

CLAIMS

What is claimed is:

1. An antibody or an immunogenic fragment thereof that specifically binds to KIR3DL3 protein.
2. The antibody or the immunogenic fragment thereof of claim 1, wherein the antibody or the immunogenic fragment thereof specifically binds to a KIR3DL3 epitope comprising the whole extracellular domain or a portion thereof.
3. The antibody or the immunogenic fragment of claim 2, wherein the antibody or the immunogenic fragment thereof binds to the KIR3DL3 D0 domain, the KIR3DL3 D1 domain, or KIR3DL3 D2 domain.
4. The antibody or immunogenic fragment thereof of claim 1 or claim 2, 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.
5. The antibody or immunogenic fragment thereof of claim 1 or claim 2, 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.
6. The antibody or immunogenic fragment thereof of claim 1 or claim 2, 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.

7. The antibody or immunogenic fragment thereof of claim 1 or claim 2, 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.

8. The antibody or immunogenic fragment thereof of claim 1 or claim 2, 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.

9. The antibody or immunogenic fragment thereof of claim 1 or claim 2, 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.

10. The antibody or immunogenic fragment thereof of claim 1 or claim 2, 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. The antibody or immunogenic fragment thereof of claim 1 or claim 2, 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. The antibody of any one of claims 1–11, wherein the antibody is a monoclonal antibody.

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

14. The antibody or the immunogenic fragment thereof any one of claims 1–11, 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. The antibody of claim 12, 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. The antibody of claim 13, 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. A fusion polypeptide comprising the antibody or the immunogenic fragment thereof of any one of claims 1–16.

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

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

20. The composition of claim 18 or claim 19, 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.

22. 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 the production of 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.

25. A method of treating a subject having a condition, comprising administering to the subject a therapeutically effective amount of 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.

26. The method of claim 25, wherein the subject has a condition and wherein the condition is cancer.

27. The method of claim 26, 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.

28. The method of claim 26, 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.

29. The method of claim 26, wherein the cancer is a human hematologic malignancy.

30. The method of claim 29, 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).

31. The method of claim 26, wherein the cancer is a metastatic cancer.

32. The method of claim 26, further comprising subjecting the subject to one or more additional cancer therapies selected from chemotherapy, radiation therapy, immunotherapy, surgery, and a combination thereof.

33. The method of claim 25, wherein the subject has a condition and wherein the condition is an infection.

34. The method of claim 33, wherein the infection is caused by a pathogen.

35. The method of claim 34, wherein the pathogen is a virus.

36. The method of claim 35, wherein the virus is selected from the group consisting of human immunodeficiency viruses, influenza viruses, papillomaviruses, coronaviruses, hepatitis viruses, or herpesviruses.

37. The method of claim 34, wherein the pathogen is a bacterium.

38. The method of claim 37, wherein the bacterium is mycobacterium tuberculosis.

39. The method of claim 34, wherein the pathogen is a prion.

40. The method of claim 34, wherein the pathogen is a fungus.

41. The method of claim 40, wherein the fungus is *Pneumocystis jirovecii* (PJP).

42. The method of claim 34, wherein the pathogen is a parasite.

43. The method of claim 25, wherein the subject has a condition and wherein the condition is an autoimmune disease or disorder.

44. The method of claim 43, 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.

45. The method of claim 43, wherein the autoimmune disease or disorder is adult rheumatoid arthritis.

46. The method of claim 25, wherein the subject has a condition and wherein the condition is a transplant.

47. The method of claim 46, wherein the transplant is selected from a stem cell transplant or a bone marrow transplant.

48. The method of claim 46, 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.