

WHAT IS CLAIMED IS:

1. An isolated anti-LILRB4 antibody or an antigen-binding fragment thereof, comprising:
 - a) a heavy chain variable region comprising a heavy chain complementarity determining region (HC-CDR) 1 having an amino acid sequence of SEQ ID NO: 5, an HC-CDR2 having an amino acid sequence of SEQ ID NO: 6 and an HC-CDR3 having an amino acid sequence of SEQ ID NO: 7; and
 - b) a light chain variable region comprising a light chain complementarity determining region (LC-CDR) 1 having an amino acid sequence of SEQ ID NO: 8 with a mutation at amino acid residues NS, an LC-CDR2 having an amino acid sequence of SEQ ID NO: 9 and an LC-CDR3 having an amino acid sequence of SEQ ID NO: 10.
2. The antibody or antigen-binding fragment thereof of claim 1, wherein the LC-CDR1 having an amino acid sequence of SEQ ID NO: 28.
3. The antibody or antigen-binding fragment thereof of claim 1, wherein the heavy chain variable region has an amino acid sequence of SEQ ID NO: 1 or at least about 90% identical to SEQ ID NO: 1; and wherein the light chain variable region has an amino acid sequence of SEQ ID NO: 27 or at least about 90% identical to SEQ ID NO: 27.
- ~~4. The antibody or antigen-binding fragment thereof of claim 1, wherein the heavy chain variable region has an amino acid sequence of SEQ ID NO: 1; and wherein the light chain variable region has an amino acid sequence of SEQ ID NO: 27.~~
- ~~5.4.~~ The antibody or antigen-binding fragment thereof of any of the preceding claims, further comprising an immunoglobulin constant region, optionally a constant region of Ig, or optionally a constant region of human IgG.
- ~~6.5.~~ The antibody or antigen-binding fragment thereof of any of the preceding claims, which is humanized.
- ~~7.6.~~ The antibody or antigen-binding fragment thereof of any of the preceding claims, which is a camelized single domain antibody, a diabody, a scFv, a scFv dimer, a BsFv, a dsFv, a (dsFv)₂, a dsFv-dsFv', an Fv fragment, a Fab, a Fab', a F(ab')₂, a bispecific antibody, a ds diabody, a nanobody, a domain antibody, or a bivalent antibody; optionally the bispecific

antibody is an antibody against LILRB4 and CD3.

~~8. The antibody or antigen-binding fragment thereof of claim 7, which is a bispecific antibody against LILRB4 and CD3.~~

9.7. The antibody or antigen-binding fragment thereof of any of the preceding claims linked to one or more conjugate moieties; optionally the conjugate moiety comprises a clearance-modifying agent, a toxin, a detectable label, a chemotherapeutic agent, a cytokine, or purification moiety.

~~10. The antibody or antigen-binding fragment thereof of claim 9, wherein the conjugate moiety comprises a clearance-modifying agent, a toxin, a detectable label, a chemotherapeutic agent, a cytokine, or purification moiety.~~

11.8. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any of the preceding claims, and a pharmaceutically acceptable carrier.

12.9. An isolated polynucleotide encoding the antibody or antigen-binding fragment thereof of claims 1-~~7~~10.

13.10. A vector comprising the isolated polynucleotide of claim ~~9~~12.

14.11. A host cell comprising the vector of claim ~~10~~13.

15.12. A method of expressing the antibody or antigen-binding fragment thereof of any one of claims 1-~~7~~10, comprising culturing the host cell of claim ~~11~~14 under the condition at which the vector of claim ~~10~~13 is expressed.

~~16.13. A method of treating or ameliorating the effect of a cancer in a subject, comprising administering to the subject Use of a therapeutically effective amount of an~~ antibody or antigen-binding fragment thereof of any one of claims 1-~~7~~10 or the pharmaceutical composition of claim ~~8~~11 in the manufacture of a medication for treating or ameliorating the effect of a cancer in a subject, wherein the subject is human.

~~17.14.~~ The ~~usemethod~~ of claim ~~1316~~, wherein the cancer is selected from the group consisting of adrenal cancer, bone cancer, brain cancer, breast cancer, colorectal cancer, esophageal cancer, eye cancer, gastric cancer, head and neck cancer, kidney cancer, liver cancer, lung cancer, non-small cell lung cancer, bronchioloalveolar cell lung cancer, mesothelioma, head and neck cancer, squamous cell carcinoma, melanoma, oral cancer, ovarian cancer, cervical cancer, penile cancer, prostate cancer, pancreatic cancer, skin cancer, sarcoma, testicular cancer, thyroid cancer, uterine cancer, vaginal cancer, lymphoma, lymphocytic leukemia, Hodgkin's Disease, acute myeloid leukemia (AML), acute lymphocytic/lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia (CML), myelodysplastic syndrome (MDS), myeloproliferative neoplasms, and/or chronic myelomonocytic leukemia (CMML).

~~18.15.~~ The ~~usemethod~~ of claim ~~1316~~, wherein the cancer has an immunosuppressive microenvironment, and wherein the antibody or antigen-binding fragment thereof kills at least one myeloid-derived suppressor cell (MDSC).

~~19. The method of claim 16, wherein the cancer is selected from the group consisting of lymphoma, lymphocytic leukemia, Hodgkin's Disease, acute myeloid leukemia (AML), acute lymphocytic/lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia (CML), myelodysplastic syndrome (MDS), myeloproliferative neoplasms, and chronic myelomonocytic leukemia (CMML).~~

~~20. The method of any of claims 16-19, wherein the subject is human.~~

~~21.16.~~ The ~~usemethod~~ of any one of claims ~~13-1516-20~~, wherein the antibody or an antigen-binding fragment thereof is to be administered intravenously, intra-arterially, intra-tumorally, or subcutaneously.

~~22.17.~~ The ~~usemethod~~ of any one of claims ~~13-1616-21~~, further comprising to be administeredadministering to the subject one or more drugs selected from the group consisting of a topoisomerase inhibitor, an anthracycline topoisomerase inhibitor, an anthracycline, a daunorubicin, a nucleoside metabolic inhibitor, a cytarabine, a hypomethylating agent, a low dose cytarabine (LDAC), a combination of daunorubicin and cytarabine, a daunorubicin and cytarabine liposome for injection, Vyxeos®, an

azacytidine, Vidaza®, a decitabine, an all-trans-retinoic acid (ATRA), an arsenic, an arsenic trioxide, a histamine dihydrochloride, Ceplene®, an interleukin-2, an aldesleukin, Proleukin®, a gemtuzumab ozogamicin, Mylotarg®, an FLT-3 inhibitor, a midostaurin, Rydapt®, a clofarabine, a farnesyl transferase inhibitor, a decitabine, an IDH1 inhibitor, an ivosidenib, Tibsovo®, an IDH2 inhibitor, an enasidenib, Idhifa®, a smoothened (SMO) inhibitor, a glasdegib, an arginase inhibitor, an IDO inhibitor, an epacadostat, a BCL-2 inhibitor, a venetoclax, Venclexta®, a platinum complex derivative, oxaliplatin, a kinase inhibitor, a tyrosine kinase inhibitor, a PI3 kinase inhibitor, a BTK inhibitor, an ibrutinib, IMBRUVICA®, an acalabrutinib, CALQUENCE®, a zanubrutinib, a PD-1 antibody, a PD-L1 antibody, a CTLA-4 antibody, a LAG3 antibody, an ICOS antibody, a TIGIT antibody, a TIM3 antibody, a CD40 antibody, a 4-1BB antibody, a CD47 antibody, a SIRP1 α antibody or fusions protein, an antagonist of E-selectin, an antibody binding to a tumor antigen, an antibody binding to a T-cell surface marker, an antibody binding to a myeloid cell or NK cell surface marker, an alkylating agent, a nitrosourea agent, an antimetabolite, an antitumor antibiotic, an alkaloid derived from a plant, a hormone therapy medicine, a hormone antagonist, an aromatase inhibitor, and/or a P-glycoprotein inhibitor.

~~23.18. A method for treating or ameliorating an autoimmune or inflammatory disease in a subject, comprising administering to the subject Use of~~ a therapeutically effective amount of ~~an~~the antibody or antigen-binding fragment thereof of any ~~one~~ of claims 1-740 or the pharmaceutical composition of claim ~~844 in the manufacture of a medicament for treating or ameliorating an autoimmune or inflammatory disease in a subject.~~

~~24.19. The use~~method of claim ~~1823~~, wherein the autoimmune or inflammatory disease is selected from the group consisting of Acquired Immunodeficiency Syndrome (AIDS), alopecia areata, ankylosing spondylitis, antiphospholipid syndrome, autoimmune Addison's disease, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune inner ear disease (AIED), autoimmune lymphoproliferative syndrome (ALPS), autoimmune thrombocytopenic purpura (ATP), Behcet's disease, cardiomyopathy, celiac sprue-dermatitis hepeticiformis, chronic fatigue immune dysfunction syndrome (CFIDS), chronic inflammatory demyelinating polyneuropathy (CIPD), cicatricial pemphigoid, cold agglutinin disease, crest syndrome, Crohn's disease, Degos' disease, dermatomyositis-juvenile, discoid lupus, essential mixed cryoglobulinemia,

fibromyalgia-fibromyositis, Graves' disease, Guillain-Barre syndrome, Hashimoto's thyroiditis, idiopathic pulmonary fibrosis, idiopathic thrombocytopenia purpura (ITP), IgA nephropathy, insulin-dependent diabetes mellitus, juvenile chronic arthritis (Still's disease), juvenile rheumatoid arthritis, Meniere's disease, mixed connective tissue disease, multiple sclerosis, myasthenia gravis, pernicious anemia, polyarteritis nodosa, polychondritis, polyglandular syndromes, polymyalgia rheumatica, polymyositis and dermatomyositis, primary agammaglobulinemia, primary biliary cirrhosis, psoriasis, psoriatic arthritis, Raynaud's phenomena, Reiter's syndrome, rheumatic fever, rheumatoid arthritis, sarcoidosis, scleroderma, systemic scleroderma, progressive systemic sclerosis (PSS), systemic sclerosis (SS), Sjogren's syndrome, stiff-man syndrome, systemic lupus erythematosus (SLE), Takayasu arteritis, temporal arteritis/giant cell arteritis, inflammatory bowel disease (IBD), ulcerative colitis, Cohn's disease, intestinal mucosal inflammation, wasting disease associated with colitis, uveitis, vitiligo and Wegener's granulomatosis, Alzheimer's disease, asthma, atopic allergy, allergy, atherosclerosis, bronchial asthma, eczema, glomerulonephritis, graft vs. host disease, hemolytic anemias, osteoarthritis, sepsis, stroke, transplantation of tissue and organs, vasculitis, diabetic retinopathy, ventilator induced lung injury, viral infections and/or autoimmune diabetes.

~~25.20. A method of killing a cell in a subject, comprising administering to the subject the Use of an antibody or antigen-binding fragment thereof of any one of claims 1-740 in the manufacture of a medicament for killing a cell in a subject.~~

~~26.21. The use method of claim 2025, wherein the cell is a monocyte, a plasmacytoid dendritic cell (pDC), a macrophage, a myeloid-derived suppressor cell (MDSC), a monocyte-derived macrophage, a monocyte-derived dendritic cell, or a cancerous cell; optionally wherein the cell has antigen-presentation function; optionally wherein the cell has at least 2,000, at least 50,000, at least 100,000 or at least 150,000 copies of LILRB4 protein expressed on the surface of the cell.~~

~~27. A method of claim 25, wherein the cell has antigen-presentation function.~~

~~28. The method of claim 25, wherein the cell has at least 2,000, at least 50,000, at least 100,000 or at least 150,000 copies of LILRB4 protein expressed on the surface of the cell.~~

~~29.22.~~ The ~~use method~~ of claim ~~2025~~, wherein the cell is killed via antibody-dependent cellular cytotoxicity (ADCC), ~~or~~ antibody-dependent cellular phagocytosis (ADCP) ~~or T cell cytotoxicity~~.

~~30. The method of claim 25, wherein the cell is killed via T cell cytotoxicity.~~

~~31.23.~~ A method of activating a T cell, comprising contacting the T cell with ~~an the~~ antibody or an antigen-binding fragment thereof of any one of claims 1-~~740~~, optionally in the presence of a cancerous cell, where the cancerous cell increases antigen-presenting activity.

~~32. A method of activating a T cell, comprising contacting the T cell with the antibody or an antigen-binding fragment thereof of any of claims 1-10 in the presence of a cancerous cell.~~

~~33. A method of claim 32, where the cancerous cell increases antigen-presenting activity.~~

~~34.24.~~ The method of claim ~~23s 31-32~~, wherein the T cell is cultured in vitro.

~~35.25.~~ A method of detecting a cancer cell or cancer stem cell in a sample or subject, wherein the sample is a body fluid or biopsy, optionally wherein the sample is blood, sputum, tears, saliva, mucous, serum, urine or feces, comprising:

- (a) contacting ~~thea~~ subject or ~~thea~~ sample from the subject with ~~an the~~ antibody or an antigen-binding fragment thereof of any one of claims 1-~~740~~; and
- (b) detecting binding of said antibody to ~~thea~~ cancer cell or ~~the~~ cancer stem cell in said subject or said sample; optionally
- (c) performing steps (a) and (b) a second time or additional times and determining a change in detection levels as compared to the first time.

~~36. The method of claim 35, wherein the sample is a body fluid or biopsy.~~

~~37. The method of claim 35, wherein the sample is blood, sputum, tears, saliva, mucous, serum, urine or feces.~~

~~38.26.~~ The method of claim ~~2535~~, wherein detection comprises immunohistochemistry, flow cytometry or FACS, immunoassays (including ELISA, RIA etc.) or Western blot.

~~39. The method of claim 35, further comprising performing steps (a) and (b) a second time or additional times and determining a change in detection levels as compared to the first time.~~

~~40. Use of the antibody or antigen-binding fragment thereof of any of claims 1-10 in the manufacture of a medication for treating cancer in a subject.~~

~~41.27.~~ A kit comprising the antibody or antigen-binding fragment thereof of any one of claims 1-~~710~~, useful in detecting LILRB4.

~~42.28.~~ A chimeric antigen receptor (CAR) protein, comprising:

- a) a heavy chain variable region comprising an HC-CDR1 having an amino acid sequence of SEQ ID NO: 5, an HC-CDR2 having an amino acid sequence of SEQ ID NO: 6 and an HC-CDR3 having an amino acid sequence of ~~SEQ ID NO:~~ SEQ ID NO: 7; and
- b) a light chain variable region comprising an LC-CDR1 having an amino acid sequence of SEQ ID NO: 8 with a mutation at amino acid residues NS, an LC-CDR2 having an amino acid sequence of SEQ ID NO: 9 and an LC-CDR3 having an amino acid sequence of SEQ ID NO: 10.

~~43.29.~~ The CAR protein of claim ~~2842~~, wherein the LC-CDR1 having an amino acid sequence of SEQ ID NO: 28.

~~44.30.~~ The CAR protein of claim ~~2842~~, wherein the heavy chain variable region has an amino acid sequence of SEQ ID NO: 1 or at least about 90% identical to SEQ ID NO: 1; and wherein the light chain variable region has an amino acid sequence of SEQ ID NO: 27 or at least about 90% identical to SEQ ID NO: 27.

~~45. The CAR protein of claim 42, wherein the heavy chain variable region has an amino acid sequence of SEQ ID NO: 1; and wherein the light chain variable region has an amino acid sequence of SEQ ID NO: 27.~~

~~46.31.~~ The CAR protein of claim 2842, comprising a single- chain variable fragment (scFv) having an amino acid sequence identical to SEQ ID NOS: 66 or 68, or at least 85%, 90%, 95% or 99% identical to SEQ ID NO: 66 or 68.

~~47. The CAR protein of claim 42, comprising a scFv having an amino acid sequence identical to SEQ ID NOS: 66 or 68.~~

~~48.32.~~ The CAR protein of claim 2842, further comprising a CD8 α transmembrane domain or a CD28 transmembrane domain.

~~49.33.~~ The CAR protein of claim 2842, further comprising a 4-1BB intracellular co-stimulatory signaling domain, ~~or~~ a CD28 intracellular co-stimulatory signaling domain or a CD3 ζ intracellular T cell signaling domain.

~~50. The CAR protein of claim 42, further comprising a CD3 ζ intracellular T cell signaling domain.~~

~~51.34.~~ A polynucleotide molecule encoding a CAR protein according to any one of claims 28-33 ~~42-50~~.

~~52.35.~~ The polynucleotide molecule of claim 3451, further comprising a promoter active in eukaryotic cells.

~~53.36.~~ The polynucleotide molecule of claim 3451, further defined as an expression vector.

~~54.37.~~ An engineered cell comprising the polynucleotide molecule of claim 3451, optionally wherein the engineered cell is a T cell, an NK cell or a macrophage.

~~55. The cell of claim 54, wherein the cell is a T cell, an NK cell or a macrophage.~~

~~56.38.~~ A method of treating or ameliorating cancer in a subject in need thereof comprising administering to the subject a cell therapy comprising Use of a therapeutically effective amount of ~~the~~ cells in accordance with claim 3754 or 55 in the manufacture of a cell therapy for treating or ameliorating cancer in a subject in need thereof.

~~57.39.~~ The ~~usemethod~~ of claim ~~3856~~, wherein said cell therapy is to be administered local to cancer site, regional to a cancer site, or systemically.

~~58.40.~~ The ~~usemethod~~ of claim ~~3957~~, further comprising ~~administering~~ to said human subject an administration of a second cancer therapy.

~~59.41.~~ The ~~usemethod~~ of claim ~~4058~~, wherein said second cancer therapy is chemotherapy, immunotherapy, radiotherapy, hormone therapy or surgery; optionally wherein said second cancer therapy is to be administered at the same time, before, or after the cell therapy.

~~60.~~ ~~The method of claim 58, wherein said second cancer therapy is administered at the same time as the cell therapy.~~

~~61.~~ ~~The method of claim 58, wherein said second cancer therapy is administered before or after the cell therapy.~~

~~62.42.~~ The ~~usemethod~~ of claim ~~3957~~, further comprising to be administered ~~administering~~ to said human subject a second administration of an effective amount of one or more cells in accordance with claim ~~3754 or 55.~~

~~63.~~ ~~The method of claim 56, wherein said cancer is a metastatic, recurrent or drug-resistant cancer.~~

~~64.~~ ~~The method of claim 56, wherein said cancer is AML.~~

~~65.43.~~ The ~~usemethod~~ of claim ~~3856~~, wherein said cancer is selected from the group consisting of pre-B acute lymphocytic leukemia (Pre-B ALL), B-cell leukemia, chronic lymphoblastic leukemia (CLL), multiple myeloma (MM), chronic myelomonocytic leukemia (CMML), myelodysplastic syndrome (MDS), myeloproliferative neoplasms, and blastic plasmacytoid dendritic cell neoplasm (BPDCN), AML, breast cancer, lung cancer, pancreatic cancer, and/or prostate cancer; optionally wherein said cancer is metastatic, recurrent or drug-resistant cancer.

~~66. The method of claim 56, wherein said cancer is breast cancer, lung cancer, pancreatic cancer, or prostate cancer.~~

~~67.44. A method for treating or ameliorating an autoimmune or inflammatory disease in a subject, comprising administering to the subject a cell therapy comprising Use of a therapeutically effective amount of the cells in accordance with claim 3754 or 55 in the manufacture of a cell therapy for treating or ameliorating an autoimmune or inflammatory disease in a subject.~~

~~68.45. The usemethod of claim 4467, wherein the autoimmune or inflammatory disease is selected from the group consisting of Acquired Immunodeficiency Syndrome (AIDS), alopecia areata, ankylosing spondylitis, antiphospholipid syndrome, autoimmune Addison's disease, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune inner ear disease (AIED), autoimmune lymphoproliferative syndrome (ALPS), autoimmune thrombocytopenic purpura (ATP), Behcet's disease, cardiomyopathy, celiac sprue-dermatitis hepeticiformis, chronic fatigue immune dysfunction syndrome (CFIDS), chronic inflammatory demyelinating polyneuropathy (CIPD), cicatricial pemphigoid, cold agglutinin disease, crest syndrome, Crohn's disease, Degos' disease, dermatomyositis-juvenile, discoid lupus, essential mixed cryoglobulinemia, fibromyalgia-fibromyositis, Graves' disease, Guillain-Barre syndrome, Hashimoto's thyroiditis, idiopathic pulmonary fibrosis, idiopathic thrombocytopenia purpura (ITP), IgA nephropathy, insulin-dependent diabetes mellitus, juvenile chronic arthritis (Still's disease), juvenile rheumatoid arthritis, Meniere's disease, mixed connective tissue disease, multiple sclerosis, myasthenia gravis, pernicious anemia, polyarteritis nodosa, polychondritis, polyglandular syndromes, polymyalgia rheumatica, polymyositis and dermatomyositis, primary agammaglobulinemia, primary biliary cirrhosis, psoriasis, psoriatic arthritis, Raynaud's phenomena, Reiter's syndrome, rheumatic fever, rheumatoid arthritis, sarcoidosis, scleroderma, systemic scleroderma, progressive systemic sclerosis (PSS), systemic sclerosis (SS), Sjogren's syndrome, stiff-man syndrome, systemic lupus erythematosus (SLE), Takayasu arteritis, temporal arteritis/giant cell arteritis, inflammatory bowel disease (IBD), ulcerative colitis, Cohn's disease, intestinal mucosal inflammation, wasting disease associated with colitis, uveitis, vitiligo and Wegener's granulomatosis, Alzheimer's disease, asthma, atopic allergy, allergy, atherosclerosis, bronchial asthma, eczema, glomerulonephritis, graft vs. host disease, hemolytic anemias,~~

osteoarthritis, sepsis, stroke, transplantation of tissue and organs, vasculitis, diabetic retinopathy, ventilator induced lung injury, viral infections and autoimmune diabetes.

~~69.46.~~ A bispecific antibody or antigen-binding fragment capable of binding to LILRB4 and CD3.

~~70.47.~~ The bispecific antibody or antigen-binding fragment of claim ~~4669~~, comprising

- (a) a first antigen-binding region comprising a first light chain variable (V_L) domain and a first heavy chain variable (V_H) domain; and
- (b) a second antigen-binding region comprising a second V_L domain and a second V_H domain,

wherein the first antigen-binding region is capable of binding to LILRB4 and the second antigen-binding region is capable of binding to CD3, or vice versa.

~~71.48.~~ The bispecific antibody or antigen-binding fragment of claim ~~4770~~, wherein the first V_L domain and the first heavy chain variable domain link to a first pair of constant domains, respectively, and wherein the second V_L domain and the second V_H domain link to a second pair of constant domains, respectively.

~~72.49.~~ The bispecific antibody or antigen-binding fragment of claim ~~4871~~, wherein

- (a) the first V_L domain links to a first light chain constant (C_L) domain, and the first V_H domain links to a first heavy chain constant domain 1 (C_{H1}), or
- (b) the first V_L domain links to a first C_{H1} domain, and the V_H domain links to a second C_L domain.

~~73.50.~~ The bispecific antibody or antigen-binding fragment of claim ~~4972~~, wherein

- (a) the second V_L domain links to a second C_L domain, and the second V_H domain links to a second C_{H1} domain, or
- (b) the second V_L domain links to a second C_{H1} domain, and the second V_H domain links to a second C_L domain, or
- (c) the second V_L domain links to a T cell receptor (TCR) α chain constant domain, and the second V_H domain links to a TCR β chain constant domain, or
- (d) the second V_L domain links to a TCR β chain constant domain, and the second V_H domain links to a TCR α chain constant domain; optionally wherein the TCR α chain constant domain has a S91A mutation.

~~74. The bispecific antibody or antigen-binding fragment of claim 73, wherein the TCR α chain constant domain has a S91A mutation.~~

~~75.51.~~ The bispecific antibody or antigen-binding fragment of claim ~~4770~~, wherein the first antigen-binding region and/or the second antigen-binding region is a single chain variable fragment (scFv).

~~76.52.~~ The bispecific antibody or antigen-binding fragment of claim ~~4770~~, further comprising a third antigen-binding region comprising a third V_L domain and a third V_H domain, wherein the third antigen-binding region is capable of binding to LILRB4 or CD3.

~~77.53.~~ The bispecific antibody or antigen-binding fragment of claim ~~5276~~, wherein the third V_L domain and the third heavy chain variable domain link to a first pair of constant domains, respectively.

~~78.54.~~ The bispecific antibody or antigen-binding fragment of claim ~~5377~~, wherein

- (a) the third V_L domain links to a third C_L domain, and the third V_H domain links to a third C_{H1} domain, or
- (b) the third V_L domain links to a third C_{H1} domain, and the third V_H domain links to a third C_L domain, or
- (c) the third V_L domain links to a second TCR α chain constant domain, and the third V_H domain links to a second TCR β chain constant domain, or
- (d) the third V_L domain links to a second TCR β chain constant domain, and the third V_H domain links to a second TCR α chain constant domain.

~~79.55.~~ The bispecific antibody or antigen-binding fragment of claim ~~4770~~, wherein

- (a) the first V_H domain comprising a first HC-CDR 1 having an amino acid sequence of SEQ ID NO: 5, a first HC-CDR2 having an amino acid sequence of SEQ ID NO: 6 and a first HC-CDR3 having an amino acid sequence of SEQ ID NO: 7; and
- (b) a first V_L domain comprising a first LC-CDR1 having an amino acid sequence of SEQ ID NO: 8 with a mutation at amino acid residues NS, a first LC-CDR2 having an amino acid sequence of SEQ ID NO: 9 and a first LC-CDR3 having an amino acid sequence of SEQ ID NO: 10.