

WHAT IS CLAIMED IS:

1. An isolated polypeptide comprising at least 95% sequence identity to a polypeptide of an extracellular domain of HER2 polypeptide having a sequence of amino acids 563 to 652 of SEQ ID NO: 23 linked to a transmembrane domain, wherein the isolated polypeptide specifically binds to an antibody that binds to an epitope in Domain IV of Her2, and wherein the isolated polypeptide excludes the full length mature HER2.
2. The isolated polypeptide of claim 1, wherein the HER2 polypeptide comprises amino acids glutamic acid 580, aspartic acid 582, aspartic acid 592, phenylalanine 595, and glutamine 624 of SEQ ID NO:23.
3. The isolated polypeptide of claim 2, wherein the HER2 polypeptide comprises amino acids 563-652 of SEQ ID NO: 23.
4. The isolated polypeptide of any one of claims 1-3 wherein the transmembrane domain comprises amino acids 653-675 of SEQ ID NO: 23.
5. The isolated polypeptide of any one of claims 1-4, further comprising a leader peptide that provides for cell surface expression.
6. The isolated polypeptide of claim 5, wherein the leader peptide comprises an amino acid sequence set forth in SEQ ID NO: 17.
7. The isolated polypeptide of any one of claims 1-6, wherein the antibody is trastuzumab.
8. An isolated nucleic acid encoding the polypeptide of any one of claims 1-7 or 38-44.
9. The isolated nucleic acid of claim 8 further comprising a promoter.
10. The isolated nucleic acid of claim 8 or claim 9 further comprising a transgene.

11. The isolated nucleic acid of claim 10, wherein the transgene comprises a polynucleotide encoding a chimeric antigen receptor.
12. The isolated nucleic acid of claim 11, wherein the chimeric antigen receptor comprising an antigen binding domain, a spacer domain, a transmembrane domain and at least one stimulatory domain.
13. The isolated nucleic acid of any one of claims 10 to 12, wherein the polynucleotide encoding the transgene is linked to the nucleic acid encoding the HER2 polypeptide of claim 1 with a self-cleaving linker.
14. The isolated nucleic acid of claim 13, wherein the self-cleaving linker is a T2A linker having the sequence of L E G G G E G R G S L L T C G (SEQ ID NO: 26).
15. The isolated nucleic acid of any one of claims 11-14, wherein the chimeric antigen receptor comprises the amino acid sequence set forth in SEQ ID NO: 2.
16. The isolated nucleic acid of any one of claims 11-14, wherein the chimeric antigen receptor comprises the amino acid sequence set forth in SEQ ID NO: 25. (CD20CAR).
17. A host cell comprising the isolated nucleic acid of any one claims 8-16.
18. The isolated host cell of claim 17, wherein the host cell is selected from the group consisting of CD8 T cells, CD4 T cells, CD4 naïve T cells, CD8 naïve T cells, CD8 central memory cells, CD4 central memory cells, and combinations thereof.
19. The isolated host cell of claims 17 or claim 18, wherein the host cell is autologous.

20. The isolated host cell of any one of claims 17-19 wherein the host cell is antigen specific.
21. A composition comprising the host cells of any one of claims 17-20 or 45 -46.
22. A method of manufacturing a composition comprising:
- a) Introducing an isolated nucleic acid of any one of claims 8-16 into a host cell; and
 - b) Culturing the host cells in a medium comprising at least one growth factor.
23. The method of claim 22, wherein the growth factor is selected from the group consisting of IL-15, IL-7, IL-21, IL-2, and combinations thereof.
24. The method of claim 22 or claim 23, further comprising selecting cells that express the Her2t polypeptide.
25. The method of any one of claims 22-24, wherein the cells are selected before culturing the cells in the medium.
26. The method of any one of claims 24-25, wherein the cells are selected using an antibody that binds to Domain IV of Her2.
27. The method of claim 26, wherein the antibody is trastuzumab.
28. The method of any one of claims 22-27, further comprising introducing a second isolated nucleic acid coding for a chimeric antigen receptor linked to a second genetic tag.
29. The method of claim 28, further comprising selecting cells expressing the second genetic tag.

30. The method of any one of claims 28-29 wherein the second genetic tag comprises EGFRt.
31. A method of treating patient having cancer expressing a tumor antigen comprising administering an effective amount of a composition of claim 21, wherein the cells of the composition express a chimeric antigen receptor that comprises an antigen binding domain that binds to the tumor antigen expressed on the cancer cell and a genetic tag.
32. A use of a composition of claim 21 for treating a cancer having a tumor antigen recognized by the chimeric antigen receptor on the cells.
33. A method of treating patient having cancer expressing a tumor antigen comprising administering an effective amount of a composition of claim 21 and an antibody that specifically binds to the genetic tag, wherein the cells of the composition express a chimeric antigen receptor that comprises an antigen binding domain that binds to the tumor antigen expressed on the cancer cell and a genetic tag.
34. A use of a composition of claim 21 for treating a cancer having a tumor antigen recognized by the chimeric antigen receptor on the cells of the composition and an antibody that specifically binds the genetic tag.
35. The method or use of any one of claims 31 to 34 where the antibody is Herceptin or Erbitux.
36. The method or use of any one of claims 31-35, wherein the antibody is conjugated to a cytotoxic agent.
37. The method or use of any one of claims 31-35, wherein the antibody is detectably labelled.
38. An isolated polypeptide comprising at least 95% sequence identity to a polypeptide of an extracellular domain of HER2 polypeptide having a sequence of amino acids 563

to 652 of SEQ ID NO: 23 linked to a transmembrane domain, wherein the isolated polypeptide specifically binds to an antibody that binds to an epitope in Domain IV of Her2, and wherein the isolated polypeptide excludes the full length mature HER, and wherein the extracellular domain of HER2 polypeptide having the sequence of amino acids 563 to 652 of SEQ ID NO: 23 is linked to the transmembrane domain by a sequence comprising amino acids GGGSGGGS (SEQ ID NO: 45).

39. The isolated polypeptide of claim 38, wherein the HER2 polypeptide comprises amino acids glutamic acid 580, aspartic acid 582, aspartic acid 592, phenylalanine 595, and glutamine 624 of SEQ ID NO:23.
40. The isolated polypeptide of claim 39, wherein the HER2 polypeptide comprises amino acids 563-652 of SEQ ID NO: 23.
41. The isolated polypeptide of any one of claims 38-40 wherein the transmembrane domain comprises amino acids 653-675 of SEQ ID NO: 23.
42. The isolated polypeptide of any one of claims 38-41, further comprising a leader peptide that provides for cell surface expression.
43. The isolated polypeptide of claim 42, wherein the leader peptide comprises an amino acid sequence set forth in SEQ ID NO: 17.
44. The isolated polypeptide of any one of claims 38-43, wherein the antibody is trastuzumab.
45. The host cell of claim 17, wherein the host cell is a precursor T cell.
46. The host cell of claim 17, wherein the host cell is a hematopoietic stem cell.
47. The host cell of any one of claims 22-30, wherein the host cell is a precursor T cell.
48. The host cell of any one of claims 22-30, wherein the host cell is a hematopoietic stem cell.

CLAIMS

1. A polypeptide comprising an extracellular domain of a HER2 polypeptide comprising an amino acid sequence with at least 95% sequence identity to the sequence of amino acids 563 to 652 of SEQ ID NO:23 linked via a spacer to a transmembrane domain, wherein the spacer is selected from the group consisting of an IgG4 hinge domain, a CD28 hinge domain, and a polypeptide comprising the amino acid sequence of SEQ ID NO:45 having 0-3 conservative substitutions thereof.
2. The polypeptide of claim 1, wherein the spacer comprises the IgG4 hinge domain.
3. The polypeptide of claim 2, wherein the IgG4 hinge domain comprises the amino acid sequence of any one of SEQ ID NOs:09-13 having 0-3 conservative substitutions thereof.
4. The polypeptide of claim 3, wherein the IgG4 hinge domain comprises the amino acid sequence of SEQ ID NO:09 having 0-3 conservative substitutions thereof.
5. The polypeptide of claim 3, wherein the IgG4 hinge domain comprises the amino acid sequence of SEQ ID NO:09.
6. The polypeptide of claim 1, wherein the spacer comprises the amino acid sequence of SEQ ID NO:45 having 0-3 conservative substitutions thereof.
7. The polypeptide of claim 6, wherein the spacer comprises the amino acid sequence of SEQ ID NO:45.
8. The polypeptide of claim 1, wherein the spacer comprises the CD28 hinge domain.
9. The polypeptide of any one of claims 1-8, further comprising a leader peptide that provides for cell surface expression.
10. The polypeptide of claim 9, wherein the leader peptide comprises the amino acid sequence set forth in SEQ ID NO:17.
11. The polypeptide of any one of claims 1-8, wherein the polypeptide specifically binds to trastuzumab.
12. A nucleic acid encoding the polypeptide of any one of claims 1-8.
13. The nucleic acid of claim 12, further comprising a transgene, wherein the transgene encodes a first chimeric antigen receptor (CAR).
14. An isolated host cell comprising the nucleic acid of claim 12.

15. The isolated host cell of claim 14, further comprising a transgene encoding a first chimeric antigen receptor (CAR).

16. The isolated host cell of claim 14, wherein the isolated host cell is selected from the group consisting of a CD8 T cell, a CD4 T cell, a CD4 naïve T cell, a CD8 naïve T cell, a CD8 central memory cell, and a CD4 central memory cell.

17. The isolated host cell of claim 14, wherein the isolated host cell is a precursor T cell or a hematopoietic stem cell.

18. A pharmaceutical composition comprising the isolated host cell of claim 14 and a pharmaceutically acceptable excipient.

19. The isolated host cell of claim 15, for use in the manufacture of a medicament to treat or inhibit a cancer in a subject, wherein the isolated host cell expresses the first CAR and the polypeptide, and wherein the first CAR is capable of specifically binding to a tumor antigen expressed by the cancer.

20. The isolated host cell of claim 19, for use in the manufacture of a medicament to treat or inhibit a cancer in a subject, wherein the isolated host cell is administered in combination with an antibody that specifically binds to the polypeptide.

21. The isolated host cell of claim 20, where the antibody is trastuzumab.

22. The isolated host cell of claim 20, wherein the antibody is conjugated to a cytotoxic agent.

23. The isolated host cell of claim 20, wherein the antibody is detectably labeled.

24. An *ex vivo* method for preparing a population of cells for an infusion, the method comprising:

(a) introducing the nucleic acid of claim 12 into a cell; and

(b) culturing the cell to obtain a population of cells.

25. The method of claim 24, further comprising (c) enriching for cells expressing the nucleic acid.