FCRL1. It is known that binding an immunotoxin to an anti-FCRL1 antibody exerts cellular cytotoxicity against a cancer cell line (Non-Patent Literature 4).

CITATION LIST

PATENT LITERATURE

[0006] Patent Literature 1: WO2005/097185

Patent Literature 2: US Patent Application Publication No. 2006/0216232

Patent Literature 3: WO2006/037048

NON-PATENT LITERATURE

[0007] Non-Patent Literature 1: Davis RS., et al. "Identification of a family of Fc receptor homologs with preferential B cell expression" Proceedings of the National Academy of Sciences of the United States of America 98. 17 (2001): 9772-9777.

Non-Patent Literature 2: Du X., et al. "FCRL1 on chronic lymphocytic leukemia, hairy cell leukemia, and B-cell non-Hodgkin lymphoma as a target of immunotoxins" Blood 111. 1 (2008): 338-343.

Non-Patent Literature 3: Auat M., et al. "Evaluation of CD307a expression patterns during normal B-cell maturation and in B-cell malignancies by flow cytometry" Cytometry Part B: Clinical Cytometry 94. 4 (2018): 588-595.

Non-Patent Literature 4: Yousefi Z., et al. "Fc Receptor-Like 1 as a Promising Target for Immunotherapeutic Interventions of B-Cell-Related Disorders" Biomarker Insights 14 (2018): 1-9.

SUMMARY

TECHNICAL PROBLEM

[0008] An object of the present disclosure is to provide a novel monoclonal antibody or an antibody fragment thereof that binds to an extracellular region of FCRL1, a hybridoma that produces the antibody, a nucleic acid comprising a nucleotide sequence that encodes the antibody or the antibody fragment thereof, a transformed cell obtained by introducing a vector comprising the nucleic acid into a host cell, a method for producing the antibody or the antibody fragment thereof using the hybridoma or the transformed cell, an antibody-drug conjugate comprising the antibody or the antibody fragment thereof, a therapeutic agent and a diagnostic

agent, each of which comprises the antibody or the antibody fragment thereof, and a therapeutic method and a diagnostic method for a disease associated with FCRL1 using the antibody, the antibody fragment thereof, or the antibody-drug conjugate comprising the antibody or the antibody fragment thereof.

SOLUTION TO PROBLEM

[0009] The present disclosure relates to the following 1 to 26.

1. An antibody or an antibody fragment thereof, which is a monoclonal antibody or an antibody fragment thereof that binds to Fc receptor-like protein 1 (hereinafter, abbreviated as FCRL1), in which

the antibody is any one antibody selected from the following (a) to (g):

(a) an antibody in which complementarity determining regions (hereinafter, abbreviated as CDR) 1 to 3 of a heavy chain variable region (hereinafter, abbreviated as VH) comprise the amino acid sequences represented by SEQ ID NOs: 20 to 22, respectively, and CDRs 1 to 3 of a light chain variable region (hereinafter, abbreviated as VL) comprise the amino acid sequences represented by SEQ ID NOs: 24 to 26, respectively,

(b) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 28 to 30, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 32 to 34, respectively,

(c) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 36 to 38, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 40 to 42, respectively,

(d) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 44 to 46, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 48 to 50, respectively,

(e) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 52 to 54, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 56 to 58, respectively, and

(f) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 60 to 62, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 64 to 66, respectively, and

(g) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 36 to 38, respectively, and CDRs 1 to 3 of a VL comprise the

the antibody or the antibody fragment thereof according to any one of the above 1 to 7, or the antibody-drug conjugate according to the above 13 or 14.

20. The therapeutic agent according to the above 19, in which

the disease associated with FCRL1 is cancer, an autoimmune disease, or an inflammatory disease.

21. A diagnostic method for a disease associated with FCRL1, including:

using the antibody or the antibody fragment thereof according to any one of the above 1 to 7, or the antibody-drug conjugate according to the above 13 or 14.

22. A therapeutic method for a disease associated with FCRL1, including:

administering the antibody or the antibody fragment thereof according to any one of the above 1 to 7, or the antibody-drug conjugate according to the above 13 or 14.

23. Use of the antibody or the antibody fragment thereof according to any one of the above 1 to 7, or the antibody-drug conjugate according to the above 13 or 14, for manufacturing a diagnostic agent for a disease associated with FCRL1.

24. Use of the antibody or the antibody fragment thereof according to any one of the above 1 to 7, or the antibody-drug conjugate according to the above 13 or 14, for manufacturing a therapeutic agent for a disease associated with FCRL1.

25. Use of the antibody or the antibody fragment thereof according to any one of the above 1 to 7, or the antibody-drug conjugate according to the above 13 or 14, for use as a diagnostic agent for a disease associated with FCRL1.

26. Use of the antibody or the antibody fragment thereof according to any one of the above 1 to 7, or the antibody-drug conjugate according to the above 13 or 14, for use as a therapeutic agent for a disease associated with FCRL1.

[0009a] In one aspect, the present disclosure refers to an antibody or an antibody fragment thereof, which is a monoclonal antibody or an antibody fragment thereof that binds to Fc receptor-like protein 1 (hereinafter, abbreviated as FCRL1), wherein

the antibody is any one antibody selected from the following (a) to (g):

(a) an antibody in which complementarity determining regions (hereinafter, abbreviated as CDR) 1 to 3 of a heavy chain variable region (hereinafter, abbreviated as VH) comprise the amino acid sequences represented by SEQ ID NOs: 20 to 22, respectively, and CDRs 1 to 3 of a light chain variable region (hereinafter, abbreviated as VL) comprise the amino acid sequences represented by SEQ ID NOs: 24 to 26, respectively,

(b) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 28 to 30, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 32 to 34, respectively,

(c) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 36 to 38, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 40 to 42, respectively,

(d) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 44 to 46, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 48 to 50, respectively,

(e) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 52 to 54, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 56 to 58, respectively, and

(f) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 60 to 62, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 64 to 66, respectively, and

(g) an antibody in which CDRs 1 to 3 of a VH comprise the amino acid sequences represented by SEQ ID NOs: 36 to 38, respectively, and CDRs 1 to 3 of a VL comprise the amino acid sequences represented by SEQ ID NOs: 40, 71, and 42, respectively.

[0009b] In one aspect, the present disclosure refers to an antibody or an antibody fragment thereof, which is a monoclonal antibody or an antibody fragment thereof that binds to FCRL1, wherein

the antibody is any one antibody selected from the following (2b-1) to (2b-4), (2c-1), (2c-2), and (2g-1):

(2b-1) an antibody in which a VH comprises the amino acid sequence represented by SEQ ID NO: 72 and a VL comprises the amino acid sequence represented by SEQ ID NO: 68,

(2b-2) an antibody in which a VH comprises the amino acid sequence represented by SEQ ID NO: 73 and a VL comprises the amino acid sequence represented by SEQ ID NO: 74,

(2b-3) an antibody in which a VH comprises the amino acid sequence represented by SEQ ID NO: 72 and a VL comprises the amino acid sequence represented by SEQ ID NO: 74,

(2b-4) an antibody in which a VH comprises the amino acid sequence represented by SEQ ID NO: 73 and a VL comprises the amino acid sequence represented by SEQ ID NO: 68,

(2c-1) an antibody in which a VH comprises the amino acid sequence represented by SEQ ID NO: 75 and a VL comprises the amino acid sequence represented by SEQ ID NO: 76,

(2c-2) an antibody in which a VH comprises the amino acid sequence represented by SEQ ID NO: 77 and a VL comprises the amino acid sequence represented by SEQ ID NO: 76, and

(2g-1) an antibody in which a VH comprises the amino acid sequence represented by SEQ ID NO: 77 and a VL comprises the amino acid sequence represented by SEQ ID NO: 78.

[0009c] In one aspect, the present disclosure refers to a hybridoma that produces the antibody as disclosed herein.

[0009d] In one aspect, the present disclosure refers to a nucleic acid comprising a nucleotide sequence that encodes the antibody or the antibody fragment thereof as disclosed herein.

[0009e] In one aspect, the present disclosure refers to a vector comprising the nucleic acid as disclosed herein.

[0009f] In one aspect, the present disclosure refers to a transformed cell obtained by introducing the vector as disclosed herein into a host cell.

[0009g] In one aspect, the present disclosure refers to a method for producing the antibody or the antibody fragment thereof as disclosed herein, comprising: culturing the hybridoma as disclosed herein or the transformed cell as disclosed herein in a medium, and collecting the antibody or the antibody fragment thereof from a culture.

[0009h] In one aspect, the present disclosure refers to an antibody-drug conjugate comprising: the antibody or the antibody fragment thereof as disclosed herein.

[0009i] In one aspect, the present disclosure refers to a composition comprising: the antibody or the antibody fragment thereof as disclosed herein, or the antibody-drug conjugate as disclosed herein.

[0009j] In one aspect, the present disclosure refers to a reagent for detecting or measuring FCRL1, comprising: the antibody or the antibody fragment thereof as disclosed herein, or the antibody-drug conjugate as disclosed herein.

[0009k] In one aspect, the present disclosure refers to a diagnostic agent for a disease associated with FCRL1, comprising: the antibody or the antibody fragment thereof as disclosed herein, or the antibody-drug conjugate as disclosed herein.

[0009l] In one aspect, the present disclosure refers to a therapeutic agent for a disease associated with FCRL1, comprising: the antibody or the antibody fragment thereof as disclosed herein, or the antibody-drug conjugate as disclosed herein.

[0009m] In one aspect, the present disclosure refers to use of the antibody or the antibody fragment thereof as disclosed herein, or the antibody-drug conjugate as disclosed herein, in the

manufacture of a diagnostic agent for diagnosing a disease associated with FCRL1.

[0009n] In one aspect, the present disclosure refers to use of the antibody or the antibody fragment thereof as disclosed herein, or the antibody-drug conjugate as disclosed herein, in the manufacture of a therapeutic agent for treating a disease associated with FCRL1.

[0009o] In one aspect, the present disclosure refers to the antibody or the antibody fragment thereof as disclosed herein, or the antibody-drug conjugate as disclosed herein, for use as a diagnostic agent for a disease associated with FCRL1.

[0009p] In one aspect, the present disclosure refers to the antibody or the antibody fragment thereof as disclosed herein, or the antibody-drug conjugate as disclosed herein, for use as a therapeutic agent for a disease associated with FCRL1.

ADVANTAGEOUS EFFECTS OF DISCLOSURE

[0010] The monoclonal antibody or the antibody fragment thereof of the present disclosure selectively binds to an extracellular region of human FCRL1. In particular, the monoclonal antibody or the antibody fragment thereof of the present disclosure exhibits an excellent effect when used in an antibody-drug conjugate (hereinafter, also referred to as ADC), as compared with an existing FCRL1 antibody. Therefore, the monoclonal antibody or the antibody fragment thereof of the present disclosure can be used as a therapeutic agent or a diagnostic agent for a disease associated with human FCRL1.