first polynucleotide sequence and the fourth polynucleotide sequence together comprise a fourth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 162; the third polynucleotide sequence and the second polynucleotide sequence together comprise a fifth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 166; or the first polynucleotide sequence, the fourth polynucleotide sequence, and the fifth polynucleotide sequence together comprise a tenth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 167.

[0064] In some embodiment examples, the fourth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 233; the fifth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 234; or the tenth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 239.

[0065] In some embodimentexamples, the third polynucleotide sequence and the second polynucleotide sequence together comprise a fifth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 166; and the first polynucleotide sequence, the fourth polynucleotide sequence, and the fifth polynucleotide sequence together comprise a tenth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 167.

[0066] In some embodimentexamples, the third polynucleotide sequence and the second polynucleotide sequence together comprise a fifth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 186; and the first polynucleotide sequence, the fourth polynucleotide sequence, and the fifth polynucleotide sequence together comprise a tenth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 187 or 217.

[0067] In some embodimentexamples, the fifth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 234; and the tenth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 239.

[0068] In some embodimentexamples, the fifth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 254; and the tenth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 259 or 279.

[0069] In some embodimentexamples, the polycistronic polynucleotide comprises, in order from 5' to 3': the third polynucleotide sequence, the fourth polynucleotide sequence, the first polynucleotide sequence, the second polynucleotide sequence, and the fifth polynucleotide sequence.

[0070] In some embodimentexamples, the first polynucleotide sequence and the second polynucleotide sequence together comprise a first combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 160; the third polynucleotide sequence, and the fourth polynucleotide sequence together comprise a second combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 168; or the first polynucleotide sequence, the second polynucleotide sequence, and the fifth polynucleotide sequence together comprise a seventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 169.

[0071] In some embodimentexamples, the first combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 230; the second combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 231; or the seventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 236.

[0072] In some embodimentexamples, the third polynucleotide sequence, and the fourth polynucleotide sequence together comprise a second combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 168; and the first polynucleotide sequence, the second polynucleotide sequence, and the fifth polynucleotide sequence together comprise a seventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 169.

[0073] In some embodimentexamples, the third polynucleotide sequence, and the fourth polynucleotide sequence together comprise a second combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 188; and the first polynucleotide sequence, the second polynucleotide sequence, and the fifth polynucleotide sequence together comprise a seventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 189 or 219.

[0074] In some embodimentexamples, the second combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 231; and the seventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 236.

[0075] In some embodimentexamples, the second combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 251; and the seventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 256 or 276.

[0076] In some embodimentexamples, the polycistronic polynucleotide comprises, in order from 5' to 3': the third polynucleotide sequence, the second polynucleotide sequence, the fifth polynucleotide sequence, the fourth polynucleotide sequence, and the first polynucleotide sequence.

[0077] In some embodimentexamples, the third polynucleotide sequence and the second polynucleotide sequence together comprise a fifth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 166; the third polynucleotide sequence, the second polynucleotide sequence, and the fifth polynucleotide sequence together comprise a sixth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 163; the fifth polynucleotide sequence and the fourth polynucleotide sequence together comprise an eighth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 173; or the third polynucleotide sequence, the second polynucleotide sequence, the fifth polynucleotide sequence, and the fourth polynucleotide sequence together comprise a thirteenth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 170.

[0078] In some embodimentexamples, the fifth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 234; the sixth combination polynucleotide sequence

comprises the polynucleotide sequence of SEQ ID NO: 235; the eighth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 237; or the thirteenth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 242.

[0079] In some [embodimentexamples](#), the third polynucleotide sequence, the second polynucleotide sequence, the fifth polynucleotide sequence, and the fourth polynucleotide sequence together comprise a thirteenth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 170; and the first polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 40.

[0080] In some [embodimentexamples](#), the third polynucleotide sequence, the second polynucleotide sequence, the fifth polynucleotide sequence, and the fourth polynucleotide sequence together comprise a thirteenth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 190; and the first polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 41 or 42.

[0081] In some [embodimentexamples](#), the thirteenth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 242; and the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 57.

[0082] In some [embodimentexamples](#), the thirteenth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 262; and the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 55 or 58.

[0083] In some [embodimentexamples](#), the polycistronic polynucleotide comprises, in order from 5' to 3': the third polynucleotide sequence, the fourth polynucleotide sequence, the fifth polynucleotide sequence, the second polynucleotide sequence, and the first polynucleotide sequence.

[0084] In some [embodimentexamples](#), the third polynucleotide sequence and the fourth polynucleotide sequence together comprise a second combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 168; the third polynucleotide sequence, the fourth polynucleotide sequence, and the fifth polynucleotide sequence together comprise a third combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 161; the fifth polynucleotide sequence and the second polynucleotide sequence together comprise an eleventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 172; or the third polynucleotide sequence, the fourth polynucleotide sequence, the fifth polynucleotide sequence, and the second polynucleotide sequence together comprise a fourteenth combination

polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 171.

[0085] In some embodimentexamples, the second combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 231; the third combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 232; the eleventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 240; or the fourteenth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 243.

[0086] In some embodimentexamples, the third polynucleotide sequence, the fourth polynucleotide sequence, the fifth polynucleotide sequence, and the second polynucleotide sequence together comprise a fourteenth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 171; and the first polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 40.

[0087] In some embodimentexamples, the third polynucleotide sequence, the fourth polynucleotide sequence, the fifth polynucleotide sequence, and the second polynucleotide sequence together comprise a fourteenth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 191; and the first polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 41 or 42.

[0088] In some embodimentexamples, the fourteenth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 243; and the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 57.

[0089] In some embodimentexamples, the fourteenth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 263; and the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 55 or 58.

[0090] In some embodimentexamples, the polycistronic polynucleotide comprises, in order from 5' to 3': the fifth polynucleotide sequence, the second polynucleotide sequence, the first polynucleotide sequence, the fourth polynucleotide sequence, and the third polynucleotide sequence.

[0091] In some embodimentexamples, the first polynucleotide sequence and the fourth polynucleotide sequence together comprise a fourth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 162; or the fifth polynucleotide sequence and the second polynucleotide sequence together comprise an eleventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 172.

[0092] In some embodimentexamples, the fourth combination polynucleotide sequence comprises the

polynucleotide sequence of SEQ ID NO: 233; or the eleventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 240.

[0093] In some embodimentexamples, the first polynucleotide sequence and the fourth polynucleotide sequence together comprise a fourth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 162; the fifth polynucleotide sequence and the second polynucleotide sequence together comprise an eleventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 172; and the third polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 50.

[0094] In some embodimentexamples, the first polynucleotide sequence and the fourth polynucleotide sequence together comprise a fourth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 182 or 212; the fifth polynucleotide sequence and the second polynucleotide sequence together comprise an eleventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 222; and the third polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 51.

[0095] In some embodimentexamples, the fourth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 233; and the eleventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 240; and the third polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 59.

[0096] In some embodimentexamples, the fourth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 253 or 273; the eleventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 240; and the third polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 56.

[0097] In some embodimentexamples, the polycistronic polynucleotide comprises, in order from 5' to 3': the fifth polynucleotide sequence, the fourth polynucleotide sequence, the first polynucleotide sequence, the second polynucleotide sequence, and the third polynucleotide sequence.

[0098] In some embodimentexamples, the first polynucleotide sequence and the second polynucleotide sequence together comprise a first combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 160; or the fifth polynucleotide sequence and the fourth polynucleotide sequence together comprise an eighth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 173.

[0099] In some embodimentexamples, the first combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 230; or the eighth combination polynucleotide sequence

comprises the polynucleotide sequence of SEQ ID NO: 237.

[00100] In some embodimentexamples, the first polynucleotide sequence and the second polynucleotide sequence together comprise a first combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 160; the fifth polynucleotide sequence and the fourth polynucleotide sequence together comprise an eighth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 173; and the third polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 50.

[00101] In some embodimentexamples, the first polynucleotide sequence and the second polynucleotide sequence together comprise a first combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 180 or 210; the fifth polynucleotide sequence and the fourth polynucleotide sequence together comprise an eighth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 223; and the third polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 51.

[00102] In some embodimentexamples, the first combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 230; the eighth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 237; and the third polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 59. In some embodimentexamples, the first combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 250 or 270; the eighth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 237; and the third polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 56.

[00103] In some embodimentexamples, the polycistronic polynucleotide comprises, in order from 5' to 3': the fifth polynucleotide sequence, the second polynucleotide sequence, the third polynucleotide sequence, the fourth polynucleotide sequence, and the first polynucleotide sequence.

[00104] In some embodimentexamples, the third polynucleotide sequence and the fourth polynucleotide sequence together comprise a second combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 168; or the fifth polynucleotide sequence and the second polynucleotide sequence together comprise an eleventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 172.

[00105] In some embodimentexamples, the second combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 231; or the eleventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 240.

[00106] In some embodimentexamples, the third polynucleotide sequence and the fourth polynucleotide sequence together comprise a second combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 168; the fifth polynucleotide sequence and the second polynucleotide sequence together comprise an eleventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 172; and the first polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 40.

[00107] In some embodimentexamples, the third polynucleotide sequence and the fourth polynucleotide sequence together comprise a second combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 188; the fifth polynucleotide sequence and the second polynucleotide sequence together comprise an eleventh combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 222; and the first polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 41 or 42.

[00108] In some embodimentexamples, the second combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 231; the eleventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 240; and the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 57.

[00109] In some embodimentexamples, the second combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 251; the eleventh combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 240; and the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 55 or 58.

[00110] In some embodimentexamples, the polycistronic polynucleotide comprises, in order from 5' to 3': the fifth polynucleotide sequence, the fourth polynucleotide sequence, the third polynucleotide sequence, the second polynucleotide sequence, and the first polynucleotide sequence.

[00111] In some embodimentexamples, the third polynucleotide sequence and the second polynucleotide sequence together comprise a fifth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 166; or the fifth polynucleotide sequence and the fourth polynucleotide sequence together comprise an eighth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 173.

[00112] In some embodimentexamples, the fifth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 234; or the eighth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 237.

[00113] In some embodimentexamples, the third polynucleotide sequence and the second

polynucleotide sequence together comprise a fifth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 166; the fifth polynucleotide sequence and the fourth polynucleotide sequence together comprise an eighth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 173; and the first polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 40.

[00114] In some [embodimentexamples](#), the third polynucleotide sequence and the second polynucleotide sequence together comprise a fifth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 186; the fifth polynucleotide sequence and the fourth polynucleotide sequence together comprise an eighth combination polynucleotide sequence that encodes the amino acid sequence of SEQ ID NO: 223; and the first polynucleotide sequence encodes the amino acid sequence of SEQ ID NO: 41 or 42.

[00115] In some [embodimentexamples](#), the fifth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 234; the eighth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 237; and the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 57.

[00116] In some [embodimentexamples](#), the fifth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 254; the eighth combination polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 237; and the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 55 or 58.

[00117] In some [embodimentexamples](#), the polycistronic polynucleotide further comprises a sixth polynucleotide sequence that comprises a third 2A element; and a seventh polynucleotide sequence that comprises a marker protein.

[00118] In some [embodimentexamples](#), the third 2A element is a P2A element, a T2A element, an F2A element, or an E2A element.

[00119] In some [embodimentexamples](#), the 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.

[00120] In some [embodimentexamples](#), the domain III of HER1, or a functional fragment or functional variant thereof, comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 104.

[00121] In some [embodimentexamples](#), the N-terminal portion of domain IV of HER1 comprises amino acids 1-40, 1-39, 1-38, 1-37, 1-36, 1-35, 1-34, 1-33, 1-32, 1-31, 1-30, 1-29, 1-28, 1-27, 1-26, 1-25,

1-24, 1-23, 1-22, 1-21, 1-20, 1-19, 1-18, 1-17, 1-16, 1-15, 1-14, 1-13, 1-12, 1-11, or 1-10 of SEQ ID NO: 105.

[00122] In some [embodimentexamples](#), the N-terminal portion of domain IV of HER1 comprises amino acids 1-21 of SEQ ID NO: 105.

[00123] In some [embodimentexamples](#), the N-terminal portion of domain IV of HER1 comprises the amino acid sequence of SEQ ID NO: 106, or the amino acid sequence of SEQ ID NO: 106, comprising 1, 2, or 3 amino acid modifications.

[00124] In some [embodimentexamples](#), the transmembrane region of CD28 comprises the amino acid sequence of SEQ ID NO: 107, or the amino acid sequence of SEQ ID NO: 107, comprising 1, 2, or 3 amino acid modifications.

[00125] In some [embodimentexamples](#), the marker protein comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 100, 103, or 112.

[00126] In some [embodimentexamples](#), the V α region comprises complementarity determining region 1 α (CDR1 α), CDR2 α , and CDR3 α , comprising the amino acid sequences of SEQ ID NO: 1001 + 10n, 1002 + 10n, and 1003 + 10n, respectively, wherein n is an integer from 0 to 79. In some [embodimentexamples](#), n=0.

[00127] In some [embodimentexamples](#), the V β region comprises CDR1 β , CDR2 β , and CDR3 β , comprising the amino acid sequences of SEQ ID NO: 2001 + 10n, 2002 + 10n, and 2003 + 10n, respectively, wherein n is an integer from 0 to 79. In some [embodimentexamples](#), n=0.

[00128] In some [embodimentexamples](#), the V α region comprises the CDR1 α , CDR2 α , and CDR3 α from a V α region comprising the amino acid sequence of SEQ ID NO: 1004 + 10n, 1005 + 10n, 1006 + 10n, or 1007 + 10n, wherein n is an integer from 0 to 79. In some [embodimentexamples](#), n=0.

[00129] In some [embodimentexamples](#), the V β region comprises the CDR1 β , CDR2 β , and CDR3 β from a V β region comprising the amino acid sequence of SEQ ID NO: 2004 + 10n, 2005 + 10n, 2006 + 10n, or 2007 + 10n, wherein n is an integer from 0 to 79. In some [embodimentexamples](#), n=0.

[00130] In some [embodimentexamples](#), the V α region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1004 + 10n, 1005 + 10n, 1006 + 10n, or 1007 + 10n, wherein n is an integer from 0 to 79. In some [embodimentexamples](#), n=0.

[00131] In some [embodimentexamples](#), the V β region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence

of SEQ ID NO: 2004 + 10n, 2005 + 10n, 2006 + 10n, or 2007 + 10n, wherein n is an integer from 0 to 79. In some [embodimentexamples](#), n=0.

[00132] In some [embodimentexamples](#), the V α region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1004 + 10n, wherein the V β region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 2004 + 10n, and wherein n is an integer from 0 to 79; wherein the V α region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1005 + 10n, wherein the V β region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 2005 + 10n, and wherein n is an integer from 0 to 79; wherein the V α region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1006 + 10n, wherein the V β region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 2006 + 10n, and wherein n is an integer from 0 to 79; wherein the V α region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1007 + 10n, wherein the V β region comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 2007 + 10n, wherein n is an integer from 0 to 79. In some [embodimentexamples](#), n=0.

[00133] In some [embodimentexamples](#), the TCR alpha chain comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1008 + 10n, wherein n is an integer from 0 to 79. In some [embodimentexample](#)s, the TCR alpha chain comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1009 + 10n, wherein n is an integer from 0 to 79.

[00134] In some [embodimentexamples](#), the TCR alpha chain comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1010 + 10n, wherein n is an integer from 0 to 79.

[00135] In some [embodimentexamples](#), the TCR beta chain comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid

sequence of SEQ ID NO: 2008 + 10n, wherein n is an integer from 0 to 79. In some [embodimentexamples](#), n=0.

[00136] In some [embodimentexamples](#), the TCR beta chain comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 2009 + 10n, wherein n is an integer from 0 to 79.

[00137] In some [embodimentexamples](#), the TCR beta chain comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 2010 + 10n, wherein n is an integer from 0 to 79.

[00138] In some [embodimentexamples](#), transcriptional regulatory element comprises a promoter.

[00139] In some [embodimentexamples](#), the promoter is a human elongation factor 1-alpha (hEF-1 α) hybrid promoter.

[00140] In some [embodimentexamples](#), the promoter comprises a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO:150.

[00141] In some [embodimentexamples](#), the recombinant vector further comprises a polyA sequence at the 3' end of the polycistronic expression cassette.

[00142] In some [embodimentexamples](#), the polyA sequence comprises a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO:151.

[00143] In some [embodimentexamples](#), the recombinant vector further comprises a Left inverted terminal repeat (ITR) and a Right ITR, wherein the Left ITR and the Right ITR flank the polycistronic expression cassette.

[00144] In some [embodimentexamples](#), the recombinant vector comprises, in order from 5' to 3': the Left ITR; the transcriptional regulatory element; the first polynucleotide sequence; the second polynucleotide sequence; the third polynucleotide sequence; the fourth polynucleotide sequence; the fifth polynucleotide sequence; and the Right ITR.

[00145] In some [embodimentexamples](#), the recombinant vector is a non-viral vector.

[00146] In some [embodimentexamples](#), the non-viral vector is a plasmid.

[00147] In some [embodimentexamples](#), the recombinant vector is a viral vector.

[00148] In some [embodimentexamples](#), the recombinant vector is a polynucleotide.

[00149] Also provided herein is a polynucleotide encoding an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to an amino acid

sequence selected from the group consisting of SEQ ID NOs: 161, 163, 164, 165, 167, 169, 170, and 171.

[00149a] In one aspect, the present disclosure refers to a polynucleotide, wherein the polynucleotide encodes an amino acid sequence at least 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 161, 163, 164, 165, 167, 169, 170, and 171; or wherein the polynucleotide comprises a polynucleotide sequence at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NOs: 232, 235, 236, 238, 239, 241, 242, and 243.

[00150] Also provided herein is a polynucleotide comprising a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NOs: 232, 235, 236, 238, 239, 241, 242, and 243.

[00151] Also provided herein is a population of cells that comprises any recombinant vector provided herein, or any polynucleotide provided herein.

[00152] In some embodimentexamples, the recombinant vector or the polynucleotide is integrated into the genome of the population of cells.

[00153] In some embodimentexamples, the cells are immune effector cells.

[00154] In some embodimentexamples, the immune effector cells are selected from the group consisting of T cells, natural killer (NK) cells, B cells, mast cells, and myeloid-derived phagocytes.

[00155] In some embodimentexamples, the immune effector cells are T cells.

[00156] In some embodimentexamples, the T cells are selected from the group consisting of naïve T cells (CD4⁺ or CD8⁺); killer CD8⁺ T cells; cytotoxic CD4⁺ T cells; helper CD4⁺ T cells; CD4⁺ T cells corresponding to Th1, Th2, Th9, Th17, Th22, follicular helper (T_{fh}), regulatory (T_{reg}) lineages; tumor infiltrating lymphocytes (TILs); and memory T cells (central memory, effector memory, stem cell memory, stem cell-like memory).

[00157] In some embodimentexamples, the population of cells comprises alpha/beta T cells, gamma/delta T cells, or natural killer T (NKT) cells.

[00158] In some embodimentexamples, the population of cells comprises CD4⁺ T cells, CD8⁺ T cells, or both CD4⁺ T cells and CD8⁺ T cells.

[00159] In some embodimentexamples, the cells are *ex vivo*.

[00160] In some embodimentexamples, the cells are human.

[00161] In some embodimentexamples, the population of cells are T cells that comprise more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% or 50% CD45RA⁺CD45RO⁻CD62L⁺CD95⁺ cells.

[00162] In some embodimentexamples, the population of cells are T cells that comprise more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% or 50% CD45RA⁺CD45RO⁺CD62L⁺CD95⁺ cells.

[00163] Also provided herein is a population of cells comprising a polycistronic expression cassette comprising a first cistron comprising a 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; a second cistron comprising a polynucleotide sequence that encodes a TCR beta chain comprising a V β region and a C β region; and a third cistron comprising a polynucleotide sequence that encodes a TCR alpha chain comprising a V α region and a C α region, wherein the population of cells are T cells that comprise more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% or 50% CD45RA+CD45RO-CD62L+CD95+ cells.

[00164] Also provided herein is a population of cells comprising a polycistronic expression cassette comprising a first cistron comprising a 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; a second cistron comprising a polynucleotide sequence that encodes a TCR beta chain comprising a V β region and a C β region; and a third cistron comprising a polynucleotide sequence that encodes a TCR alpha chain comprising a V α region and a C α region, wherein the population of cells are T cells that comprise more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% or 50% CD45RA+CD45RO+CD62L+CD95+ cells.

[00164a] In one aspect, the present disclosure refers to a population of cells comprising a polycistronic expression cassette comprising a. a first cistron comprising a 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; b. a second cistron comprising a polynucleotide sequence that encodes a TCR beta chain comprising a V β region and a C β region; and c. a third cistron comprising a polynucleotide sequence that encodes a TCR alpha chain comprising a V α region and a C α region, wherein the population of cells are T cells that comprise i) more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% or 50% CD45RA+CD45RO-CD62L+CD95+ cells, or ii) more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45% or 50% CD45RA+CD45RO+CD62L+CD95+ cells.

[00165] Also provided herein is a method of producing a population of engineered cells, comprising introducing into a population of cells any recombinant vector provided herein, and a DNA transposase or a polynucleotide encoding a DNA transposase; and culturing the population of cells under conditions wherein the transposase integrates the polycistronic expression cassette into the genome of the population of cells, thereby producing the population of engineered cells.

[00166] In some **embodimentexamples**, the Left ITR and the Right ITR are ITRs of a DNA transposon selected from the group consisting of a *Sleeping Beauty* transposon, a piggyBac transposon, a TcBuster transposon, and a Tol2 transposon.

[00167] In some **embodimentexamples**, the DNA transposon is the *Sleeping Beauty* transposon.

[00168] In some **embodimentexamples**, the transposase is a *Sleeping Beauty* transposase.

[00169] In some **embodimentexamples**, the *Sleeping Beauty* transposase is selected from the group consisting of SB11, SB10, SB100X, hSB110, and hSB81.

[00170] In some **embodimentexamples**, the *Sleeping Beauty* transposase is SB11.

[00171] In some **embodimentexamples**, the SB11 comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 300.

[00172] In some **embodimentexamples**, the SB11 is encoded by a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 301.

[00173] In some [embodimentexamples](#), the polynucleotide encoding the DNA transposase is a DNA vector or an RNA vector.

[00174] In some [embodimentexamples](#), the Left ITR comprises a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 290 or 291; and the Right ITR comprises a polynucleotide sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the polynucleotide sequence of SEQ ID NO: 292, 293 or 294.

[00175] In some [embodimentexamples](#), the recombinant vector, and the DNA transposase or polynucleotide encoding the DNA transposase, are introduced to the population of cells using electroporation, sonication, calcium phosphate precipitation, lipofection, particle bombardment, microinjection, or mechanical deformation by passage through a microfluidic device, or a colloidal dispersion system.

[00176] In some [embodimentexample](#)s, the recombinant vector, and the DNA transposase or polynucleotide encoding the DNA transposase, are introduced to the population of cells using electroporation.

[00177] In some [embodimentexamples](#), the method is completed within 30 days, 25 days, 20 days, 15 days, 14 days, 10 days, 7 days, 6 days, 5 days, 4 days, 3 days, 2 days, or 1 day.

[00178] In some [embodimentexamples](#), wherein the method is completed in less than 30 days, 25 days, 20 days, 15 days, 14 days, 10 days, 7 days, 6 days, 5 days, 4 days, 3 days, 2 days, or 1 day.

[00179] In some [embodimentexample](#)s, the population of cells is cryopreserved and thawed before introduction of the recombinant vector and the DNA transposase or polynucleotide encoding the DNA transposase.

[00180] In some [embodimentexamples](#), the population of cells is rested before introduction of the recombinant vector and the DNA transposase or polynucleotide encoding the DNA transposase.

[00181] In some [embodimentexamples](#), the population of cells is not rested before introduction of the recombinant vector and the DNA transposase or polynucleotide encoding the DNA transposase.

[00182] In some [embodimentexamples](#), the population of cells comprises expanded human *ex vivo* cells.

[00183] In some [embodimentexamples](#), the population of cells is not activated *ex vivo*.

[00184] In some [embodimentexamples](#), the population of cells comprises T cells.

[00185] Also provided herein is a method of treating cancer in a subject in need thereof comprising administering to the subject a therapeutically effective amount of any of the populations of cells provided herein, thereby treating the cancer.

[00186] In some embodiment examples, the cancer is selected from lung, cholangiocarcinoma, pancreatic, colorectal, gynecological, and ovarian cancer.

[00187] Also provided herein is a method of treating an autoimmune disease or disorder in a subject in need thereof comprising administering to the subject a therapeutically effective amount any of the populations of cells provided herein, thereby treating the autoimmune disease or disorder.

[00187a] In one aspect, the present disclosure refers to use of a population of cells comprising the recombinant vector disclosed herein, or a population of cells comprising the polynucleotide disclosed herein, or the population of cells disclosed herein in the manufacture of a medicament for treating cancer or an autoimmune disease or disorder in a subject in need thereof.

4. BRIEF DESCRIPTION OF THE RAWINGS

[00188] The accompanying drawings which are incorporated in and constitute a part of this specification, illustrate exemplary embodiments of the present disclosure and, together with the description, serve to explain principles of the present disclosure.

[00189] **FIG. 1** is a set of schematics of the structures of TCR α (A), TCR β (B), and mbIL15 (15), shown from N terminus (left) to C terminus (right).

[00190] **FIG. 2A** is a set of schematics of the ORFs of tricistronic Cassettes APBT15, ATBP15, AP15TB, AT15PB, BPAT15, BTAP15, BP15TA, and BT15PA. **FIG. 2B** is a set of schematics of the ORFs of control Cassettes 15, APB, and BPA.

[00191] **FIG. 3** is a schematic diagram depicting double transposition and single transposition approaches using a *Sleeping Beauty* transposon/transposase system to generate T cells expressing TCR α /TCR β and mbIL15.

[00192] **FIG. 4** is a set of 2-parameter flow plots showing transgene co-expression as assessed after electroporation and overnight incubation for each of Groups 1-14.

[00193] **FIG. 5A** is a set of 2-parameter flow plots showing representative TCR transgene expression in CD3⁺ cells after overnight incubation for each of Groups 1-14. **FIG. 5B** provides TCR expression data from three donors presented as % mTCR⁺ cells out of CD3⁺ cells.

[00194] **FIG. 6A-6C** shows TCR and mbIL15 expression after first phase expansion (Day 13). **FIG. 6A** provides representative TCR and mbIL15 expression data from each of Groups 1-14. **FIG. 6B** provides TCR expression data from three donors presented as % mTCR⁺ cells out of CD3⁺ cells. **FIG. 6C** provides TCR and mbIL15 co-expression data from three donors presented as % TCR⁺mbIL15⁺ cells out of CD3⁺ cells.

[00195] **FIG. 7A-7B** shows total numbers of TCR⁺ and TCR⁺mbIL15⁺ cells after first phase expansion (Day 13). **FIG. 7A** provides TCR expression data from three donors presented as total