

What is Claimed is: Claims

1. A multispecific antibody comprising:
 - (a) a first binding domain that binds to T Cell Receptor Delta Variable 2 (TRDV2), and
 - (b) a second binding domain that binds to an antigen on the surface of a cancer cell.
2. The multispecific antibody of claim 1, wherein the first binding domain comprises:
 - (i) a VH comprising a VH CDR1, a VH CDR2, and a VH CDR3 having an amino acid sequence of a VH CDR1, a VH CDR2, and a VH CDR3, respectively, of a VH having ~~an~~the amino acid sequence of SEQ ID NO:7; and
 - ~~_____~~(ii) a VL comprising a VL CDR1, a VL CDR2, and a VL CDR3 having an amino acid sequence of a VL CDR1, a VL CDR2, and a VL CDR3, respectively, of a VL having ~~an~~the amino acid sequence of SEQ ID NO:8-
3. ~~The multispecific antibody of claim 2,~~ optionally wherein
 - ~~(i)~~ (i) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the first binding domain are according to the Kabat numbering system; the Chothia numbering system, the AbM numbering system, the Contact numbering system, the IMGT numbering system, or the Exemplary numbering system.
 - ~~(ii)~~ (ii) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the first binding domain are according to the Chothia numbering system;
 - ~~(iii)~~ (iii) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the first binding domain are according to the AbM numbering system;
 - ~~(iv)~~ (iv) the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the first binding domain are according to the Contact numbering system;

- (v) ~~the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the first binding domain are according to the IMGT numbering system; or~~
- (vi) ~~the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the first binding domain are according to the Exemplary numbering system.~~

4.3. The multispecific antibody of claim 1 or 2, wherein the first binding domain comprises:

- (i) a VH comprising a VH CDR1 having ~~an~~the amino acid sequence of SEQ ID NO:1, a VH CDR2 having ~~an~~the amino acid sequence of SEQ ID NO:2, and a VH CDR3 having ~~an~~the amino acid sequence of SEQ ID NO:3; and
- (ii) a VL comprising a VL CDR1 having ~~an~~the amino acid sequence of SEQ ID NO:4, a VL CDR2 having ~~an~~the amino acid sequence of SEQ ID NO:5, and a VL CDR3 having ~~an~~the amino acid sequence of SEQ ID NO:6.

~~5.4.~~ The multispecific antibody of ~~claim 2~~any one of claims 1-3, wherein

- (i) the first binding domain comprises a VH having ~~an~~the amino acid sequence of SEQ ID NO:7;
- (ii) the first binding domain comprises a VL having ~~an~~the amino acid sequence of SEQ ID NO:8; or
- (iii) the first binding domain comprises a VH having ~~an~~the amino acid sequence of SEQ ID NO:7, and a VL having ~~an~~the amino acid sequence of SEQ ID NO:8.

~~6.5.~~ The multispecific antibody of any one of claims 1 to ~~54~~, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2 and VL CDR3 of the first binding domain form a binding site for an antigen of the TRDV2 or an epitope of the TRDV2, optionally wherein TRDV2 is present on the surface of a T cell.

~~7.6.~~ The multispecific antibody of any one of claims 1 to ~~65~~, wherein the ~~TRDV2~~ is present on the surface of a T cell.;

~~8.~~ The multispecific antibody of any one of claims 1 to 7, wherein (A) _____ the cancer cell is a cell of an adrenal cancer, anal cancer, appendix cancer, bile duct cancer, bladder cancer, bone cancer, brain cancer, breast cancer, cervical cancer, colorectal cancer, esophageal cancer, gallbladder cancer, gestational trophoblastic, head and neck cancer, Hodgkin lymphoma, intestinal cancer, kidney cancer, leukemia, liver cancer, lung cancer, melanoma, mesothelioma, multiple myeloma, neuroendocrine tumor, non-Hodgkin lymphoma, oral cancer, ovarian cancer, pancreatic cancer, prostate cancer, sinus cancer, skin cancer, soft tissue sarcoma spinal cancer, stomach cancer, testicular cancer, throat cancer, thyroid cancer, uterine cancer endometrial cancer, vaginal cancer, or vulvar cancer-; and/or

~~9.~~ The multispecific antibody of any one of claims 1 to 8, wherein (B) _____ the antigen on the surface of the cancer cell is angiopoietin, BCMA, CD19, CD20, CD22, CD25 (IL2-R), CD30, CD33, CD37, CD38, CD52, CD56, CD123 (IL-3R), cMET, DLL/Notch, EGFR, EpCAM, FGF, FGF-R, GD2, HER2, Mesothelin, Nectin-4, PAP, PDGFR α , PSA, PSA3, PSMA, RANKL, SLAMF7, STEAP1, TARP, TROP2, VEGF, VEGF-R, CEA, immature laminin receptor, TAG-72, HPV E6, HPV E7, BING-4, calcium-activated chloride channel 2, cyclin-B1, 9D7, EpCAM, EphA3, Her2/neu, telomerase, mesothelin, SAP-1, surviving, a BAGE family antigen, CAGE family antigen, GAGE family antigen, MAGE family antigen, SAGE family antigen, XAGE family antigen, NY-ESO-1/LAGE-1, PRAME, SSX-2, Melan-A, MART-1, Gp100, pmel17, tyrosinase, TRP-1, TRP-2, P. polypeptide, MC1R, prostate-specific antigen, β -catenin, or BRCA1.

~~10.~~ The multispecific antibody of any one of claims 1 to ~~96~~, wherein the antigen on the surface of the cancer cell is CD33-; optionally

~~11.~~ The multispecific antibody of claim 10, wherein the second binding domain that binds to CD33 comprises:

(i) —a VH comprising a VH CDR1, a VH CDR2, and a VH CDR3 having an amino acid sequence of a VH CDR1, a VH CDR2, and a VH

CDR3, respectively, of a VH having ~~an~~the amino acid sequence of SEQ ID NO:15; and

- (ii) —a VL comprising a VL CDR1, a VL CDR2, and a VL CDR3 having an amino acid sequence of a VL CDR1, a VL CDR2, and a VL CDR3, respectively, of a VL having ~~an~~the amino acid sequence of SEQ ID NO:16;

~~12. The multispecific antibody of claim 11;~~ optionally wherein

~~7. (i) —the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the second binding domain are according to the Kabat numbering system;~~ the Chothia numbering system, the AbM numbering system, the Contact numbering system, the IMGT numbering system, or the Exemplary numbering system.

~~(ii) —the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the second binding domain are according to the Chothia numbering system;~~

~~(iii) —the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the second binding domain are according to the AbM numbering system;~~

~~(iv) —the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the second binding domain are according to the Contact numbering system;~~

~~(v) —the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the second binding domain are according to the IMGT numbering system; or~~

~~(vi) —the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2, and VL CDR3 amino acid sequences of the second binding domain are according to the Exemplary numbering system.~~

~~13-8. The multispecific antibody of claim 10~~ any one of claims 1-7, wherein the second binding domain comprises:

- ~~(iv)~~ (i) —a VH comprising a VH CDR1 having ~~an~~the amino acid sequence of SEQ ID NO:9, a VH CDR2 having ~~an~~the amino acid

sequence of SEQ ID NO:10, and a VH CDR3 having ~~an~~the amino acid sequence of SEQ ID NO:11; and

- (ii) a VL comprising a VL CDR1 having ~~an~~the amino acid sequence of SEQ ID NO:12, a VL CDR2 having ~~an~~the amino acid sequence of SEQ ID NO:13, and a VL CDR3 having ~~an~~the amino acid sequence of SEQ ID NO:14.

~~14.~~—The multispecific antibody of ~~claim 13~~any one of claims 1-8, wherein

- ~~(i)~~—the second binding domain comprises a VH having ~~an~~the amino acid sequence of SEQ ID NO:15;

~~9.~~ ~~(ii)~~—the second binding domain comprises, and/or a VL having ~~an~~the amino acid sequence of SEQ ID NO:16; ~~or~~;

- ~~(iii)~~—the second binding domain comprises a VH having ~~an~~ amino acid sequence of SEQ ID NO:15, and a VL having ~~an~~ amino acid sequence of SEQ ID NO:16.

~~15.~~—The multispecific antibody of ~~any one of claims 10 to 14~~, wherein the VH CDR1, VH CDR2, VH CDR3, VL CDR1, VL CDR2 and VL CDR3 of the second binding domain form a binding site for an antigen of the CD33 or an epitope of the CD33.

~~16.~~—The multispecific antibody of ~~any one of claims 1 to 15~~, wherein

- ~~(i)~~—the first binding domain is multivalent, the second binding domain is multivalent, or wherein both the first binding domain and the second binding domain are multivalent;
- ~~(ii)~~—the first binding domain is capable of binding at least three antigens, or wherein the second binding domain is capable of binding at least three antigens;
- ~~(iii)~~—the first binding domain is capable of binding at least four antigens, or wherein the second binding domain is capable of binding at least four antigens; or
- ~~(iv)~~—the first binding domain is capable of binding at least five antigens, or wherein the second binding domain is capable of binding at least five antigens.

10. ~~17.~~ The multispecific antibody of any one of claims 1 to ~~16~~9, wherein

~~17.~~(i) the multispecific antibody is a bispecific antibody, a trispecific antibody, or a quadraspecific antibody.

~~18.~~ ~~The multispecific antibody of any one of claims 1 to 17, wherein (ii)~~ the antibody

~~(i)~~ is a humanized antibody,

~~(ii)~~ ~~(iii)~~ the antibody is an IgG antibody, optionally wherein the IgG antibody is an IgG1, IgG2, IgG3, or IgG4 antibody,

~~(iii)~~ ~~(iv)~~ the antibody comprises a kappa light chain or a lambda light chain, or

~~(iv)~~ ~~(v)~~ the antibody is a monoclonal antibody.

~~19.~~ ~~A multispecific antibody comprising: a first means capable of binding TRDV2 on the surface of a $\gamma\delta$ T cell; and a second means capable of binding a cancer antigen.~~

~~20.~~11. A nucleic acid encoding the multispecific antibody of any one of claims 1 to ~~19~~10.

~~21.~~12. A vector comprising the nucleic acid of claim ~~20~~11.

~~22.~~13. A host cell comprising the vector of claim ~~21~~12.

~~23.~~14. A kit comprising the vector of claim ~~13~~12 and packaging for the same.

~~24.~~15. A pharmaceutical composition comprising the multispecific antibody of any one of claims 1 to ~~19~~10, and a pharmaceutically acceptable carrier.

~~25.~~ A process for making an antibody that binds to more than one target molecule, ~~the molecule comprising: a step for performing a function of obtaining a~~

binding domain capable of binding to TRDV2 antigen on a $\gamma\delta$ T cell; ~~a step for performing a function of obtaining a binding domain capable of binding to an antigen on the surface of a cancer cell; and a step for performing a function of providing an antibody capable of binding to a TRDV2 antigen on a $\gamma\delta$ T cell and an antigen on the surface of a cancer cell.~~

~~26.16. The process of claim 25;~~ optionally wherein the step for performing a function of obtaining a binding domain capable of binding to an antigen on the surface of a cancer cell is repeated n times and further comprising comprises n steps for performing a function of providing a binding domain capable of binding to a TRDV2 antigen on a $\gamma\delta$ T cell and n number of target molecules, wherein n is at least 2.

~~A method of~~

~~27.17. The multispecific antibody of any one of claims 1 to 10 for use in directing a $\gamma\delta$ T cell expressing TRDV2 to a cancer cell, the method comprising contacting the $\gamma\delta$ T cell with the multispecific antibody of any one of claims 1 to 19, wherein the contacting directs the $\gamma\delta$ T cell to the cancer cell.~~

~~A method of~~

~~28. The multispecific antibody of any one of claims 1 to 10 for use in inhibiting growth or proliferation of a cancer cell expressing a cancer antigen on the cell surface, the method comprising contacting the cancer cells with the multispecific antibody of any one of claims 1 to 19, wherein contacting the cancer cells with the pharmaceutical composition inhibits growth or proliferation of the cancer cells.~~

~~29.18. The method of claim 28, wherein the cancer cells are;~~ optionally wherein the cancer cell is in the presence of a $\gamma\delta$ T cell expressing TRDV2 while in contact with the multispecific antibody.

~~A method for~~

~~19. The multispecific antibody of any one of claims 1 to 10 for use in eliminating a cancer cell in a subject or treating cancer in a subject.~~

~~30. The, comprising administering an effective amount of the multispecific antibody of any one of claims 1 to 19 to the subject.~~

- ~~31. A method for treating cancer in a subject, comprising administering an effective amount of the multispecific antibody of any one of claims 1 to 19 to the subject.~~
- ~~32. The method of claim 30 or 31, wherein the subject is a subject in need thereof.~~
- ~~33. A method of 10 for use in activating a $\gamma\delta$ T cell expressing TRDV2, comprising contacting the $\gamma\delta$ T cell with the multispecific antibody of any one of claims 1 to 19.~~

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