CLAIMS

1. A recombinant polypeptide comprising an extracellular region, a transmembrane region, and an intracellular region, wherein

the extracellular region comprises a human epidermal growth factor receptor (EGFR) Domain III sequence, and

the intracellular region (i) comprises a juxtamembrane domain that is net-neutral or net-positively charged in the first at least three amino acids (ii) but lacks an active EGFR tyrosine kinase domain.

2. The recombinant polypeptide of claim 1, wherein more than half of the amino acids of the juxtamembrane domain are glycine, serine, arginine, lysine, threonine, asparagine, glutamine, aspartic acid, glutamic acid, tyrosine, tryptophan, histidine, and/or proline.

3. The recombinant polypeptide of claim 1 or 2, wherein the amino acid at each position of the juxtamembrane domain is selected according to Table 1.

4. The recombinant polypeptide of claim 1, wherein the juxtamembrane domain comprises RRRHIVRKR (SEQ ID NO:16), RRRHIVRK (SEQ ID NO:17), RRRHIVR (SEQ ID NO:18), RRRHIV (SEQ ID NO:19), RRRHI (SEQ ID NO:20), RRRH (SEQ ID NO:21), RRR, RKR, or RR.

5. The recombinant polypeptide of any one of the preceding claims, wherein the intracellular region does not contain any residue that is phosphorylated.

6. The recombinant polypeptide of any one of the preceding claims, wherein the Domain III sequence comprises SEQ ID NO:2.

7. The recombinant polypeptide of any one of the preceding claims, wherein the extracellular region further comprises, C-terminal to the Domain III sequence, (i) a sequence derived from EGFR Domain IV, (ii) an artificial sequence, or (iii) both (i) and (ii).

8. The recombinant polypeptide of claim 7, wherein the extracellular region comprises amino acids 334-504, 334-525, or 334-645 of SEQ ID NO:1.

9. The recombinant polypeptide of any one of the preceding claims, wherein the transmembrane region is derived from a human EGFR transmembrane domain, optionally comprising SEQ ID NO:5.

10. The recombinant polypeptide of any one of the preceding claims, further comprising a signal peptide derived from human EGFR, human granulocyte-macrophage colony-stimulating factor (GM-CSF), human Ig kappa, mouse Ig kappa, or human CD33.

11. The recombinant polypeptide of claim 1, comprising SEQ ID NO:26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40; or an amino acid sequence at least 90% identical thereto.

12. A nucleic acid molecule comprising a coding sequence for the recombinant polypeptide of any one of the preceding claims.

13. The nucleic acid molecule of claim 12, further comprising a coding sequence for a chimeric antigen receptor (CAR).

14. The nucleic acid molecule of claim 13, wherein

the coding sequences for the recombinant polypeptide and the CAR are operably linked to the same promoter such that the two coding sequences are co-transcribed, and

optionally the two coding sequences are separated by (i) an internal ribosome entry site (IRES) or (ii) a coding sequence for a self-cleaving peptide wherein the coding sequences for the recombinant polypeptide, the CAR, and the self-cleaving peptide are in frame with each other.

15. The nucleic acid molecule of claim 13, further comprising a coding sequence for a third polypeptide, optionally wherein the third polypeptide is human c-Jun or a functional analog thereof.

16. The nucleic acid molecule of claim 15, wherein

the coding sequences for the recombinant polypeptide, the CAR, and the human c-Jun are operably linked to the same promoter such that the three coding sequences are co-transcribed, and

optionally the three coding sequences are separated from each other by (i) an internal ribosome entry site (IRES) or (ii) a coding sequence for a self-cleaving peptide wherein the coding sequences for the recombinant polypeptide, the CAR, the human c-Jun, and the self-cleaving peptide(s) are in frame with each other.

17. The nucleic acid molecule of any one of claims 12-16, wherein

the promoter is a constitutive or inducible promoter, optionally wherein the promoter is an MND promoter,

the self-cleaving peptide is a 2A peptide, and/or

the CAR is specific for a tumor antigen, optionally selected from AFP, BCMA, CD19, CD20, CD22, CD123, EpCAM, GPC2, GPC3, HER2, MUC16, ROR1, and ROR2.

18. The nucleic acid molecule of any one of claims 12-17, wherein the nucleic acid molecule is a viral vector, optionally a lentiviral or retroviral vector.

19. A cell comprising the nucleic acid molecule of any one of claims 12-18.

20. The cell of claim 19, wherein the cell is a human T cell.

21. A pharmaceutical composition comprising the cell of claim 19 or 20, the nucleic acid molecule of any one of claims 12-18, or a recombinant virion comprising the nucleic acid molecule of claim 18; and a pharmaceutically acceptable carrier.

22. The cell of claim 19 or 20 for use in treating a patient in need thereof, optionally wherein the cell is derived from the patient.

23. Use of the cell of claim 19 or 20 in the manufacture of a medicament for treating cancer in a patient, wherein the cell is a T cell expressing a CAR, a T cell receptor (TCR), an engineered TCR, or a TCR mimic that is specific for a tumor antigen present in cancer.

24. The use of the cell in the manufacture of the medicament of claim 23, wherein the cell is derived from the patient.

25. The cell for use of claim 22 or the use of the cell in the manufacture of the medicament of claim 23 or 24, wherein the cell is to be administered to the patient prior to administration of an effective amount of an antibody specific for human EGFR, wherein the antibody elicits cytotoxicity against cells expressing the recombinant polypeptide, and optionally the antibody is IgG_1 or IgG_2, optionally wherein the antibody is cetuximab.

26. A method of making a genetically engineered human cell, comprising providing an isolated human cell, and introducing the nucleic acid molecule of any one of claims 12-18 into the human cell.

27. The method of claim 26, wherein the human cell is a human T cell.