CLAIMS

What is claimed is:

1. A chimeric antibody-T cell receptor (TCR) construct (caTCR) comprising:
   a) a multispecific antigen-binding module comprising a first antigen-binding domain that specifically binds to a first target antigen and a second antigen-binding domain that specifically binds to a second target antigen;
   b) a TCR module (TCRM), wherein the TCRM comprises a first TCR domain (TCRD) (TCRD1) comprising a first TCR transmembrane domain (TCR-TM) and a second TCRD (TCRD2) comprising a second TCR-TM; wherein the TCRM facilitates recruitment of at least one TCR-associated signaling molecule; and
   c) a stabilization module, wherein the stabilization module comprises a first stabilization domain comprising a first immunoglobulin constant domain, and a second stabilization domain comprising a second immunoglobulin constant domain;

   wherein the multispecific antigen-binding module is fused to the N-terminus of the stabilization module, and the stabilization module is fused to the N-terminus of the TCRM.

2. The caTCR of claim 1, wherein the first antigen-binding domain comprises a first heavy chain variable domain (VH1) and a first light chain variable domain (VL1), wherein the second antigen-binding domain comprises a second VH (VH2) and a second VL (VL2); and wherein the caTCR comprises:
   (i) a first polypeptide chain comprising from the N-terminus to the C-terminus: V_H1-L1-V_H2-C_H1-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: V_L1-L2-V_L2-C_L-TCRD2;
   (ii) a first polypeptide chain comprising from the N-terminus to the C-terminus: V_H1-L1-V_L2-C_L-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: V_L1-L2-V_H2-C_H1-TCRD2;
   (iii) a first polypeptide chain comprising from the N-terminus to the C-terminus: V_L1-L1-V_H2-C_H1-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: V_H1-L2-V_L2-C_L-TCRD2;
   (iv) a first polypeptide chain comprising from the N-terminus to the C-terminus: V_L1-L1-V_L2-C_L-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: V_H1-L2-V_H2-C_H1-TCRD2;

(v) a first polypeptide chain comprising from the N-terminus to the C-terminus: VH1-L1-VH2-CH1-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: VL2-L2-VL1-CL-TCRD2;

(vi) a first polypeptide chain comprising from the N-terminus to the C-terminus: VL1-L1-VL2-CL-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: VH2-L2-VH1-CH1-TCRD2;

(vii) a first polypeptide chain comprising from the N-terminus to the C-terminus: VH1-L1-VH2-CH1-TCRD2, and a second polypeptide chain comprising from the N-terminus to the C-terminus: VL2-L2-VL1-CL-TCRD1; or

(viii) a first polypeptide chain comprising from the N-terminus to the C-terminus: VL1-L1-VL2-CL-TCRD2, and a second polypeptide chain comprising from the N-terminus to the C-terminus: VH2-L2-VH1-CH1-TCRD1;

wherein L1 and L2 are peptide linkers.

3. The caTCR of claim 1, wherein the first antigen-binding domain is a first scFv (scFv1) and the second antigen-binding domain is a second scFv (scFv2), and wherein the caTCR comprises:

(i) a first polypeptide chain comprising from the N-terminus to the C-terminus: scFv1-L1-C_H1-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: scFv2-L2-C_L-TCRD2;

(ii) a first polypeptide chain comprising from the N-terminus to the C-terminus: scFv2-L1-C_H1-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: scFv1-L2-C_L-TCRD2;

(iii) a first polypeptide chain comprising from the N-terminus to the C-terminus: scFv1-L1-CL-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: scFv2-L2-CH1-TCRD2; or

(iv) a first polypeptide chain comprising from the N-terminus to the C-terminus: scFv2-L1-CL-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: scFv1-L2-CH1-TCRD2;

wherein L1 and L2 are peptide linkers.

4. The caTCR of claim 1, wherein the first antigen-binding domain is an scFv and the second antigen-binding domain comprises a VH and a VL, and wherein the caTCR comprises:

(i) a first polypeptide chain comprising from the N-terminus to the C-terminus: scFv-L1-V_H-C_H1-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: V_L-C_L-TCRD2;

(ii) a first polypeptide chain comprising from the N-terminus to the C-terminus: V_H-C_H1-TCRD1, and a second polypeptide chain comprising from the N-terminus to the C-terminus: scFv-L2-V_L-C_L-TCRD2;

(iii) a first polypeptide chain comprising from the N-terminus to the C-terminus: VH-CH1-TCRD2, and a second polypeptide chain comprising from the N-terminus to the C-terminus: scFv-L2-VL-CL-TCRD1; or

(iv) a first polypeptide chain comprising from the N-terminus to the C-terminus: scFv-L1-VH-CH1-TCRD2, and a second polypeptide chain comprising from the N-terminus to the C-terminus: VL-CL-TCRD1;

wherein L1 and L2 are peptide linkers.

5. The caTCR of claim 2, wherein L1 and/or L2 are about 5 to about 50 amino acids long.

6. The caTCR of claim 1, wherein the first target antigen is a first cell surface antigen, and the second target antigen is a second cell surface antigen.

7. The caTCR of claim 6, wherein

(i) the first target antigen is CD19 and the second target antigen is CD22, or

(ii) the first target antigen is CD22 and the second target antigen is CD19.

8. The caTCR of claim 7,

wherein the antigen-binding domain that specifically binds to CD22 comprises HC-CDR1, HC-CDR2, and HC-CDR3 of a V_H comprising the amino acid sequence of SEQ ID NO: 65, and LC-CDR1, LC-CDR2, and LC-CDR3 of a V_L comprising the amino acid sequence of SEQ ID NO: 69; and/or

wherein the antigen-binding domain that specifically binds to CD19 comprises HC-CDR1, HC-CDR2, and HC-CDR3 of a VH comprising the amino acid sequence of SEQ ID NO: 74, and LC-CDR1, LC-CDR2, and LC-CDR3 of a VL comprising the amino acid sequence of SEQ ID NO: 78.

9. The caTCR of claim 1, wherein at least one of the TCR-TMs is non-naturally occurring.

10. The caTCR of claim 1, wherein the TCRD1 further comprises a first connecting peptide or fragment thereof of a first TCR subunit; and/or wherein the TCRD2 further comprises a second connecting peptide or fragment thereof of a second TCR subunit.

11. The caTCR of claim 1, wherein the TCRD1 further comprises a first TCR intracellular domain comprising a first TCR intracellular sequence; and/or wherein the TCRD2 further comprises a second TCR intracellular domain comprising a second TCR intracellular sequence.
12. One or more nucleic acids encoding the caTCR of claim 1.
13. A complex comprising the caTCR of claim 1 and at least one TCR-associated signaling molecule selected from the group consisting of CD3δε, CD3γε, and ζζ.
14. An effector cell presenting on its surface the caTCR of claim 1.
15. An *in vitro* method of killing a target cell presenting a target antigen, comprising contacting the target cell with the effector cell of claim 14, wherein the caTCR specifically binds to the target antigen.
16. Use of the effector cell of claim 14 in the manufacture of a pharmaceutical composition for treating a target antigen-associated disease in an individual in need thereof, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier, and wherein the caTCR specifically binds to the target antigen.
17. The caTCR of claim 1, wherein the stabilization module is selected from the group consisting of: i) a CH1-CL module, ii) a CH2-CH2 module, iii) a CH3-CH3 module, and iv) a CH4-CH4 module.
18. The caTCR of claim 1, wherein the first stabilization domain is CH1 and the second stabilization domain is CL, and wherein: i) the CH1 is fused to the N-terminus of the TCRD1, and the CL is fused to the N-terminus of the TCRD2; or ii) the CH1 is fused to the N-terminus of the TCRD2, and the CL is fused to the N-terminus of the TCRD1.
19. The caTCR of claim 1, wherein:

    i) the first TCR-TM comprises the transmembrane domain of TCRα or a variant thereof, and the second TCR-TM comprises the transmembrane domain of TCRβ or a variant thereof;

    ii) the first TCR-TM comprises the transmembrane domain of TCRβ or a variant thereof, and the second TCR-TM comprises the transmembrane domain of TCRα or a variant thereof;

    iii) the first TCR-TM comprises the transmembrane domain of TCRγ or a variant thereof, and the second TCR-TM comprises the transmembrane domain of TCRδ or a variant thereof; or

iv) the first TCR-TM comprises the transmembrane domain of TCRδ or a variant thereof, and the second TCR-TM comprises the transmembrane domain of TCRγ or a variant thereof.

20. Use of the effector cell of claim 14 in the manufacture of a medicament for killing a target cell presenting a target antigen, wherein the target cell is to be contacted with the effector cell, wherein the caTCR specifically binds to the target antigen.