CLAIMS

What is claimed is:

1. An antibody that specifically binds to human T-cell immunoreceptor with Ig and ITIM domains (TIGIT), wherein the antibody comprises the following six hypervariable regions (HVRs):

an HVR-H1 comprising the amino acid sequence of SYPMN (SEQ ID NO: 17);

an HVR-H2 comprising the amino acid sequence of WINTNTGNPTYVQGFTG (SEQ ID NO: 18);

an HVR-H3 comprising the amino acid sequence of TGGHTYDSYAFDV (SEQ ID NO: 19);

an HVR-L1 comprising the amino acid sequence of RASQVISSSLA (SEQ ID NO: 20);

an HVR-L2 comprising the amino acid sequence of AASTLQS (SEQ ID NO: 21); and

an HVR-L3 comprising the amino acid sequence of QHLHGYPX_1N (SEQ ID NO: 22), wherein X_1 is C or S.

2. The antibody of claim 1, wherein antibody comprises the following six HVRs:

an HVR-H1 comprising the amino acid sequence of SYPMN (SEQ ID NO: 17);

an HVR-H2 comprising the amino acid sequence of WINTNTGNPTYVQGFTG (SEQ ID NO: 18);

an HVR-H3 comprising the amino acid sequence of TGGHTYDSYAFDV (SEQ ID NO: 19);

an HVR-L1 comprising the amino acid sequence of RASQVISSSLA (SEQ ID NO: 20);

an HVR-L2 comprising the amino acid sequence of AASTLQS (SEQ ID NO: 21); and

an HVR-L3 comprising the amino acid sequence of QHLHGYPSN (SEQ ID NO: 23).

3. The antibody of any one of claim 1 or 2, wherein the antibody further comprises the following heavy chain variable region framework regions (FRs):

an FR-H1 comprising the amino acid sequence of EVQLVQSGSDLKKPGASVRVSCKASGYTFT (SEQ ID NO: 24);

an FR-H2 comprising the amino acid sequence of WVRQAPGHGLEWMG (SEQ ID NO: 25);

an FR-H3 comprising the amino acid sequence of RFVFSLDTSVNTAYLQISSLKAEDTAVYFCAR (SEQ ID NO: 26); and

an FR-H4 comprising the amino acid sequence of WGQGTMVTVSS (SEQ ID NO: 27).

4. The antibody of claim 1, wherein antibody comprises the following six HVRs:

an HVR-H1 comprising the amino acid sequence of SYPMN (SEQ ID NO: 17);

an HVR-H2 comprising the amino acid sequence of WINTNTGNPTYVQGFTG (SEQ ID NO: 18);

an HVR-H3 comprising the amino acid sequence of TGGHTYDSYAFDV (SEQ ID NO: 19);

an HVR-L1 comprising the amino acid sequence of RASQVISSSLA (SEQ ID NO: 20);

an HVR-L2 comprising the amino acid sequence of AASTLQS (SEQ ID NO: 21); and

an HVR-L3 comprising the amino acid sequence of QHLHGYPCN (SEQ ID NO: 28).

5. The antibody of claim 4, wherein the antibody further comprises the following heavy chain variable region FRs:

an FR-H1 comprising the amino acid sequence of QVQLVQSGSDLKKPGASVRVSCKASGYTFT (SEQ ID NO: 29);

an FR-H2 comprising the amino acid sequence of WVRQAPGHGLEWMG (SEQ ID NO: 25);

an FR-H3 comprising the amino acid sequence of RFVFSLDTSVNTAYLQISSLKAEDTAVYFCAR (SEQ ID NO: 26); and

an FR-H4 comprising the amino acid sequence of WGQGTMVTVSS (SEQ ID NO: 27).

6. The antibody of any one of claims 1-5, wherein the antibody further comprises the following light chain variable region FRs:

an FR-L1 comprising the amino acid sequence of DIQLTQSPTFLSASVGDRVTITC (SEQ ID NO: 30);

an FR-L2 comprising the amino acid sequence of WYQQNPGKAPKLLIY (SEQ ID NO: 31);

an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTEFTLTISSLQPEDFVTYYC (SEQ ID NO: 32); and

an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 33).

7. The antibody of any one of claims 1-6, wherein the antibody comprises (a) a heavy chain variable region (VH) having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 37 and (b) a light chain variable region (VL) having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 38.

8. An antibody that specifically binds to human TIGIT, wherein the antibody comprises (a) a VH having the amino acid sequence of SEQ ID NO: 37 and (b) a VL having the amino acid sequence of SEQ ID NO: 38.

9. The antibody of any one of claims 1-8, wherein the antibody is capable of binding to both human TIGIT and cynomolgus monkey (cyno) TIGIT, wherein optionally the antibody binds human TIGIT with a Kd of about 10 nM or lower and cyno TIGIT with a Kd of about 10 nM or lower.

10. The antibody of any one of claims 1-9, wherein the antibody is an antagonist antibody; wherein optionally the antagonist antibody specifically binds TIGIT and inhibits or blocks TIGIT interaction with poliovirus receptor (PVR); and wherein optionally the antagonist antibody inhibits intracellular signaling mediated by TIGIT binding to PVR.

11. The antibody of claim 10, wherein (i) the antagonist antibody inhibits or blocks binding of human TIGIT to human PVR with an IC50 value of 10 nM or lower; wherein optionally (ii) the antagonist antibody inhibits or blocks binding of human TIGIT to human PVR with an IC50 value of 1 nM to about 10 nM; and wherein optionally (iii) the antagonist antibody inhibits or blocks binding of cyno TIGIT to cyno PVR with an IC50 value of 50 nM or lower.

12. The antibody of claim 11, wherein the antagonist antibody inhibits or blocks binding of cyno TIGIT to cyno PVR with an IC50 value of 1 nM to about 50 nM; wherein optionally the antagonist antibody inhibits or blocks binding of cyno TIGIT to cyno PVR with an IC50 value of 1 nM to about 5 nM.

13. The antibody of any one of claims 1-12, wherein the antibody is monoclonal.

14. The antibody of any one of claims 1-12, wherein the antibody is human, humanized, or chimeric; wherein optionally at least a portion of the framework sequence is a human consensus framework sequence.

15. The antibody of any one of claims 1-14, wherein the antibody is a full-length antibody.

16. The antibody of any one of claims 1-15, wherein the antibody has a clearance following intravenous injection of about 3 ml/kg/day to about 10 ml/kg/day.

17. The antibody of any one of claims 1-14, wherein the antibody is an antibody fragment that binds TIGIT; wherein optionally the antibody fragment is selected from the group consisting of Fab, Fab', Fab'-SH, Fv, single chain variable fragment (scFv), and $(Fab')_2$ fragments.

18. The antibody of any one of claims 1-16, wherein the antibody is an IgG class antibody; wherein optionally the IgG class antibody is an IgG1 subclass antibody.

19. The antibody of any one of claims 1-18, wherein the antibody exhibits effector function.

20. A polynucleotide encoding the antibody of any one of claims 1-19.

21. A vector comprising the polynucleotide of claim 20.

22. A host cell comprising the vector of claim 21.

23. The host cell of claim 22, wherein the host cell is: (a) prokaryotic, wherein optionally the host cell is *Escherichia coli*; or (b) eukaryotic, wherein optionally the host cell is a 293 cell, a CHO cell, a yeast cell, or a plant cell.

24. A method of producing the antibody of any one of claims 1-19, the method comprising culturing the host cell of claim 22 or 23 in a culture medium.

25. The method of claim 24, wherein the method further comprises recovering the antibody from the host cell or culture medium.

26. A composition comprising the antibody of any one of claims 1-19.

27. The composition of claim 26, further comprising a pharmaceutically acceptable carrier, excipient, or diluent; wherein optionally the composition is a pharmaceutical composition.

28. The composition of claim 26 or 27, wherein the composition further comprises a PD-1 axis binding antagonist or an additional therapeutic agent.

29. The antibody of any one of claims 1-19 for use as a medicament.

30. The antibody of any one of claims 1-19 for use in treating or delaying progression of a cancer in a subject in need thereof.

31. The antibody for use of claim 30, wherein the cancer is selected from the group consisting of a non-small cell lung cancer, a small cell lung cancer, a renal cell cancer, a colorectal cancer, an ovarian cancer, a breast cancer, a pancreatic cancer, a gastric carcinoma, a bladder cancer, an esophageal cancer, a mesothelioma, a melanoma, a head and neck cancer, a thyroid cancer, a sarcoma, a prostate cancer, a glioblastoma, a cervical cancer, a thymic carcinoma, a leukemia, a lymphoma, a myeloma, mycosis fungoides, a Merkel cell cancer, and a hematologic malignancy; wherein optionally the myeloma is multiple myeloma (MM).

32. Use of the antibody of any one of claims 1-19 in the manufacture of a medicament for treating or delaying progression of a cancer.

33. The use of claim 32, wherein the cancer is selected from the group consisting of a non-small cell lung cancer, a small cell lung cancer, a renal cell cancer, a colorectal cancer, an ovarian cancer, a breast cancer, a pancreatic cancer, a gastric carcinoma, a bladder cancer, an esophageal cancer, a mesothelioma, a melanoma, a head and neck cancer, a thyroid cancer, a sarcoma, a prostate cancer, a glioblastoma, a cervical cancer, a thymic carcinoma, a leukemia, a lymphoma, a myeloma, mycosis fungoides, a Merkel cell cancer, and a hematologic malignancy; wherein optionally the myeloma is MM.

34. The use of claim 32 or 33, wherein the medicament is to be administered with a PD-1 axis binding antagonist; wherein optionally the PD-1 axis binding antagonist is to be administered prior to or subsequent to the administration of the antibody, or concurrently with the antibody.

35. The use of claim 34, wherein the PD-1 axis binding antagonist is a PD-L1 binding antagonist; wherein optionally the PD-L1 binding antagonist is an anti-PD-L1 antibody.

36. The use of claim 35, wherein the anti-PD-L1 antibody is atezolizumab.

37. The use of any one of claims 32-36, wherein the medicament is to be administered with an additional therapeutic agent; wherein optionally the additional therapeutic agent is a chemotherapeutic agent.

38. The use of any one of claims 32-37, wherein the antibody is to be administered subcutaneously or intravenously.

39. A kit comprising the antibody of any one of claims 1-19 and a package insert comprising instructions for using the antibody for treating or delaying progression of a cancer in a subject.