CLAIMS

We claim:

1. An anti-TIGIT antibody that binds to a TIGIT polypeptide on one or more amino acid residues comprising D51, wherein the TIGIT polypeptide has an amino acid sequence corresponding to SEQ ID NO:1.

2. The anti-TIGIT antibody of claim 1, wherein the antibody is a monoclonal antibody.

3. The anti-TIGIT antibody of claim 1 or claim 2, wherein the antibody is chimeric, humanized, or veneered.

4. The anti-TIGIT antibody of claim 1, wherein the antibody is a human antibody.

5. The anti-TIGIT antibody of any one of claims 1-4, wherein the antibody does not bind to one or more amino acid residues comprising L44, I47, or H55.

6. The anti-TIGIT antibody of any one of claims 1-5, wherein the antibody comprises a mature light chain variable region of SEQ ID NO:14 and mature heavy chain variable region of SEQ ID NO:10.

7. The recombinant anti-TIGIT antibody of any one of claims 1-6, wherein the antibody binds to the same epitope as TIG1 on the amino acid sequence corresponding to SEQ ID NO:1.

8. The anti-TIGIT antibody of any one of claims 1-7, comprising three light chain CDRs comprising SEQ ID NOs: 15-17 and three heavy chain CDRs comprising SEQ ID NOs: 11-13.

9. The anti-TIGIT antibody of any one of claims 1-7, comprising a mature heavy chain variable region with at least 90% sequence identity to SEQ ID NO:35 and a mature light chain variable region with at least 90% sequence identity to SEQ ID NO:37.

10. The anti-TIGIT antibody of claim 9, wherein the mature heavy chain variable region comprises the amino acid sequence of SEQ ID NO:35 and the mature light chain variable region comprises the amino acid sequence of SEQ ID NO:37.

11. The antibody of claim 9 or claim 10, wherein the mature heavy chain variable region

is linked to a heavy chain constant region comprising SEQ ID NO:40 provided that the C-terminal lysine may or may not be present, and the mature light chain variable region is linked to the light chain constant region comprising SEQ ID NO:41.

12. A monoclonal antibody that competes with any of TIG1, TIG2 or TIG3 for binding to human TIGIT, wherein antibody TIG1 is characterized by a mature light chain variable region of SEQ ID NO:14 and mature heavy chain variable region of SEQ ID NO:10, antibody TIG2 is characterized by a mature light chain variable region of SEQ ID NO:22 and a mature heavy chain variable region of SEQ ID NO:18, and antibody TIG3 is characterized by a mature light chain variable region of SEQ ID NO:30 and a mature heavy chain variable region of SEQ ID NO:26, for specific binding to CD155.

13. The monoclonal antibody of claim 12 that binds to the same epitope on human TIGIT as any of TIG1, TIG2 or TIG3.

14. The antibody of any one of claims 1-13 that inhibits binding of CD155 to human TIGIT.

15. The monoclonal antibody of claim 12 comprising three light chain CDRs and three heavy chain CDRs corresponding to three light chain and three heavy chain CDRs of any one of TIG1, TIG2 or TIG3.

16. The monoclonal antibody of claim 12 comprising three heavy chain CDRs and three light chain CDRs of any one of TIG1, TIG2 or TIG3.

17. The monoclonal antibody of claim 12 comprising three heavy chain CDRs as defined by Kabat and three light chain CDRs as defined by Kabat of any one of TIG1 (SEQ ID NOs: 15-17 light chain and 11-13 heavy chain), TIG2 (SEQ ID NOs. 23-25 light chain, 19-21 heavy chain) or TIG3 (SEQ ID NOs: 31-33 light chain and 27-29 heavy chain).

18. The monoclonal antibody of any one of claims 12-17 that is chimeric, humanized, or veneered.

19. The monoclonal antibody of claim 12 that is a human antibody.

20. The monoclonal antibody of any one of claims 12-19 that has human IgG1 kappa isotype.

21. The monoclonal antibody of any one of claims 12-20 that is an intact antibody.

22. The monoclonal antibody of any of claims 12-20 that is a single-chain antibody, Fab or $F(ab')_2$ fragment.

23. The monoclonal antibody of any of claim 12-21 comprising a mature heavy chain variable region with at least 90% sequence identity to SEQ ID NO:35 and a mature light chain variable region with at least 90% sequence identity to SEQ ID NO:37.

24. The monoclonal antibody of claim 23, wherein the mature heavy chain variable region has at least 95% sequence identity to SEQ ID NO:35 and the mature light chain variable region has at least 95% sequence identity to SEQ ID NO:37.

25. The monoclonal antibody of claim 24, wherein the mature heavy chain variable region has the amino acid sequence of SEQ ID NO:35 and the mature light chain variable region has the amino acid sequence of SEQ ID NO:37.

26. The monoclonal antibody of claim 25, wherein the mature heavy chain variable region is linked to a heavy chain constant region comprising SEQ ID NO:40 provided that the C-terminal lysine may or may not be present, and the mature light chain variable region is linked to a light chain constant region comprising SEQ ID NO:41.

27. The monoclonal antibody of claim 25, wherein the mature heavy chain variable region is linked to a heavy chain constant region comprising SEQ ID NO:60 provided that the C-terminal lysine may or may not be present, and the mature light chain variable region is linked to a light chain constant region comprising SEQ ID NO:64.

28. The monoclonal antibody of claim 25, wherein the mature heavy chain variable region is linked to a heavy chain constant region comprising SEQ ID NO:61 provided that the C-terminal lysine may or may not be present, and the mature light chain variable region is linked to a light chain constant region comprising SEQ ID NO:64.

29. The monoclonal antibody of any of claim 12-21 comprising a mature heavy chain variable region with at least 90% sequence identity to SEQ ID NO:43 and a mature light chain variable region with at least 90% sequence identity to SEQ ID NO:45.

30. The monoclonal antibody of claim 29, wherein the mature heavy chain variable

region has at least 95% sequence identity to SEQ ID NO:43 and the mature light chain variable region has at least 95% sequence identity to SEQ ID NO:45.

31. The monoclonal antibody of claim 30, wherein the mature heavy chain variable region has the amino acid sequence of SEQ ID NO:43 and the mature light chain variable region has the amino acid sequence of SEQ ID NO:45.

32. The monoclonal antibody of claim 31, wherein the mature heavy chain variable region is linked to a heavy chain constant region comprising SEQ ID NO:48 provided that the C-terminal lysine may or may not be present, and the mature light chain variable region is linked to a light chain constant region comprising SEQ ID NO:49.

33. The monoclonal antibody of claim 31, wherein the mature heavy chain variable region is linked to a heavy chain constant region comprising SEQ ID NO:62 provided that the C-terminal lysine may or may not be present, and the mature light chain variable region is linked to a light chain constant region comprising SEQ ID NO:65.

34. The monoclonal antibody of claim 31, wherein the mature heavy chain variable region is linked to a heavy chain constant region comprising SEQ ID NO:63 provided that the C-terminal lysine may or may not be present, and the mature light chain variable region is linked to a light chain constant region comprising SEQ ID NO:65.

35. A monoclonal antibody that binds to an epitope comprising residues 35 and 37 of SEQ ID NO:1 and/or residues 49 and 51 of SEQ ID NO:1.

36. The monoclonal antibody of claim 35 that binds to an epitope comprising residues 35, 37, 49 and 51 of SEQ ID NO:1.

37. The monoclonal antibody of claim 35 that binds to a peptide consisting of residues 35-51 of SEQ ID NO:1 and no more than five flanking amino acids from SEQ ID NO:1 on either side.

38. The monoclonal antibody of claim 37 that binds to a peptide consisting of residues 35-51 of SEQ ID NO:1.

39. The monoclonal antibody of claim 35, wherein the epitope consists of 3 to 20 contiguous residues of SEQ ID NO:1.

40. The monoclonal antibody of any preceding claim that has one or more of the following properties: (a) inhibiting binding of TIGIT to CD155, optionally with an IC_{50} of 15-100 ng/ml, (b) increases intrinsic T-cell activation in the presence of antigen presenting cells expressing CD155 as measured by IL-2 production, optionally 1.5-3 fold, (c) increases antigen-specific T-cell activation as measured by IL-12 production, optionally 1.5-3 fold, (d) increases natural killer cell activation as measured by production of any of IL-2, IL-6, TNFα or IFNγ, optionally by 1.5-3 fold, (e) increases T-cell production of at least one pro-inflammatory cytokine, optionally by 1.5-3 fold, and (f) reduces T-cell production of a least one anti-inflammatory cytokine, optionally by 1.5-3 fold.

41. A pharmaceutical composition comprising an antibody as defined in any preceding claim and pharmaceutically acceptable carrier.

42. A method of treating or effecting prophylaxis of cancer comprising administering to a subject having or at risk of cancer an effective regime or a therapeutically effective amount of an antibody of any preceding claim.

43. The method of claim 42, wherein the cancer is acute myeloid leukemia or adult T-cell leukemia.

44. The method of claim 42 or claim 43, wherein the subject is administered tumor infiltrating T-cells which are activated by the antibody.

45. The method of any one of claims 42-44, wherein the subject is administered a vaccine inducing an immune response against the cancer, which is enhanced by the antibody.

46. The method of claim 45, wherein the vaccine comprises an antigen or a fragment thereof expressed on the surface of cancer cells.

47. The method of any one of claims 42-46, wherein the subject is administered natural killer cells whose cytotoxicity against the cancer is enhanced by the antibody.

48. The method of any one of claims 42-47, wherein the subject is further administered a second antibody against an antigen expressed on the surface of cells of cancer, whereby an effector mediated cytotoxicity of the second antibody against the cancer is enhanced by the antibody.

49. The method of any one of claims 42-47, wherein the subject is further administered a second antibody against an antigen expressed on the surface of an immune cell.

50. The method of claim 49, wherein the immune cell is a T-cell or a natural killer cell.

51. The method of claim 49 or claim 50, wherein the antigen is CTLA-4, PD-1 or PD-L1.

52. The method of any one of claims 42-51, wherein the subject is further administered one or more therapies selected from the group consisting of chemotherapy, radiation, cell-based therapy, and surgery.

53. The method of any one of claims 42-52, wherein the subject is further administered an inhibitor of one or more immune-checkpoint receptors or ligands.

54. The method of claim 53, wherein the inhibitor is selected from the group consisting of ipilimumab, nivolumab, pembrolizumab (lambrolizumab) and atezolizumab.

55. A method of treating a subject infected with a pathogen comprising administering to the subject an effective regime or a therapeutically effective amount of an antibody of any preceding claim.

56. The method of claim 55, wherein the pathogen is a virus, bacteria, fungi, or protozoan.

57. The method of claim 56, wherein the pathogen is HIV, SIV, hepatitis, herpes virus, adenovirus, influenza virus, flavivirus, echovirus, rhinovirus, coxsackie virus, cornovirus, respiratory syncytial virus, mumps virus, rotavirus, measles virus, rubella virus, parvovirus, vaccinia virus, HTLV virus, dengue virus, papillomavirus, molluscum virus, poliovirus, rabies virus, JC virus, arboviral encephalitis virus, chlamydia, rickettsial bacteria, mycobacteria, staphylococci, treptocci, pneumonococci, meningococci, conococci, klebsiella, proteus, serratia, pseudomonas, legionella, diphtheria, salmonella, bacilli, cholera, tetanus, botulism, anthrax, plague, leptospirosis, and Lyme disease bacteria.

58. The method of any one of claims 55-57, wherein the subject is treated with a vaccine inducing an immune response against the pathogen which is enhanced by the antibody.

59. The method of claim 58, wherein the vaccine comprises a protein of the pathogen or fragment thereof.

60. The method of any one of claims 55-59, wherein the subject is further administered a second antibody against the pathogen, wherein an effector mediated cytotoxicity of the second antibody against the pathogen is enhanced by the antibody.

61. The method of any one of claims 55-60, wherein the subject is further administered one or more of an antiviral agent, an antiparasitic agent, an antibacterial agent, or an antifungal agent.

62. A method of aiding in the treatment of cancer comprising administering to a subject having cancer a therapeutically effective amount of an antibody of any preceding claim.

63. The method of claim 62, wherein the cancer is acute myeloid leukemia or adult T-cell leukemia.

64. The method of claim 62 or claim 63, wherein the subject is administered tumor infiltrating T-cells which are activated by the antibody.

65. The method of any one of claims 62-64, wherein the subject is administered a vaccine inducing an immune response against the cancer, which is enhanced by the antibody.

66. The method of claim 65, wherein the vaccine comprises an antigen expressed on the surface of cancer cells or a fragment thereof.

67. The method of any one of claims 62-66, wherein the subject is administered natural killer cells whose cytotoxicity against the cancer is enhanced by the antibody.

68. The method of any one of claims 62-67, wherein the subject is administered a second antibody against an antigen expressed on the surface of cells of cancer, whereby an effector mediated cytotoxicity of the second antibody against the cancer is enhanced by the antibody.

69. The method of any one of claims 62-67, wherein the subject is further administered a second antibody against an antigen expressed on the surface of an immune cell.

70. The method of claim 69, wherein the immune cell is a T-cell or a natural killer cell.

71. The method of claim 69 or claim 70, wherein the antigen is CTLA-4, PD-1or PD-L1.

72. The method of any one of claims 62-71, wherein the subject is further administered one or more therapies selected from the group consisting of chemotherapy, radiation, cell-

based therapy, and surgery.

73. The method of any one of claims 62-72, wherein the subject is further administered an inhibitor of one or more immune-checkpoint receptors or ligands.

74. The method of claim 73, wherein the one or more immune-checkpoint receptors or ligands are selected from the group consisting of CTLA-4, PD-1, PD-L1, TIM-3, LAG-3, BTLA, VISTA, CD96, A2aR, A2bR, Arginase, CD39, CD73, IDO and TDO.

75. The method of claim 74, wherein the inhibitor is selected from the group consisting of ipilimumab, nivolumab, pembrolizumab (lambrolizumab) and atezolizumab.