

CLAIMS

[Claim 1]

A bispecific antibody, which binds to a transferrin receptor (TfR) and a cell surface antigen, including an IgG portion that binds to TfR and an N-terminal side polypeptide that binds to the cell surface antigen, wherein the N-terminal side polypeptide binds directly or through a linker to the N terminus of a heavy chain of the IgG portion,

wherein the IgG portion includes one VH selected from the following (ai) to (ci), and VL having CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOS: 17 to 19, respectively:

(ai) VH having CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOS: 32 to 34, respectively;

(bi) VH having CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOS: 42 to 44, respectively; and

(ci) VH having CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOS: 47 to 49, respectively

wherein the cell surface antigen is EGFR, and

wherein the N-terminal side polypeptide is Fab of an antibody against EGFR, and the antibody is an antibody including VH having CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOS: 60 to 62, respectively, or SEQ ID NOS: 65 to 67, respectively, and VL having CDRs 1 to 3 containing the amino acid sequences represented by SEQ ID NOS: 17 to 19, respectively.

[Claim 2]

The bispecific antibody according to claim 1, which divalently binds to each of the TfR and the cell surface antigen.

[Claim 3]

The bispecific antibody according to claim 1 or 2, wherein the IgG portion includes VH containing the amino acid sequence represented by any one of SEQ ID NOS: 31, 41, and 46, and VL containing the amino acid sequence represented by SEQ ID NO: 16.

[Claim 4]

The bispecific antibody according to any one of claims 1 to 3, wherein a heavy chain constant region of the IgG portion contains the amino acid sequence represented by SEQ ID NO: 84 or SEQ ID NO: 86.

5 [Claim 5]

The bispecific antibody according to any one of claims 1 to 4, wherein the antibody against EGFR is an antibody of the following (a):

(a) an antibody including VH containing the amino acid sequence represented by SEQ ID NO: 59 or SEQ ID NO: 64 and VL containing the amino acid sequence represented
10 by SEQ ID NO: 16.

[Claim 6]

The bispecific antibody according to any one of claims 1 to 5, wherein the heavy chain C terminus of the Fab directly binds to the heavy chain N terminus of the IgG portion.

[Claim 7]

15 The bispecific antibody according to any one of claims 1 to 5, wherein the heavy chain C terminus of the Fab binds to the heavy chain N terminus of the IgG portion through the linker.

[Claim 8]

20 The bispecific antibody according to claim 7, wherein the amino acid sequence of the linker is composed of part or all of the amino acid sequence of a hinge region of IgG.

[Claim 9]

The bispecific antibody according to any one of claims 1 to 8, wherein the Fab and the IgG portion each include a light chain composed of the same amino acid sequence.

[Claim 10]

25 A bispecific antibody, which divalently binds to each of a transferrin receptor (TfR) and a cell surface antigen, including an IgG portion that binds to TfR and an N-terminal side polypeptide that binds to the cell surface antigen, wherein the N-terminal side polypeptide directly binds to the N terminus of a heavy chain of the IgG portion,

wherein the IgG portion includes VH containing the amino acid sequence
30 represented by SEQ ID NO: 31 and VL containing the amino acid sequence represented by SEQ ID NO: 16,

wherein the cell surface antigen is EGFR, and

wherein the N-terminal side polypeptide is Fab of an antibody against EGFR, and the antibody is an antibody including VH containing the amino acid sequence represented by SEQ ID NO: 64 and VL containing the amino acid sequence represented by SEQ ID NO: 16.
[Claim 11]

5 A bispecific antibody, which divalently binds to each of a transferrin receptor (TfR) and a cell surface antigen, including an IgG portion that binds to TfR and an N-terminal side polypeptide that binds to the cell surface antigen, wherein the N-terminal side polypeptide directly binds to the N terminus of a heavy chain of the IgG portion,

 wherein the IgG portion includes VH containing the amino acid sequence
10 represented by SEQ ID NO: 41 and VL containing the amino acid sequence represented by SEQ ID NO: 16,

 wherein the cell surface antigen is EGFR, and

 wherein the N-terminal side polypeptide is Fab of an antibody against EGFR, and the antibody is an antibody including VH containing the amino acid sequence represented by
15 SEQ ID NO: 59 and VL containing the amino acid sequence represented by SEQ ID NO: 16.
[Claim 12]

 A bispecific antibody, which divalently binds to each of a transferrin receptor (TfR) and a cell surface antigen, including an IgG portion that binds to TfR and an N-terminal side polypeptide that binds to the cell surface antigen, wherein the N-terminal side polypeptide
20 directly binds to the N terminus of a heavy chain of the IgG portion,

 wherein the IgG portion includes VH containing the amino acid sequence represented by SEQ ID NO: 41 and VL containing the amino acid sequence represented by SEQ ID NO: 16,

 wherein the cell surface antigen is EGFR, and

25 wherein the N-terminal side polypeptide is Fab of an antibody against EGFR, and the antibody is an antibody including VH containing the amino acid sequence represented by SEQ ID NO: 64 and VL containing the amino acid sequence represented by SEQ ID NO: 16.
[Claim 13]

 A DNA encoding the bispecific antibody according to any one of claims 1 to 12.

30 [Claim 14]

 A recombinant vector comprising the DNA according to claim 13.

[Claim 15]

A transformant, obtainable by introducing the recombinant vector according to claim 14 into a host cell.

[Claim 16]

5 A method for producing the bispecific antibody according to any one of claims 1 to 12, comprising culturing the transformant according to claim 15 in a culture medium, allowing the transformant to produce and accumulate the bispecific antibody according to any one of claims 1 to 12 in a culture, and collecting the bispecific antibody from the culture.

[Claim 17]

10 The bispecific antibody according to any one of claims 1 to 12 for use in therapy and/or diagnosis for a disease associated with at least one of human TfR and a cell surface antigen.

[Claim 18]

15 The bispecific antibody according to claim 17, wherein the disease associated with at least one of human TfR and a cell surface antigen is cancer.

[Claim 19]

20 Use of the bispecific antibody according to any one of claims 1 to 12 in the manufacture of a medicament for treating a disease associated with at least one of human TfR and a cell surface antigen, wherein the disease associated with at least one of human TfR and a cell surface antigen is cancer.

[Claim 20]

A reagent for detecting or measuring at least one of human TfR and a cell surface antigen, comprising the bispecific antibody according to any one of claims 1 to 12.