

WHAT IS CLAIMED IS:

1. A polynucleotide encoding a membrane-bound interleukin 15 (mbIL15) in a bicistronic configuration with a chimeric receptor, the chimeric receptor comprising:
 - (a) an extracellular receptor domain, wherein said extracellular receptor domain comprises a peptide that binds native ligands of Natural Killer Group 2 member D (NKG2D), wherein the peptide that binds native ligands of NKG2D is encoded by SEQ ID NO. 2; and
 - (b) an effector domain comprising a transmembrane region and an intracellular signaling domain, wherein the intracellular signaling domain comprises CD3zeta, and wherein the CD3zeta is encoded by a polynucleotide having at least 95% sequence identity to SEQ ID NO. 13.
2. The polynucleotide of Claim 1, wherein the transmembrane region of the effector domain comprises a CD8a transmembrane domain.
3. The polynucleotide of Claim 2, wherein the transmembrane region of the effector domain further comprises a CD8a hinge region.
4. The polynucleotide of Claim 3, wherein the CD8a hinge region is encoded by a polynucleotide having at least 95% sequence identity to SEQ ID NO. 5.
5. The polynucleotide of Claim 1, wherein the intracellular signaling domain further comprises 4-1BB, wherein the 4-1BB is encoded by a polynucleotide having at least 95% sequence identity to SEQ ID NO. 12.
6. The polynucleotide of any one of Claims 1 to 5, wherein the extracellular receptor domain comprising the peptide that binds native ligands of NKG2D is coupled to CD8a; 4-1BB; and CD3zeta.
7. The polynucleotide of Claim 6, wherein the chimeric receptor is encoded by a polynucleotide having at least 95% sequence identity to SEQ ID NO. 18.
8. The polynucleotide of Claim 6, wherein the chimeric receptor comprises an amino acid sequence having at least 95% sequence identity to SEQ ID NO. 19.

9. A polynucleotide encoding a membrane-bound interleukin 15 (mbIL15) in a bicistronic configuration with a chimeric receptor, the chimeric receptor comprising:

(a) an extracellular receptor domain, wherein said extracellular receptor domain comprises a peptide that binds native ligands of Natural Killer Group 2 member D (NKG2D), wherein the peptide that binds native ligands of NKG2D is encoded by SEQ ID NO. 2; and

(b) an effector domain comprising a transmembrane region and an intracellular signaling domain, wherein the intracellular signaling domain comprises CD3zeta, wherein the CD3zeta is encoded by a polynucleotide having at least 95% sequence identity to SEQ ID NO. 13 and

wherein the mbIL15 is encoded by a polynucleotide having at least 95% sequence identity to SEQ ID NO. 16.

10. The polynucleotide of Claim 9, wherein the transmembrane region of the effector domain comprises a CD8a transmembrane domain.

11. The polynucleotide of Claim 10, wherein the transmembrane region of the effector domain further comprises a CD8a hinge region.

12. The polynucleotide of Claim 11, wherein the CD8a hinge region is encoded by SEQ ID NO. 5.

13. The polynucleotide of any one of Claims 9 to 12, wherein mbIL15 comprises an amino acid sequence having at least 95% sequence identity to SEQ ID NO. 17.

14. The polynucleotide of any one of Claims 9 to 13, wherein the intracellular signaling domain further comprises an OX-40 domain.

15. The polynucleotide of Claim 14, wherein the extracellular receptor domain comprising the peptide that binds native ligands of NKG2D is coupled to a CD8a hinge; a CD8a transmembrane domain; the OX-40 domain; and the CD3zeta.

16. The polynucleotide of Claim 15, wherein the chimeric receptor is encoded by a polynucleotide having at least 95% sequence identity to SEQ ID NO: 90.

17. The polynucleotide of Claim 15 or Claim 16, wherein the chimeric receptor comprises an amino acid sequence having at least 95% sequence identity to SEQ ID NO. 109.

18. A polynucleotide encoding a membrane-bound interleukin 15 (mbIL15) in a bicistronic configuration with a chimeric receptor, the chimeric receptor, comprising:

(a) an extracellular receptor domain, wherein said extracellular receptor domain comprises a peptide that binds native ligands of Natural Killer Group 2 member D (NKG2D), wherein the peptide that binds native ligands of NKG2D is encoded by SEQ ID NO. 2; and

(b) an effector domain comprising a transmembrane region and an intracellular signaling domain, wherein the intracellular signaling domain comprises OX-40 and CD3zeta.

19. A vector encoding a membrane-bound interleukin 15 (mbIL15) in a bicistronic configuration with a chimeric receptor, the chimeric receptor, comprising:

(a) an extracellular receptor domain, wherein said extracellular receptor domain comprises a peptide that binds native ligands of Natural Killer Group 2 member D (NKG2D), wherein the peptide that binds native ligands of NKG2D is encoded by SEQ ID NO. 2; and

(b) an effector domain comprising a transmembrane region and an intracellular signaling domain, wherein the intracellular signaling domain comprises OX-40 and CD3zeta.

20. A genetically engineered immune cell expressing both membrane-bound interleukin 15 (mbIL15) and a chimeric receptor, the chimeric receptor, comprising:

(a) an extracellular receptor domain, wherein said extracellular receptor domain comprises a peptide that binds native ligands of Natural Killer Group 2 member D (NKG2D), wherein the peptide that binds native ligands of NKG2D is encoded by SEQ ID NO. 2; and

(b) an effector domain comprising a transmembrane region and an intracellular signaling domain, wherein the intracellular signaling domain comprises OX-40 and CD3zeta; and

wherein the mbIL15 is in a bicistronic configuration with the chimeric receptor, and the mbIL15 and the chimeric receipt are encoded by a polynucleotide.

21. The genetically engineered immune cell of Claim 20, wherein the genetically engineered immune cell is a Natural Killer (NK) cell.

22. The genetically engineered immune cell of Claim 21 for use in allogeneic treatment for cancer.

23. The genetically engineered immune cell of Claim 21 for use in enhancing NK cell cytotoxicity in a mammal.