

[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 refers to an anti-KIR3DL3 antibody or an antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises: a) a VH region comprising 3 CDRs having an amino acid sequence of SEQ ID NOs: 31, 33, and 35; and b) a VL region comprising 3 CDRs having an amino acid sequence of SEQ ID NOs: 43, 45, and 47.

[0006] In another example, the disclosure refers to an antibody or an immunogenic fragment thereof that specifically binds to KIR3DL3 protein (SEQ ID NO: 335). In certain examples, 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 examples, 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 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,

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

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

[0017] In one example, 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 example, 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 example, 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 the anti-KIR3DL3 antibody or the antigen-binding fragment thereof according to the present disclosure are provided.

[0021] In certain aspects, compositions comprising the anti-KIR3DL3 antibody or an antigen-binding fragment thereof or fusion proteins according the present disclosure are provided.

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

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

[0024] In certain 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 examples, antibodies or immunogenic fragments thereof, fusion polypeptides, or compositions according to the present disclosure for use in a therapy are provided.

[0026] In certain examples, 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, the present disclosure refers to nucleic acids comprising a nucleic acid encoding an anti-KIR3DL3 antibody or an antigen-binding 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 one aspect, the present disclosure refers to the use of the anti-KIR3DL3 antibody or the antigen-binding fragment thereof as described herein, the fusion polypeptide as described herein, or the composition as described herein, or the nucleic acid as described herein in the manufacture of a medicament for treating a subject having cancer. In certain 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 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, 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

CLAIMS

What is claimed is:

1. An anti-KIR3DL3 antibody or an antigen binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises:

a) a VH region comprising 3 CDRs having an amino acid sequence of SEQ ID NOs: 31, 33, and 35; and

b) a VL region comprising 3 CDRs having an amino acid sequence of SEQ ID NOs: 43, 45, and 47.

2. The anti-KIR3DL3 antibody or the antigen binding 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 anti-KIR3DL3 antibody of claim 1, wherein the antibody is a monoclonal antibody.

4. The anti-KIR3DL3 antibody of claim 1, wherein the antibody is a chimeric antibody or a humanized antibody.

5. A fusion polypeptide comprising the anti-KIR3DL3 antibody or the antigen-binding fragment thereof of claim 1.

6. A composition comprising the anti-KIR3DL3 antibody or the antigen-binding fragment thereof according to claim 1 or the fusion polypeptide of claim 5.

7. The composition of claim 6, further comprising a pharmaceutically acceptable carrier.

8. The composition of claim 7, further comprising a pharmaceutically acceptable excipient.

9. A nucleic acid comprising a nucleic acid encoding an anti-KIR3DL3 antibody or an antigen-binding fragment thereof of claim 1.

10. A nucleic acid comprising a nucleic acid encoding a fusion polypeptide, wherein the fusion polypeptide is the fusion polypeptide of claim 5.

11. The anti-KIR3DL3 antibody or the antigen-binding fragment thereof of claim 1, the fusion polypeptide of claim 5, the composition of any one of claims 6-8, or the nucleic acid of claims 9-10 for use as a medicament.

12. Use of the anti-KIR3DL3 antibody or the antigen-binding fragment thereof of claim 1, the fusion polypeptide of claim 5, the composition of any one of claims 6-8, or the nucleic acid of claims 9-10 in the manufacture of a medicament for treating a subject having cancer.

13. The use of claim 12, 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.

14. The use of claim 12, 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.

15. The use of claim 12, wherein the cancer is a human hematologic malignancy, 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).

16. The use of claim 12, wherein the cancer is a metastatic cancer.

17. The use of claim 12, wherein the subject is to be further subjected to one or more additional cancer therapies selected from chemotherapy, radiation therapy, immunotherapy, surgery, and a combination thereof.