

CLAIMS

WHAT IS CLAIMED IS:

1. A chimeric polypeptide comprising:
 - (a) an antigen-binding region;
 - (b) a transmembrane region; and
 - (c) a spacer region connecting the trans-membrane region with the antigen binding region, wherein the spacer region comprises: (i) a stalk region comprising about 20 to about 60 amino acids and at least one dimerization site; and (ii) one to five a stalk extension regions, wherein each stalk extension region comprises fewer dimerization sites than the stalk region
2. The chimeric polypeptide of claim 1, wherein at least one stalk extension region comprises an amino acid sequence having at least 80% sequence identity with the amino acid sequence of the stalk region.
3. The chimeric polypeptide of claim 1, wherein the stalk region is proximal to the transmembrane region.
4. The chimeric polypeptide of claim 1, wherein the stalk region is distal to the transmembrane region.
5. The chimeric polypeptide of claim 1, wherein the chimeric polypeptide exhibits increased expression on a cell surface compared to an otherwise identical polypeptide that lacks the stalk extension region.
6. The chimeric polypeptide of claim 1, wherein at least one stalk extension region lacks a dimerization site.
7. The chimeric polypeptide of claim 1, wherein each stalk extension region comprises about 20 to about 60 amino acids.

8. The chimeric polypeptide of claim 7, wherein each stalk extension region comprises an amino acid sequence that has at least about 80% sequence identity to the amino acid sequence of the stalk region.
9. The chimeric polypeptide of claim 1, wherein the stalk region comprises a sequence with at least about identity to a CD8alpha hinge domain, a CD28 hinge domain, and/or a CTLA-4 hinge domain.
10. The chimeric polypeptide of claim 1, wherein the antigen binding region binds an epitope on CD19, BCMA, CD44, α -Folate receptor, CAIX, CD30, ROR1, CEA, EGP-2, EGP-40, HER2, HER3, Folate-binding Protein, GD2, GD3, IL-13R-a2, KDR, EDB-F, mesothelin, CD22, EGFR, Folate receptor α , Mucins, MUC-1, MUC-16, GPC3, CSPG4, HER1/HER3, HER2, CD44v6, CD44v7/v8, CD20, CD174, CD138, L1-CAM, FAP, c-MET, PSCA, CS1, CD38, IL-11R α , EphA2, CLL-1, MAGE-A1, h5T4, PSMA, TAG-72, EGFR, CD20, EGFRvIII, CD123, and/or VEGF-R2.
11. The chimeric polypeptide of claim 1, wherein the chimeric polypeptide comprises a chimeric antigen receptor (CAR).
12. The chimeric polypeptide of claim 1, wherein the chimeric polypeptide comprises an engineered T-cell receptor (TCR).
13. The chimeric polypeptide of claim 12, wherein the engineered TCR is an $\alpha\beta$ TCR.
14. The chimeric polypeptide of claim 12, wherein the engineered TCR is a $\gamma\delta$ TCR.
15. The chimeric polypeptide of claim 12, wherein the antigen binding region binds an epitope on at least one of NY-ESO-1, Titin, MART-1, HPV, HBV, MAGE-A4, MAGE-A10, MAGE A3/A6, gp100, MAGE-A1, or PRAME.
16. The chimeric polypeptide of claim 11, wherein at least one stalk extension region comprises:
(a) an amino acid sequence that has at least 80% sequence identity with the amino acid sequence of stalk region; and (b) at least one amino acid substitution relative to the stalk region.

17. The chimeric polypeptide of claim 16, wherein the stalk region is capable of dimerizing with a second stalk region present in second CAR and comprises at least 80% sequence identity with the amino acid sequence of the second stalk region.
18. A method of increasing expansion of an engineered T cell expressing a chimeric polypeptide comprising engineering a nucleic acid encoding the chimeric polypeptide to comprise a stalk extension domain, thereby generating an engineered T cell.
19. The chimeric polypeptide of claim 1, wherein the antigen binding region binds an epitope on CD33, MUC-16, and/or ROR1.
20. The chimeric polypeptide of claim 1, wherein the antigen binding region binds an epitope on ROR1.
21. The chimeric polypeptide of claim 1, wherein the stalk region comprises an amino acid sequence that has at least 80% sequence identity with SEQ ID NO: 3.
22. The chimeric polypeptide of claim 1, wherein the spacer region comprises an amino acid sequence that has at least 80% sequence identity with SEQ ID NO: 5.
23. A modified effector cell that expresses the chimeric polypeptide of claim 1.
24. A modified effector cell that expresses the chimeric polypeptide of claim 20.
25. The modified effector cell of claim 24, wherein the cell is a CAR-T cell.
26. The modified effector cell of claim 23, wherein the cell expresses a cytokine.
27. The modified effector cell of claim 26, wherein the cytokine is a membrane-bound IL15.
28. The modified effector cell of claim 23, wherein the cell expresses a cell tag.

29. The modified effector cell of claim 28, wherein the cell tag comprises a truncated epidermal growth factor receptor.
30. The modified cell of claim 23, wherein the cell expresses a membrane-bound IL15 and a cell tag comprising a truncated epidermal growth factor receptor.
31. The modified cell of claim 24, wherein the cell expresses a membrane-bound IL15 and a cell tag comprising a truncated epidermal growth factor receptor.
32. The modified cell of claim 23, wherein the cell has improved cytotoxicity as compared to a cell expressing an otherwise identical antigen-binding polypeptide that lacks the stalk extension region.
33. A method for making the modified effector cell of claim 23, the method comprising transfecting an immune effector cell with an expression vector encoding the chimeric polypeptide.
34. The method of claim 33, wherein the vector is a *Sleeping Beauty* transposon.