

What Is Claimed Is:

1. A bi-specific antibody, comprising:
 - (a) a first antigen binding fragment that binds human CD3, wherein the first antigen binding fragment comprises a first heavy chain comprising a first heavy chain variable region (V_H) and a first light chain comprising a first light chain variable region (V_L), wherein the first V_H comprises the same heavy chain complementary determining regions (CDRs) or no more than 5 amino acid variations relative to a first reference antibody and the first V_L comprises the same light chain CDRs or no more than 5 amino acid variations relative to the reference antibody, and wherein the first reference antibody is CTA.02, CTA.03, CTA.04, or CTA.05; and
 - (b) a second antigen binding fragment that binds a tumor associated antigen (TAA), wherein the second antigen binding fragment comprises a second heavy chain comprising a second heavy chain variable region (V_H) and a second light chain comprising a second light chain variable region (V_L).
2. The bi-specific antibody of claim 1, wherein the first heavy chain and the first light chain comprise the same V_H and V_L as the first reference antibody.
3. The bi-specific antibody of claim 1 or claim 2, wherein the second antigen binding fragment binds a TAA, which is CD20, CD19, EGFR, HER2, PSMA, CEA, EpCAM, FAP, PD-L1, CD38, CD33, cMET, CD47, TRAIL-R2, mesothelin, or GD2.
4. The bi-specific antibody of claim 3, wherein the second V_H comprises the same heavy chain complementary determining regions (CDRs) or no more than five amino acid variations relative to a second reference antibody and the second V_L comprises the same light chain CDRs or no more than 5 amino acid variations relative to the second reference antibody, and wherein the second reference antibody is CTAT.01, CTAT.02, CTAT.03, CTAT.04, CTAT.05, CTAT.06, CTAT.07, CTAT.08, CTAT.09, CTAT.10, CTAT.11, CTAT.12, CTAT.13, CTAT.14, CTAT.15, or CTAT.16.
5. The bi-specific antibody of claim 4, wherein the second antigen binding fragment comprises the same V_H and same V_L as the second reference antibody.

6. The bi-specific antibody of any one of claims 1-5, wherein the first antigen binding fragment is a Fab fragment and the second antigen binding fragment is a single chain variable fragment (scFv), and wherein the Fab fragment comprises the first heavy chain, which comprises the first V_H and a CH1 fragment, and the first light chain, which comprises the first V_L and a light chain constant region.

7. The bi-specific antibody of claim 6, wherein the Fab fragment comprises the first heavy chain and the first light chain, which respectively comprise the amino acid sequences of (a) SEQ ID NO: 10 and SEQ ID NO: 11, (b) SEQ ID NO: 23 and SEQ ID NO: 24, 25, or 228, (c) SEQ ID NO: 35 and SEQ ID NO: 36, or (d) SEQ ID NO: 46 and SEQ ID NO: 47.

8. The bi-specific antibody of claim 6 or claim 7, wherein the scFv of the second antigen binding fragment comprises the amino acid sequence of any one of SEQ ID NOs: 254-271.

9. The bi-specific antibody of any one of claims 6-8, wherein the scFv is linked to the CH1 fragment or the light chain constant region via a peptide linker.

10. The bi-specific antibody of claim 7, wherein the bi-specific antibody comprises a first polypeptide comprising the first light chain and a second polypeptide comprising, from N-terminus to C-terminus, the first heavy chain, the peptide linker, and the scFv.

11. The bi-specific antibody of claim 8, wherein the first polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 229-248.

12. The bi-specific antibody of claim 10 or claim 11, wherein the second polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 24, 25, and 228.

13. The bi-specific antibody of any one of claims 1-5, wherein the first antigen binding fragment is a single chain variable fragment (scFv) and the second antigen binding fragment is a Fab fragment, wherein the Fab fragment comprises the second heavy chain,

which comprises the second V_H and a CH1 fragment, and the second light chain, which comprises the second V_L and a light chain constant region.

14. The bi-specific antibody of claim 13, wherein the scFv comprises the amino
5 acid sequence of any one of SEQ ID NOs:250-253.

15. The bi-specific antibody of claim 13 or claim 14, wherein the Fab fragment
comprises the first heavy chain and the first light chain, which respectively comprise the
amino acid sequences of (1) SEQ ID NO:57 and SEQ ID NO: 58, (2) SEQ ID NO: 72 and
10 SEQ ID NO: 73, (3) SEQ ID NO: 83 and SEQ ID NO: 84, (4) SEQ ID NO: 94 and SEQ ID
NO: 95, (5) SEQ ID NO:105 and SEQ ID NO:106, (6) SEQ ID NO: 116 and SEQ ID
NO:117, (7) SEQ ID NO: 127 and SEQ ID NO:128, (8) SEQ ID NO:138 and SEQ ID
NO:139, (9) SEQ ID NO:149 and SEQ ID NO:150, (10) SEQ ID NO:160 and SEQ ID
NO:161, (11) SEQ ID NO: 171 and SEQ ID NO:172, (12) SEQ ID NO:182 and SEQ ID
15 NO:183, (13) SEQ ID NO:193 and SEQ ID NO:194, (14) SEQ ID NO:204 and SEQ ID
NO:205, (15) SEQ ID NO:215 and SEQ ID NO:216, or (16) SEQ ID NO:226 and SEQ ID
NO:227.

16. The bi-specific antibody of any one of claims 13-15, wherein the scFv is
20 linked to the CH1 fragment or the light chain constant region via a peptide linker, which
optionally is at least 5 amino acids in length.

17. The bi-specific antibody of any one of claims 1-5, wherein both the first
antigen binding fragment and the second antigen binding fragment are scFv antibodies.
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18. The bi-specific antibody of claim 13, wherein the bi-specific antibody
comprises a polypeptide comprising the two scFv antibodies.

19. An armed immune cell, comprising an immune cell that expresses surface
30 CD3, and a bi-specific antibody of any one of claims 1-18, wherein the armed immune cell
displays the bi-specific antibody on the surface via interaction between the first antigen
binding fragment in the bi-specific antibody and the CD3 expressed by the immune cell.

20. The armed immune cell of claim 19, wherein the immune cell is a T cell, a B cell, a monocyte, a macrophage, or a combination thereof.

21. The armed immune cell of claim 20, wherein the T cell is a CD4⁺ T cell, a
5 CD8⁺ T cell, a regulatory T cell, or a natural killer T cell.

22. The armed immune cell of any one of claims 19-21, wherein the immune cell is a human immune cell.

10 23. The armed immune cell of claim 22, wherein the human immune cell is derived from a human donor.

24. A method of producing the armed immune cell of claim 19, comprising cultivating a cell population comprising the immune cells in the presence of the bi-specific
15 antibody to allow for binding of the bi-specific antibody to the immune cells, thereby producing the armed immune cell.

25. The method of claim 24, wherein the cell population comprises T cells, B cells, monocytes, macrophages, or a combination thereof.

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26. The method of claim 25, wherein the cell population comprises peripheral blood mononuclear cells (PBMCs) or immune cells derived from stem cells in vitro, and optionally wherein the stem cells are hematopoietic stem cells, umbilical cord blood stem cells, or induced pluripotent stem (iPS) cells.

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27. The method of any one of claims 24-26, wherein the cultivating step is performed in a culture medium comprising a cytokine, which optionally comprises interleukin 2 (IL-2), interleukin 7 (IL-7), transforming growth factor-beta (TGF- β), or a combination thereof.

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28. A population of armed immune cells, which is produced by a method of any one of claims 24-27.

29. A method for treating cancer, comprising administering to a subject in need thereof an effective amount of a population of armed immune cells set forth in any one of claims 19-23 and 28, wherein the subject has or suspected of having a cancer that is positive with the TAA, to which the second antigen binding fragment of the bi-specific antibody
5 binds.

30. The method of claim 29, wherein the subject is a human cancer patient.

31. The method of claim 29 or claim 30, wherein the armed immune cells are
10 autologous to the subject.

32. The method of claim 29 or claim 30, wherein the armed immune cells are allogenic to the subject.

15 33. The method of any one of claims 29-32, wherein the cancer is selected from the group consisting of melanoma, esophageal carcinoma, gastric carcinoma, brain tumor, small cell lung cancer, non-small cell lung cancer, bladder cancer, breast cancer, pancreatic cancer, colon cancer, rectal cancer, colorectal cancer, renal cancer, hepatocellular carcinoma, ovary cancer, prostate cancer, thyroid cancer, testis cancer, head and neck squamous cell
20 carcinoma, leukemia, lymphoma, and myeloma.

34. A nucleic acid or a set of nucleic acids, which encodes or collectively encodes a bi-specific antibody set forth in any one of claims 1-18.

25 35. The nucleic acid or set of nucleic acids of claim 34, which is a vector or a set of vectors.

36. The nucleic acid or set of nucleic acids of claim 35, wherein the vector(s) is an expression vector(s).
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37. A host cell, comprising the nucleic acid or set of nucleic acids set forth in any one of claims 34-36.

38. The host cell of claim 37, wherein the host cell is a bacterial cell, a yeast cell, or a mammalian cell.

39. A method for producing a bi-specific antibody, comprising:
- 5 (i) culturing a host cell of claim 37 or claim 38 under conditions allowing for expressing of the bi-specific antibody; and
- (ii) harvesting the bi-specific antibody.

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