

[0005] Drugs that function to suppress immune response can be used to effectively treat patients having autoimmune diseases or to help prevent transplant rejection. For example, among currently available treatments for rheumatoid arthritis and kidney transplant are Abatacept (Orencia®) and Betacept (Nulojix®), modified antibody fusion polypeptides comprising the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) linked to the Fc region of IgG1. Conversely, drugs that activate immune responses may be used to effectively treat diseases or disorders including cancers or infectious diseases. For example, ipilimumab (Yervoy®) is a monoclonal antibody that activates immune responses by targeting CTLA-4 and can be used to treat melanoma. Pembrolizumab (Keytruda®) is a humanized antibody against human programmed death receptor-1 (PD-1) and is prescribed as an anti-PD-1 immunotherapy against certain cancers. Nivolumab (Opdivo®) is another anti-PD-1 antibody used as an immunotherapy to treat certain cancers.

SUMMARY

[0005a] In one aspect, the disclosure relates to an antibody or an immunogenic fragment thereof that specifically binds to KIR3DL3 protein, comprising a VH region comprising 3 CDRs having an amino acid sequence of SEQ ID NOs: 31, 33, and 35; and a VL region comprising 3 CDRs having an amino acid sequence of SEQ ID NOs: 43, 45, and 47.

[0006] In ~~one~~ another aspect, the disclosure relates to an antibody or an immunogenic fragment thereof that specifically binds to KIR3DL3 protein (SEQ ID NO: 335). In certain example embodiments, the disclosure relates to an antibody or an immunogenic fragment thereof that specifically binds to KIR3DL3 protein, wherein the antibody or the immunogenic fragment thereof specifically binds to a KIR3DL3 epitope comprising the whole extracellular domain or a portion thereof. In some example embodiments, the antibody or the immunogenic fragment thereof binds to the KIR3DL3 D0 domain (SEQ ID NO: 337), the KIR3DL3 D1 domain (SEQ ID NO: 338), or KIR3DL3 D2 domain (SEQ ID NO: 339).

[0007] In one aspect example, antibodies or immunogenic fragments thereof provided herein comprise a VH region comprising CDR1, CDR2, and CDR3, having an amino acid sequence of SEQ ID NOs: 7, 9, 11, 31, 33, 35, 54, 56, 76, 78, 80, 100, 102,

104, 124, 126, 128, 148, 150, 152, 172, 174, 176, 196, 198, 200, 220, 222, 224, 244, 246, 248, 268, 270, 272, 292, 294, 296, 316, 318, or 320.

[0008] In one ~~aspect~~example, antibodies or immunogenic fragments thereof provided herein comprise a VH region comprising at least one CDRs that are 80% identical to an amino acid sequence selected from SEQ ID NOs: 7, 9, 11, 31, 33, 35, 54, 56, 76, 78, 80, 100, 102, 104, 124, 126, 128, 148, 150, 152, 172, 174, 176, 196, 198, 200, 220, 222, 224, 244, 246, 248, 268, 270, 272, 292, 294, 296, 316, 318, or 320.

[0009] In one aspectexamples, antibodies or immunogenic fragments thereof provided herein comprise a VH region comprising at least two CDRs that are 80% identical to an amino acid sequence selected from SEQ ID NOs: 7, 9, 11, 31, 33, 35, 54, 56, 76, 78, 80, 100, 102, 104, 124, 126, 128, 148, 150, 152, 172, 174, 176, 196, 198, 200, 220, 222, 224, 244, 246, 248, 268, 270, 272, 292, 294, 296, 316, 318, or 320.

[0010] In one aspectexample, antibodies or immunogenic fragments thereof provided herein comprise a VH region comprising at least three CDRs that are 80% identical to an amino acid sequence selected from SEQ ID NOs: 7, 9, 11, 31, 33, 35, 54, 56, 76, 78, 80, 100, 102, 104, 124, 126, 128, 148, 150, 152, 172, 174, 176, 196, 198, 200, 220, 222, 224, 244, 246, 248, 268, 270, 272, 292, 294, 296, 316, 318, or 320.

[0011] In one aspectexample, antibodies or immunogenic fragments thereof provided herein comprise a VL region comprising CDR1, CDR2, and CDR3, having an amino acid sequence of SEQ ID NOs: 19, 21, 23, 43, 45, 47, 64, 66, 68, 88, 90, 92, 112, 114, 116, 136, 138, 140, 160, 162, 164, 184, 186, 188, 208, 210, 212, 232, 234, 236, 256, 258, 260, 280, 282, 284, 304, 306, 308, 328, 330, or 332.

[0012] In one aspectexample, antibodies or immunogenic fragments thereof provided herein comprise a VL region comprising at least one CDR that is 80% identical to an amino acid sequence selected from SEQ ID NOs: 19, 21, 23, 43, 45, 47, 64, 66, 68, 88, 90, 92, 112, 114, 116, 136, 138, 140, 160, 162, 164, 184, 186, 188, 208, 210, 212, 232, 234, 236, 256, 258, 260, 280, 282, 284, 304, 306, 308, 328, 330, or 332.

[0013] In one exampleaspect, antibodies or immunogenic fragments thereof provided herein comprise a VL region comprising at least two CDRs that are 80% identical to an amino acid sequence selected from SEQ ID NOs: 19, 21, 23, 43, 45, 47, 64, 66, 68, 88, 90, 92, 112, 114, 116, 136, 138, 140, 160, 162, 164, 184, 186, 188, 208, 210, 212, 232, 234, 236, 256, 258, 260, 280, 282, 284, 304, 306, 308, 328, 330, or 332.

[0014] In one exampleaspect, antibodies or immunogenic fragments thereof provided herein comprise a VL region comprising at least three CDRs that are 80% identical to an amino acid sequence selected from SEQ ID NOs: 19, 21, 23, 43, 45, 47, 64, 66, 68, 88, 90, 92, 112, 114, 116, 136, 138, 140, 160, 162, 164, 184, 186, 188, 208, 210, 212, 232, 234, 236, 256, 258, 260, 280, 282, 284, 304, 306, 308, 328, 330, or 332.

[0015] In certain exampleaspects, antibodies or immunogenic fragments thereof provided herein comprise a monoclonal antibody.

[0016] In certain exampleaspects, antibodies or immunogenic fragments thereof provided herein comprise a chimeric antibody, a human antibody, or a humanized antibody.

[0017] In one exampleaspect, antibodies or immunogenic fragments thereof provided herein comprise an amino acid sequence selected from SEQ ID NOs: 7, 9, 11, 19, 21, 23, 31, 33, 35, 43, 45, 47, 54, 56, 64, 66, 68, 76, 78, 80, 88, 90, 92, 100, 102, 104, 112, 114, 116, 124, 126, 128, 136, 138, 140, 148, 150, 152, 160, 162, 164, 172, 174, 176, 184, 186, 188, 196, 198, 200, 208, 210, 212, 220, 222, 224, 232, 234, 236, 244, 246, 248, 256, 258, 260, 268, 270, 272, 280, 282, 284, 292, 294, 296, 304, 306, 308, 316, 318, 320, 328, 330, or 332.

[0018] In one exampleaspect, antibodies or immunogenic fragments thereof are provided herein, wherein the antibody is monoclonal 8G7, monoclonal 26E10, monoclonal 26E2, monoclonal 31C4, monoclonal 34B10, monoclonal 37A3, monoclonal 12A10, monoclonal 3B7, monoclonal 11G8, monoclonal 14F8, monoclonal 15D2, monoclonal 29H7, monoclonal 30D10, or monoclonal 51C3.

[0019] In one exampleaspect, antibodies or immunogenic fragments thereof are provided herein, wherein the antibody is humanized 8G7, humanized 26E10, humanized 26E2, humanized 31C4, humanized 34B10, humanized 37A3, humanized 12A10, humanized 3B7, humanized 11G8, humanized 14F8, humanized 15D2, humanized 29H7, humanized 30D10, or humanized 51C3.

[0020] In another aspect, fusion polypeptides comprising an antibody or an immunogenic fragment thereof according to the present disclosure are provided.

[0021] In certain aspects, compositions comprising an antibody or an immunogenic fragment thereof or fusion proteins according the present disclosure are provided.

[0022] In another exampleaspect, compositions provided herein further comprise a pharmaceutically acceptable carrier.

[0023] In another exampleaspect, compositions provided herein further comprise a pharmaceutically acceptable excipient.

[0024] In certain ~~aspects~~examples, antibodies or immunogenic fragments thereof, fusion polypeptides, or compositions according to the present disclosure may be or comprise a component of a chimeric antigen receptor or an antibody-drug conjugate (e.g., an antibody or immunogenic fragment thereof attached to a cytotoxic agent or molecule).

[0025] In certain aspects, antibodies or immunogenic fragments thereof, fusion polypeptides, or compositions according to the present disclosure for use in a therapy are provided.

[0026] In certain aspects, antibodies or immunogenic fragments thereof, fusion polypeptides, or compositions according to the present disclosure for use in the production of a medicament are provided.

[0027] In another aspect, nucleic acids comprising a nucleic acid encoding an antibody or an immunogenic fragment thereof according to the present disclosure are provided.

[0028] In another aspect, nucleic acids comprising a nucleic acid encoding a fusion polypeptide according to the present disclosure are provided.

[0029] In certain ~~aspects~~examples, methods of treating a subject having a condition, comprising administering to the subject a therapeutically effective amount of an antibody or an immunogenic fragment thereof, a fusion polypeptide, or a composition according to the present disclosure are provided.

[0030] In some ~~aspects~~examples, methods of treating a subject having a condition comprising administering to the subject a therapeutically effective amount of an antibody or an immunogenic fragment thereof, a fusion polypeptide, or a composition according to the present disclosure are provided, wherein the subject has a condition and wherein the condition is cancer. In some examples~~embodiments~~, the cancer is selected from the group consisting of chronic lymphocytic leukemia (CLL), acute leukemia, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell lymphoma, B-cell lymphoma, T-cell acute lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), B-cell prolymphocytic leukemia, T-cell lymphoma, Hodgkin's Disease, B-cell non-Hodgkin's lymphoma, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell follicular lymphoma, large cell follicular lymphoma, malignant

lymphoproliferative conditions, mucosa-associated lymphoid tissue (MALT) lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenström macroglobulinemia, or preleukemia. In other examplesembodiments, the cancer is selected from the group consisting of colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, lung cancer, kidney cancer, gastric cancer, gallbladder cancer, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, environmentally induced cancers, combinations of the cancers, and metastatic lesions of the cancers. In other examplesembodiments, the cancer is a human hematologic malignancy. In certain examplesembodiments, the human hematologic malignancy is selected from myeloid neoplasm, acute myeloid leukemia (AML), AML with recurrent genetic abnormalities, AML with myelodysplasia-related changes, therapy-related AML, acute leukemias of ambiguous lineage, myeloproliferative neoplasm, essential thrombocythemia, polycythemia vera, myelofibrosis (MF), primary myelofibrosis, systemic mastocytosis, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, chronic myeloid leukemia, chronic neutrophilic leukemia, chronic eosinophilic leukemia, myelodysplastic syndromes (MDS), refractory anemia with ringed sideroblasts, refractory cytopenia with multilineage dysplasia, refractory anemia with excess blasts (type 1), refractory anemia with excess blasts (type 2), MDS with isolated del (5q), unclassifiable MDS, myeloproliferative/myelodysplastic syndromes, chronic myelomonocytic leukemia, atypical chronic myeloid leukemia, juvenile myelomonocytic leukemia, unclassifiable

myeloproliferative/myelodysplastic syndromes, lymphoid neoplasms, precursor lymphoid neoplasms, B lymphoblastic leukemia, B lymphoblastic lymphoma, T lymphoblastic leukemia, T lymphoblastic lymphoma, mature B-cell neoplasms, diffuse large B-cell lymphoma, primary central nervous system lymphoma, primary mediastinal B-cell lymphoma, Burkitt's lymphoma/leukemia, follicular lymphoma, chronic lymphocytic leukemia, small lymphocytic lymphoma, B-cell prolymphocytic leukemia, lymphoplasmacytic lymphoma, Waldenström macroglobulinemia, mantle cell lymphoma, marginal zone lymphomas, post-transplant lymphoproliferative disorders, HIV-associated lymphomas, primary effusion lymphoma, intravascular large B-cell lymphoma, primary cutaneous B-cell lymphoma, hairy cell leukemia, multiple myeloma, monoclonal gammopathy of unknown significance (MGUS), smoldering multiple myeloma, or solitary plasmacytomas (solitary bone and extramedullary).

[0031] In some ~~embodiments~~examples, the cancer is a metastatic cancer.

[0032] In some ~~embodiments~~examples, methods of treating a subject having cancer comprising administering to the subject a therapeutically effective amount of an antibody or an immunogenic fragment thereof, a fusion polypeptide, or a composition according to the present disclosure further comprise subjecting the subject to one or more additional cancer therapies selected from chemotherapy, radiation therapy, immunotherapy, surgery and a combination thereof.

[0033] In some ~~aspects~~examples, methods of treating a subject having a condition comprising administering to the subject a therapeutically effective amount of an antibody or an immunogenic fragment thereof, a fusion polypeptide, or a composition according to the present disclosure are provided, wherein the subject has a condition and wherein the condition is an infection. In certain ~~embodiments~~examples, the infection is caused by a pathogen. In certain example~~embodiments~~, the pathogen is a virus. In some ~~embodiments~~examples, the virus is selected from the group consisting of human immunodeficiency viruses, influenza viruses, papillomaviruses, coronaviruses, hepatitis viruses, or herpesviruses. In other ~~embodiments~~examples, the pathogen is a bacterium. In some example~~embodiments~~, the bacterium is mycobacterium tuberculosis. In other ~~embodiments~~examples, the pathogen is a prion. In other ~~embodiments~~examples, the pathogen is a fungus. In certain example~~embodiments~~, the fungus is *Pneumocystis jirovecii* (PJP). In other example~~embodiments~~, the pathogen is a parasite.

[0034] In some examplesaspects, methods of treating a subject having a condition comprising administering to the subject a therapeutically effective amount of an antibody or an immunogenic fragment thereof, a fusion polypeptide, or a composition according to the present disclosure are provided, wherein the subject has a condition and wherein the condition is an autoimmune disease or disorder. In some examplesembodiments, the autoimmune disease or disorder is selected from the group consisting of acute disseminated encephalomyelitis (ADEM), alopecia areata, antiphospholipid syndrome, autoimmune cardiomyopathy, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune inner ear disease, autoimmune lipoproliferative syndrome, autoimmune peripheral neuropathy, autoimmune pancreatitis, autoimmune polyendocrine syndrome, autoimmune progesterone dermatitis, autoimmune thrombocytopenic purpura, autoimmune urticarial, autoimmune uveitis, Behçet's disease, celiac disease, Chagas disease, cold agglutinin disease, Crohn's disease, dermatomyositis, diabetes mellitus type 1, eosinophilic fasciitis, gastrointestinal pemphigoid, Goodpasture's syndrome, Grave's syndrome, Guillain-Barré syndrome, Hashimoto's encephalopathy, Hashimoto's thyroiditis, lupus erythematosus, Miller-Fisher syndrome, mixed connective tissue disease, myasthenia gravis, pemphigus vulgaris, pernicious anemia, polymyositis, psoriasis, psoriatic arthritis, relapsing polychondritis, rheumatoid arthritis, rheumatic fever, Sjögren's syndrome, temporal arteritis, transverse myelitis, ulcerative colitis, undifferentiated connective tissue disease, vasculitis, and Wegener's granulomatosis. In certain examplesembodiments, the autoimmune disease or disorder is adult rheumatoid arthritis.

[0035] In some examplesaspects, methods of treating a subject having a condition comprising administering to the subject a therapeutically effective amount of an antibody or an immunogenic fragment thereof, a fusion polypeptide, or a composition according to the present disclosure are provided, wherein the subject has a condition and wherein the condition is a transplant. In some examplesembodiments, the transplant is selected from a stem cell transplant or a bone marrow transplant. In some embodiments, the transplant is selected from the group consisting of a kidney transplant, a lung transplant, a heart transplant, a pancreas transplant, a cornea transplant, or a liver transplant.

[0036] In certain examples~~aspects~~, compositions comprising an antibody, an immunogenic fragment thereof, a fusion polypeptide, or a combination thereof according to the present technology for use in treating a subject having a condition are provided.

[0037] In some examples~~aspects~~, compositions comprising an antibody, an immunogenic fragment thereof, a fusion polypeptide, or a combination thereof according to the present technology for use in treating a subject having a condition are provided, wherein the condition is cancer. In some examples~~aspects~~, the cancer is selected from the group consisting of chronic lymphocytic leukemia (CLL), acute leukemia, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell lymphoma, B-cell lymphoma, T-cell acute lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), B-cell prolymphocytic leukemia, T-cell lymphoma, Hodgkin's Disease, B-cell non-Hodgkin's lymphoma, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell follicular lymphoma, large cell follicular lymphoma, malignant lymphoproliferative conditions, mucosa-associated lymphoid tissue (MALT) lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenström macroglobulinemia, or preleukemia. In other examples~~aspects~~, the cancer is selected from the group consisting of colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, lung cancer, kidney cancer, gastric cancer, gallbladder cancer, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, environmentally induced cancers, combinations of the cancers, and metastatic

lesions of the cancers. In other example embodiments, the cancer is a human hematologic malignancy. In certain example embodiments, the human hematologic malignancy is selected from myeloid neoplasm, acute myeloid leukemia (AML), AML with recurrent genetic abnormalities, AML with myelodysplasia-related changes, therapy-related AML, acute leukemias of ambiguous lineage, myeloproliferative neoplasm, essential thrombocythemia, polycythemia vera, myelofibrosis (MF), primary myelofibrosis, systemic mastocytosis, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, chronic myeloid leukemia, chronic neutrophilic leukemia, chronic eosinophilic leukemia, myelodysplastic syndromes (MDS), refractory anemia with ringed sideroblasts, refractory cytopenia with multilineage dysplasia, refractory anemia with excess blasts (type 1), refractory anemia with excess blasts (type 2), MDS with isolated del (5q), unclassifiable MDS, myeloproliferative/myelodysplastic syndromes, chronic myelomonocytic leukemia, atypical chronic myeloid leukemia, juvenile myelomonocytic leukemia, unclassifiable myeloproliferative/myelodysplastic syndromes, lymphoid neoplasms, precursor lymphoid neoplasms, B lymphoblastic leukemia, B lymphoblastic lymphoma, T lymphoblastic leukemia, T lymphoblastic lymphoma, mature B-cell neoplasms, diffuse large B-cell lymphoma, primary central nervous system lymphoma, primary mediastinal B-cell lymphoma, Burkitt's lymphoma/leukemia, follicular lymphoma, chronic lymphocytic leukemia, small lymphocytic lymphoma, B-cell prolymphocytic leukemia, lymphoplasmacytic lymphoma, Waldenström macroglobulinemia, mantle cell lymphoma, marginal zone lymphomas, post-transplant lymphoproliferative disorders, HIV-associated lymphomas, primary effusion lymphoma, intravascular large B-cell lymphoma, primary cutaneous B-cell lymphoma, hairy cell leukemia, multiple myeloma, monoclonal gammopathy of unknown significance (MGUS), smoldering multiple myeloma, or solitary plasmacytomas (solitary bone and extramedullary).

[0038] In some example embodiments, the cancer is a metastatic cancer.

[0039] In some example embodiments, compositions comprising an antibody, an immunogenic fragment thereof, a fusion polypeptide, or a combination thereof according to the present technology for use in treating a subject having a condition are provided, wherein the compositions are co-administered to the subject with one or more additional cancer therapies selected from chemotherapy, radiation therapy, immunotherapy, surgery, or a combination thereof.

[0040] In some examplesaspects, compositions comprising an antibody, an immunogenic fragment thereof, a fusion polypeptide, or a combination thereof according to the present technology for use in treating a subject having a condition are provided, wherein the condition is an infection. In certain exampleembodiments, the infection is caused by a pathogen. In certain exampleembodiments, the pathogen is a virus. In some exampleembodiments, the virus is selected from the group consisting of human immunodeficiency viruses, influenza viruses, papillomaviruses, coronaviruses, hepatitis viruses, or herpesviruses. In other exampleembodiments, the pathogen is a bacterium. In some exampleembodiments, the bacterium is mycobacterium tuberculosis. In other exampleembodiments, the pathogen is a prion. In other exampleembodiments, the pathogen is a fungus. In certain exampleembodiments, the fungus is *Pneumocystis jirovecii* (PJP). In other exampleembodiments, the pathogen is a parasite.

[0041] In some examplesaspects, compositions comprising an antibody, an immunogenic fragment thereof, a fusion polypeptide, or a combination thereof according to the present technology for use in treating a subject having a condition are provided, wherein the condition is an autoimmune disease or disorder. In some exampleembodiments, the autoimmune disease or disorder is selected from the group consisting of acute disseminated encephalomyelitis (ADEM), alopecia areata, antiphospholipid syndrome, autoimmune cardiomyopathy, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune inner ear disease, autoimmune lipoproliferative syndrome, autoimmune peripheral neuropathy, autoimmune pancreatitis, autoimmune polyendocrine syndrome, autoimmune progesterone dermatitis, autoimmune thrombocytopenic purpura, autoimmune urticarial, autoimmune uveitis, Behçet's disease, celiac disease, Chagas disease, cold agglutinin disease, Crohn's disease, dermatomyositis, diabetes mellitus type 1, eosinophilic fasciitis, gastrointestinal pemphigoid, Goodpasture's syndrome, Grave's syndrome, Guillain-Barré syndrome, Hashimoto's encephalopathy, Hashimoto's thyroiditis, lupus erythematosus, Miller-Fisher syndrome, mixed connective tissue disease, myasthenia gravis, pemphigus vulgaris, pernicious anemia, polymyositis, psoriasis, psoriatic arthritis, relapsing polychondritis, rheumatoid arthritis, rheumatic fever, Sjögren's syndrome, temporal arteritis, transverse myelitis, ulcerative colitis, undifferentiated connective tissue disease, vasculitis, and Wegener's granulomatosis. In certain exampleembodiments, the autoimmune disease or disorder is adult rheumatoid arthritis.

[0042] In some examples~~aspects~~, compositions comprising an antibody, an immunogenic fragment thereof, a fusion polypeptide, or a combination thereof according to the present technology for use in treating a subject having a condition are provided, wherein the condition is a transplant. In some examples~~embodiments~~, the transplant is selected from a stem cell transplant or a bone marrow transplant. In some examples~~embodiments~~, the transplant is selected from the group consisting of a kidney transplant, a lung transplant, a heart transplant, a pancreas transplant, a cornea transplant, and liver transplant.

[0043] This listing is intended to be exemplary and illustrative rather than comprehensive and limiting. Additional aspects and embodiments may be set out in, or apparent from, the remainder of this technology and the claims.

DESCRIPTION OF THE DRAWINGS

[0044] Figures (FIGS.) 1A–1B show that KIR3DL3 protein is expressed on the cell surface of human adaptive immune cells and innate immune cells. FIG. 1A depicts a series of plots showing Fluorescence-Activated Cell Sorting (FACS) analysis of peripheral blood mononuclear cells (PBMCs). FACS analysis showed that KIR3DL3 protein was detected on the cells surface of human innate immune cells, including natural killer (NK) cells, natural killer T (NKT) cells and $\gamma\delta$ T cells, and adaptive immune cells, including CD8⁺ T cells and CD4⁺ T cells. FIG. 1B is a chart depicting the percentage of KIR3DL3 positive cells in different populations of immune cells in PBMCs from six different donors.

[0045] FIGS. 2A–2C show that HHLA2 binds KIR3DL3, but not its closest homologues KIR3DL1 and KIR3DL2, and that the D0 domain and the whole extracellular portion of KIR3DL3 bind HHLA2. FIG. 2A depicts histograms of 3T3 cell lines expressing KIR3DL1, KIR3DL2, or KIR3DL3 stained with HHLA2-Ig fusion polypeptide (open histograms) or control Ig (shaded histograms). FIG. 2B depicts a plot showing results of an intercellular conjugate assay that indicate 3T3 cell line expressing HHLA2 bound to 3T3 cell line expressing KIR3DL3, but not the control 3T3 cell line. FIG. 2C depicts histograms of a 3T3 cell line expressing HHLA2 bound by the D0 domain (red) and the whole extracellular portion (red) of KIR3DL3.

[0046] FIGS. 3A–3B show results indicating that TMIGD2 and KIR3DL3 bind non-overlapping sites on HHLA2. FIG. 3A is a chart depicting mean fluorescent intensity

CLAIMS

What is claimed is:

1. An antibody or an immunogenic fragment thereof that specifically binds to KIR3DL3 protein, comprising a VH region comprising 3 CDRs having an amino acid sequence of SEQ ID NOs: 31, 33, and 35; and a VL region comprising 3 CDRs having an amino acid sequence of SEQ ID NOs: 43, 45, and 47.

2. The antibody or the immunogenic fragment of claim 1, comprising a VH region having an amino acid sequence of SEQ ID NO: 29; and a VL region having an amino acid sequence of SEQ ID NO: 41.

3. The antibody or the immunogenic fragment of claim 1, wherein the antibody comprises or is 26E10.

14. An antibody or an immunogenic fragment thereof that specifically binds to KIR3DL3 protein.

25. The antibody or the immunogenic fragment thereof of claim 14, wherein the antibody or the immunogenic fragment thereof specifically binds to a KIR3DL3 epitope comprising the whole extracellular domain or a portion thereof.

36. The antibody or the immunogenic fragment of claim 25, wherein the antibody or the immunogenic fragment thereof binds to the KIR3DL3 D0 domain, the KIR3DL3 D1 domain, or KIR3DL3 D2 domain.

47. The antibody or immunogenic fragment thereof of claim 14 or claim 25, comprising a VH region comprising CDR1, CDR2, and CDR3, having an amino acid sequence of SEQ ID NOs: 7, 9, 11, 31, 33, 35, 54, 56, 76, 78, 80, 100, 102, 104, 124, 126, 128, 148, 150, 152, 172, 174, 176, 196, 198, 200, 220, 222, 224, 244, 246, 248, 268, 270, 272, 292, 294, 296, 316, 318, or 320.

~~58.~~ The antibody or immunogenic fragment thereof of claim ~~1-4~~ or claim 25, comprising a VH region comprising at least one CDR that is 80% identical to an amino acid sequence selected from SEQ ID NOs: 7, 9, 11, 31, 33, 35, 54, 56, 76, 78, 80, 100, 102, 104, 124, 126, 128, 148, 150, 152, 172, 174, 176, 196, 198, 200, 220, 222, 224, 244, 246, 248, 268, 270, 272, 292, 294, 296, 316, 318, or 320.

~~69.~~ The antibody or immunogenic fragment thereof of claim ~~1-4~~ or claim 25, comprising a VH region comprising at least two CDRs that are 80% identical to an amino acid sequence selected from SEQ ID NOs: 7, 9, 11, 31, 33, 35, 54, 56, 76, 78, 80, 100, 102, 104, 124, 126, 128, 148, 150, 152, 172, 174, 176, 196, 198, 200, 220, 222, 224, 244, 246, 248, 268, 270, 272, 292, 294, 296, 316, 318, or 320.

~~710.~~ The antibody or immunogenic fragment thereof of claim ~~1-4~~ or claim 25, comprising a VH region comprising at least three CDRs that are 80% identical to an amino acid sequence selected from SEQ ID NOs: 7, 9, 11, 31, 33, 35, 54, 56, 76, 78, 80, 100, 102, 104, 124, 126, 128, 148, 150, 152, 172, 174, 176, 196, 198, 200, 220, 222, 224, 244, 246, 248, 268, 270, 272, 292, 294, 296, 316, 318, or 320.

~~811.~~ The antibody or immunogenic fragment thereof of claim ~~1-4~~ or claim 25, comprising a VL region comprising CDR1, CDR2, and CDR3, having an amino acid sequence of SEQ ID NOs: 19, 21, 23, 43, 45, 47, 64, 66, 68, 88, 90, 92, 112, 114, 116, 136, 138, 140, 160, 162, 164, 184, 186, 188, 208, 210, 212, 232, 234, 236, 256, 258, 260, 280, 282, 284, 304, 306, 308, 328, 330, or 332.

~~912.~~ The antibody or immunogenic fragment thereof of claim ~~1-4~~ or claim 25, comprising a VL region comprising at least one CDR that is 80% identical to an amino acid sequence selected from SEQ ID NOs: 19, 21, 23, 43, 45, 47, 64, 66, 68, 88, 90, 92, 112, 114, 116, 136, 138, 140, 160, 162, 164, 184, 186, 188, 208, 210, 212, 232, 234, 236, 256, 258, 260, 280, 282, 284, 304, 306, 308, 328, 330, or 332.

~~1013.~~ The antibody or immunogenic fragment thereof of claim ~~1-4~~ or claim 25, comprising a VL region comprising at least two CDRs that are 80% identical to an amino acid sequence selected from SEQ ID NOs: 19, 21, 23, 43, 45, 47, 64, 66, 68, 88, 90,

92, 112, 114, 116, 136, 138, 140, 160, 162, 164, 184, 186, 188, 208, 210, 212, 232, 234, 236, 256, 258, 260, 280, 282, 284, 304, 306, 308, 328, 330, or 332.

~~11~~14. The antibody or immunogenic fragment thereof of claim ~~1~~4 or claim ~~2~~5, comprising a VL region comprising at least three CDRs that are 80% identical to an amino acid sequence selected from SEQ ID NOs: 19, 21, 23, 43, 45, 47, 64, 66, 68, 88, 90, 92, 112, 114, 116, 136, 138, 140, 160, 162, 164, 184, 186, 188, 208, 210, 212, 232, 234, 236, 256, 258, 260, 280, 282, 284, 304, 306, 308, 328, 330, or 332.

~~12~~15. The antibody of any one of claims 1–~~11~~14, wherein the antibody is a monoclonal antibody.

~~13~~16. The antibody of any one of claims 1–~~11~~14, wherein the antibody is a chimeric antibody, a human antibody, or a humanized antibody.

~~14~~17. The antibody or the immunogenic fragment thereof any one of claims 1–~~11~~14, comprising the amino acid sequence selected from SEQ ID NOs: 7, 9, 11, 19, 21, 23, 31, 33, 35, 43, 45, 47, 54, 56, 64, 66, 68, 76, 78, 80, 88, 90, 92, 100, 102, 104, 112, 114, 116, 124, 126, 128, 136, 138, 140, 148, 150, 152, 160, 162, 164, 172, 174, 176, 184, 186, 188, 196, 198, 200, 208, 210, 212, 220, 222, 224, 232, 234, 236, 244, 246, 248, 256, 258, 260, 268, 270, 272, 280, 282, 284, 292, 294, 296, 304, 306, 308, 316, 318, 320, 328, 330, or 332.

~~15~~18. The antibody of claim ~~12~~15, wherein the antibody is monoclonal 8G7, monoclonal 26E10, monoclonal 26E2, monoclonal 31C4, monoclonal 34B10, monoclonal 37A3, monoclonal 12A10, monoclonal 3B7, monoclonal 11G8, monoclonal 14F8, monoclonal 15D2, monoclonal 29H7, monoclonal 30D10, or monoclonal 51C3.

~~16~~19. The antibody of claim ~~13~~16, wherein the antibody is humanized 8G7, humanized 26E10, humanized 26E2, humanized 31C4, humanized 34B10, humanized 37A3, humanized 12A10, humanized 3B7, humanized 11G8, humanized 14F8, humanized 15D2, humanized 29H7, humanized 30D10, or humanized 51C3.

~~17~~20. A fusion polypeptide comprising the antibody or the immunogenic fragment thereof of any one of claims 1–~~16~~19.

~~18~~21. A composition comprising the antibody or the immunogenic fragment thereof according to any one of claims 1–~~16~~19 or the fusion polypeptide of claim ~~17~~20.

~~19~~22. The composition of claim ~~18~~21, further comprising a pharmaceutically acceptable carrier.

~~20~~23. The composition of claim ~~18~~21 or claim ~~19~~22, further comprising a pharmaceutically acceptable excipient.

~~21. The antibody or the immunogenic fragment thereof of any one of claims 1–16, the fusion polypeptide of claim 17, or the composition of any one of claims 18–20 for use in a therapy.~~

~~24. A nucleic acid comprising a nucleic acid encoding an antibody or an immunogenic fragment thereof, wherein the antibody or the immunogenic fragment thereof is the antibody or the immunogenic fragment thereof according to any one of claims 1–19.~~

~~25. A nucleic acid comprising a nucleic acid encoding a fusion polypeptide, wherein the fusion polypeptide is the fusion polypeptide of claim 20.~~

~~22~~26. The antibody or the immunogenic fragment thereof of any one of claims 1–~~16~~19, the fusion polypeptide of claim ~~17~~20, ~~or the composition of any one of claims 18~~21–20 ~~23, or the nucleic acid of claims 24–25 for use in the production of~~as a medicament.

~~23. A nucleic acid comprising a nucleic acid encoding an antibody or an immunogenic fragment thereof, wherein the antibody or the immunogenic fragment thereof is the antibody or the immunogenic fragment thereof according to any one of claims 1–16.~~

~~24. A nucleic acid comprising a nucleic acid encoding a fusion polypeptide, wherein the fusion polypeptide is the fusion polypeptide of claim 17.~~

~~2527. A method of treating a subject having a condition, comprising administering to the subject a therapeutically effective amount of~~Use of ~~the antibody or the immunogenic fragment thereof of any one of claims 1–1619, the fusion polypeptide of claim 1720, or the composition of any one of claims 1821–2023, or the nucleic acid of claims 24-25 in the manufacture of a medicament for treating a subject having a condition.~~

~~2628. The method-use of claim 2527, wherein the subject has a condition and wherein the condition is cancer.~~

~~2729. The method-use of claim 2627, wherein the cancer is selected from the group consisting of chronic lymphocytic leukemia (CLL), acute leukemia, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell lymphoma, B-cell lymphoma, T-cell acute lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), B-cell prolymphocytic leukemia, T-cell lymphoma, Hodgkin's Disease, B-cell non-Hodgkin's lymphoma, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell follicular lymphoma, large cell follicular lymphoma, malignant lymphoproliferative conditions, mucosa-associated lymphoid tissue (MALT) lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenström macroglobulinemia, or preleukemia.~~

~~2830. The method-use of claim 2628, wherein the cancer is selected from the group consisting of colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, lung cancer, kidney cancer, gastric cancer, gallbladder cancer, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer,~~

testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, environmentally induced cancers, combinations of the cancers, and metastatic lesions of the cancers.

2931. The ~~method~~-use of claim 2628, wherein the cancer is a human hematologic malignancy.

3032. The ~~method~~-use of claim 2931, wherein the human hematologic malignancy is selected from myeloid neoplasm, acute myeloid leukemia (AML), AML with recurrent genetic abnormalities, AML with myelodysplasia-related changes, therapy-related AML, acute leukemias of ambiguous lineage, myeloproliferative neoplasm, essential thrombocythemia, polycythemia vera, myelofibrosis (MF), primary myelofibrosis, systemic mastocytosis, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, chronic myeloid leukemia, chronic neutrophilic leukemia, chronic eosinophilic leukemia, myelodysplastic syndromes (MDS), refractory anemia with ringed sideroblasts, refractory cytopenia with multilineage dysplasia, refractory anemia with excess blasts (type 1), refractory anemia with excess blasts (type 2), MDS with isolated del (5q), unclassifiable MDS, myeloproliferative/myelodysplastic syndromes, chronic myelomonocytic leukemia, atypical chronic myeloid leukemia, juvenile myelomonocytic leukemia, unclassifiable myeloproliferative/myelodysplastic syndromes, lymphoid neoplasms, precursor lymphoid neoplasms, B lymphoblastic leukemia, B lymphoblastic lymphoma, T lymphoblastic leukemia, T lymphoblastic lymphoma, mature B-cell neoplasms, diffuse large B-cell lymphoma, primary central nervous system lymphoma, primary mediastinal B-cell lymphoma, Burkitt's lymphoma/leukemia, follicular lymphoma, chronic lymphocytic leukemia, small lymphocytic lymphoma, B-cell prolymphocytic leukemia,

lymphoplasmacytic lymphoma, Waldenström macroglobulinemia, mantle cell lymphoma, marginal zone lymphomas, post-transplant lymphoproliferative disorders, HIV-associated lymphomas, primary effusion lymphoma, intravascular large B-cell lymphoma, primary cutaneous B-cell lymphoma, hairy cell leukemia, multiple myeloma, monoclonal gammopathy of unknown significance (MGUS), smoldering multiple myeloma, or solitary plasmacytomas (solitary bone and extramedullary).

~~3133~~. The ~~method-use~~ of claim ~~2628~~, wherein the cancer is a metastatic cancer.

~~3234~~. The ~~method-use~~ of claim ~~2628~~, wherein the subject is to be further subjected ~~further comprising subjecting the subject~~ to one or more additional cancer therapies selected from chemotherapy, radiation therapy, immunotherapy, surgery, and a combination thereof.

~~3335~~. The ~~method-use~~ of claim ~~2527~~, wherein the subject has a condition and wherein the condition is an infection.

~~3436~~. The ~~method-use~~ of claim ~~3335~~, wherein the infection is caused by a pathogen.

~~3537~~. The ~~method-use~~ of claim ~~3436~~, wherein the pathogen is a virus.

~~3638~~. The ~~method-use~~ of claim ~~3537~~, wherein the virus is selected from the group consisting of human immunodeficiency viruses, influenza viruses, papillomaviruses, coronaviruses, hepatitis viruses, or herpesviruses.

~~3739~~. The ~~method-use~~ of claim ~~3436~~, wherein the pathogen is a bacterium.

~~3840~~. The ~~method-use~~ of claim ~~3739~~, wherein the bacterium is mycobacterium tuberculosis.

~~3941~~. The ~~method-use~~ of claim ~~3436~~, wherein the pathogen is a prion.

~~4042~~. The ~~method-use~~ of claim ~~3436~~, wherein the pathogen is a fungus.

~~4143~~. The ~~method-use~~ of claim ~~4042~~, wherein the fungus is *Pneumocystis jirovecii* (PJP).

~~4244~~. The ~~method-use~~ of claim ~~3436~~, wherein the pathogen is a parasite.

~~4345~~. The ~~method-use~~ of claim ~~2527~~, wherein the subject has a condition and wherein the condition is an autoimmune disease or disorder.

~~4446~~. The ~~method-use~~ of claim ~~4345~~, wherein the autoimmune disease or disorder is selected from the group consisting of acute disseminated encephalomyelitis (ADEM), alopecia areata, antiphospholipid syndrome, autoimmune cardiomyopathy, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune inner ear disease, autoimmune lipoproliferative syndrome, autoimmune peripheral neuropathy, autoimmune pancreatitis, autoimmune polyendocrine syndrome, autoimmune progesterone dermatitis, autoimmune thrombocytopenic purpura, autoimmune urticarial, autoimmune uveitis, Behçet's disease, celiac disease, Chagas disease, cold agglutinin disease, Crohn's disease, dermatomyositis, diabetes mellitus type 1, eosinophilic fasciitis, gastrointestinal pemphigoid, Goodpasture's syndrome, Grave's syndrome, Guillain-Barré syndrome, Hashimoto's encephalopathy, Hashimoto's thyroiditis, lupus erythematosus, Miller-Fisher syndrome, mixed connective tissue disease, myasthenia gravis, pemphigus vulgaris, pernicious anemia, polymyositis, psoriasis, psoriatic arthritis, relapsing polychondritis, rheumatoid arthritis, rheumatic fever, Sjögren's syndrome, temporal arteritis, transverse myelitis, ulcerative colitis, undifferentiated connective tissue disease, vasculitis, and Wegener's granulomatosis.

~~4547~~. The ~~method-use~~ of claim ~~4345~~, wherein the autoimmune disease or disorder is adult rheumatoid arthritis.

~~4648~~. The ~~method-use~~ of claim ~~2527~~, wherein the subject has a condition and wherein the condition is a transplant.

4749. The ~~method~~use of claim 4648, wherein the transplant is selected from a stem cell transplant or a bone marrow transplant.

4850. The ~~method~~use of claim 4648, wherein the transplant is selected from the group consisting of a kidney transplant, a lung transplant, a heart transplant, a pancreas transplant, a cornea transplant, or a liver transplant.

~~49. The composition of any one of claims 18–20 for use in treating a subject having a condition.~~

~~50. The composition of claim 49, wherein the condition is cancer.~~

~~51. The composition of claim 50, wherein the cancer is selected from the group consisting of chronic lymphocytic leukemia (CLL), acute leukemia, acute lymphoid leukemia (ALL), B-cell acute lymphoid leukemia (B-ALL), T-cell lymphoma, B-cell lymphoma, T-cell acute lymphoid leukemia (T-ALL), chronic myelogenous leukemia (CML), B-cell prolymphocytic leukemia, T-cell lymphoma, Hodgkin's Disease, B-cell non-Hodgkin's lymphoma, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell follicular lymphoma, large cell follicular lymphoma, malignant lymphoproliferative conditions, mucosa-associated lymphoid tissue (MALT) lymphoma, mantle cell lymphoma, marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenström macroglobulinemia, or preleukemia.~~

~~52. The composition of claim 50, wherein the cancer is selected from the group consisting of colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, lung cancer, kidney cancer, gastric cancer, gallbladder cancer, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the~~

~~endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, environmentally induced cancers, combinations of the cancers, and metastatic lesions of the cancers.~~

53.—The composition of claim 50, wherein the cancer is a human hematologic malignancy.

54.—The composition of claim 53, wherein the human hematologic malignancy is selected from ~~myeloid neoplasm, acute myeloid leukemia (AML), AML with recurrent genetic abnormalities, AML with myelodysplasia related changes, therapy related AML, acute leukemias of ambiguous lineage, myeloproliferative neoplasm, essential thrombocythemia, polycythemia vera, myelofibrosis (MF), primary myelofibrosis, systemic mastocytosis, myelodysplastic syndromes (MDS), myeloproliferative/myelodysplastic syndromes, chronic myeloid leukemia, chronic neutrophilic leukemia, chronic eosinophilic leukemia, myelodysplastic syndromes (MDS), refractory anemia with ringed sideroblasts, refractory cytopenia with multilineage dysplasia, refractory anemia with excess blasts (type 1), refractory anemia with excess blasts (type 2), MDS with isolated del (5q), unclassifiable MDS, myeloproliferative/myelodysplastic syndromes, chronic myelomonocytic leukemia, atypical chronic myeloid leukemia, juvenile myelomonocytic leukemia, unclassifiable myeloproliferative/myelodysplastic syndromes, lymphoid neoplasms, precursor lymphoid neoplasms, B lymphoblastic leukemia, B lymphoblastic lymphoma, T lymphoblastic leukemia, T lymphoblastic lymphoma, mature B-cell neoplasms, diffuse large B-cell lymphoma, primary central nervous system lymphoma, primary mediastinal B-cell lymphoma, Burkitt's lymphoma/leukemia, follicular lymphoma, chronic lymphocytic leukemia, small lymphocytic lymphoma, B-cell prolymphocytic leukemia, lymphoplasmacytic lymphoma, Waldenström macroglobulinemia, mantle cell~~

~~lymphoma, marginal zone lymphomas, post-transplant lymphoproliferative disorders, HIV-associated lymphomas, primary effusion lymphoma, intravascular large B-cell lymphoma, primary cutaneous B-cell lymphoma, hairy cell leukemia, multiple myeloma, monoclonal gammopathy of unknown significance (MGUS), smoldering multiple myeloma, or solitary plasmacytomas (solitary bone and extramedullary).~~

~~55.—The composition of claim 50, wherein the cancer is a metastatic cancer.~~

~~56.—The composition of claim 50, wherein the composition is co-administered to the subject with one or more additional cancer therapies selected from chemotherapy, radiation therapy, immunotherapy, surgery, and a combination thereof.~~

~~57.—The composition of claim 49, wherein the condition is an infection.~~

~~58.—The composition of claim 57, wherein the infection is caused by a pathogen.~~

~~59.—The composition of claim 58, wherein the pathogen is a virus.~~

~~60.—The composition of claim 59, wherein the virus is selected from the group consisting of human immunodeficiency viruses, influenza viruses, papillomaviruses, coronaviruses, hepatitis viruses, or herpesviruses.~~

~~61.—The composition of claim 58, wherein the pathogen is a bacterium.~~

~~62.—The composition of claim 61, wherein the bacterium is mycobacterium tuberculosis.~~

~~63.—The composition of claim 58, wherein the pathogen is a prion.~~

~~64.—The composition of claim 58, wherein the pathogen is a fungus.~~

~~65.—The composition of claim 64, wherein the fungus is *Pneumocystis jirovecii* (PJP).~~

~~66.—The composition of claim 58, wherein the pathogen is a parasite.~~

~~67.—The composition of claim 49, wherein the condition is an autoimmune disease or disorder.~~

~~68.—The composition of claim 67, wherein the autoimmune disease or disorder is selected from the group consisting of acute disseminated encephalomyelitis (ADEM), alopecia areata, antiphospholipid syndrome, autoimmune cardiomyopathy, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune inner ear disease, autoimmune lipoproliferative syndrome, autoimmune peripheral neuropathy, autoimmune pancreatitis, autoimmune polyendocrine syndrome, autoimmune progesterone dermatitis, autoimmune thrombocytopenic purpura, autoimmune urticarial, autoimmune uveitis, Behçet's disease, celiac disease, Chagas disease, cold agglutinin disease, Crohn's disease, dermatomyositis, diabetes mellitus type 1, eosinophilic fasciitis, gastrointestinal pemphigoid, Goodpasture's syndrome, Grave's syndrome, Guillain-Barré syndrome, Hashimoto's encephalopathy, Hashimoto's thyroiditis, lupus erythematosus, Miller-Fisher syndrome, mixed connective tissue disease, myasthenia gravis, pemphigus vulgaris, pernicious anemia, polymyositis, psoriasis, psoriatic arthritis, relapsing polychondritis, rheumatoid arthritis, rheumatic fever, Sjögren's syndrome, temporal arteritis, transverse myelitis, ulcerative colitis, undifferentiated connective tissue disease, vasculitis, and Wegener's granulomatosis.~~

~~69.—The composition of claim 67, wherein the autoimmune disease or disorder is adult rheumatoid arthritis.~~

~~70.—The composition of claim 49, wherein the condition is a transplant.~~

~~71.—The composition of claim 70, wherein the transplant is selected from a stem cell transplant or a bone marrow transplant.~~

72.—~~The composition of claim 70, wherein the transplant is selected from the group consisting of a kidney transplant, a lung transplant, a heart transplant, a pancreas transplant, a cornea transplant, or a liver transplant.~~