# Claims

[Claim 1]

A bispecific antibody comprising a first domain which specifically binds to a mutant calreticulin protein and a second domain which specifically binds to a CD3 antigen.

[Claim 2]

The bispecific antibody according to claim 1, wherein the first domain competes with an antibody which binds to an epitope of a mutant calreticulin protein of SEQ ID NO: 1.

[Claim 3]

The bispecific antibody according to claim 1 or 2, wherein the mutant calreticulin protein has an antigen-recognition site in a polypeptide chain consisting of the amino acid sequence of SEQ ID NO: 1 or a polypeptide chain consisting of an amino acid sequence of SEQ ID NO: 1 but having deletion, substitution, or addition of one or several amino acids.

[Claim 4]

The bispecific antibody according to any one of claims 1 to 3, wherein the first domain does not bind to a wild-type calreticulin protein but has high affinity to the mutant calreticulin protein.

[Claim 5]

The bispecific antibody according to any one of claims 1 to 4, wherein the first domain has a high affinity to a mutant calreticulin protein after cleavage.

[Claim 6]

The bispecific antibody according to any one of claims 1 to 5, wherein binding of the first domain with the mutant calreticulin protein has a $K_D$ of $10^{-7}$ M or less.

[Claim 7]

The bispecific antibody according to any one of claims 1 to 6, wherein a CDR of the first domain has (a) an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 10, SEQ ID NO: 11 or 126, and SEQ ID NO: 12 (VHCDR) and an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 13, SEQ ID NO: 14 or 127, and SEQ ID NO: 15 (VLCDR); (b) an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 16 to 18 (VHCDR) and an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 19 to 21 (VLCDR); or (c) an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 22 to 24 (VHCDR) and an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 25 to 27 (VLCDR).

[Claim 8]

The bispecific antibody according to any one of claims 1 to 7, wherein the first domain has (d) a VH region having an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 2, 90, 91, 92, 93, 94, 133, 134, 135, and 136, and a VL region having an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 3, 95, 96, 97, 98, 99, 137, 138, 139, 140, and 141; (e) a VH region having an amino acid sequence having 80% or more homology to the amino acid sequence of SEQ ID NO: 4, and a VL region having an amino acid sequence having 80% or more homology to the amino acid sequence of SEQ ID NO: 5; or (f)a VH region having an amino acid sequence having 80% or more homology to the amino acid sequence of SEQ ID NO: 6, and a VL region having an amino acid sequence having 80% or more homology to the amino acid sequence of SEQ ID NO: 7.

[Claim 9]

The bispecific antibody according to any one of claims 1 to 8, wherein a CDR of the second domain has an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 28, SEQ ID NO: 29 or 128, and SEQ ID NO: 30, 129 or 130 (VHCDR), and an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 31 or 131, SEQ ID NO: 32 or 132, and SEQ ID NO: 33 (VLCDR).

[Claim 10]

The bispecific antibody according to any one of claims 1 to 9, wherein the second domain has a VH region having an amino acid sequence having 80% or more homology to the amino acid sequences of SEQ ID NO: 8, SEQ ID NO: 204, SEQ ID NO: 205, and 206, and a VL region having an amino acid sequence having 80% or more homology to the amino acid sequences of in SEQ ID NO: 9, SEQ ID NO: 207, and 208.

[Claim 11]

The bispecific antibody according to any one of claims 1 to 10, wherein a dimerization module is a hetero-H chain having one or more knob-into-hole structures, wherein an amino acid(s) at one or more positions selected from the group consisting of 349, 354, 366, 368, and 407 in a constant region of the H chain are replaced by Y349C, T366S, L368A, Y407V (hole or cavity), S354C, or T366W (knob or protrusion), the bispecific antibody comprising an Fc region of SEQ ID NO: 209 or 210.

[Claim 12]

The bispecific antibody according to any one of claims 1 to 11, comprising a mutated Fc region of SEQ ID NO: 211 with substitution of an amino acid(s) at one or more positions selected from the group consisting of 234 and 235 in a H-chain Fc region to each introduce L234A or L235A mutation.

[Claim 13]

The bispecific antibody according to any one of claims 1 to 12, which is a human antibody, a humanized antibody, a chimeric antibody of an animal-derived antibody and a human antibody, or a synthetic antibody.

[Claim 14]

A pharmaceutical composition comprising the bispecific antibody according to any one of claims 1 to 13 or a functional fragment thereof.

[Claim 15]

The pharmaceutical composition according to claim 14, which is a pharmaceutical composition for use in the treatment or diagnosis of a myeloproliferative neoplasm.

[Claim 16]

A method for detecting a mutant calreticulin protein, comprising detecting the following polypeptide (A) or (B) in a biological sample using the bispecific antibody according to any one of claims 1 to 13 or a functional fragment thereof:

(A) a polypeptide consisting of the amino acid sequence of SEQ ID NO: 1; or

(B) a polypeptide consisting of the amino acid sequence of SEQ ID NO: 1 but having deletion, substitution, or addition of one or several amino acids.

[Claim 17]

The bispecific antibody according to any one of claims 1 to 13 or a functional fragment thereof, for use in detection of a mutant calreticulin protein.

[Claim 18]

A diagnostic method for a myeloproliferative neoplasm, comprising detecting the following polypeptide (A) or (B) in a biological sample using the bispecific antibody according to any one of claims 1 to 13 or a functional fragment thereof:

(A) a polypeptide consisting of the amino acid sequence of SEQ ID NO: 1; or

(B) a polypeptide consisting of the amino acid sequence of SEQ ID NO: 1 but having deletion, substitution, or addition of one or several amino acids.

[Claim 19]

The bispecific antibody according to any one of claims 1 to 13 or a functional fragment thereof, for use in the treatment or diagnosis of a myeloproliferative neoplasm.

[Claim 20]

Use of the bispecific antibody according to any one of claims 1 to 13 or a functional fragment thereof, for producing a medicament for the treatment or diagnosis of a myeloproliferative neoplasm.

[Claim 21]

Use of the bispecific antibody according to any one of claims 1 to 13 or a functional fragment thereof for producing a medicament for the prevention or treatment of tumor, wherein the medicament is to be administered.

[Claim 22]

The use according to claim 21, wherein the tumor is a hematologic tumor, and preferably a myeloproliferative neoplasm, myeloid leukemia, thrombocytosis, polycythemia, primary myelofibrosis, or secondary myelofibrosis.