Claims

[Claim 1] An anti-human Tie2 antibody or an antigen-binding fragment thereof, comprising four heavy chain variable regions and four light chain variable regions, wherein

the heavy chain variable region comprises CDR1 consisting of the amino acid sequence of the amino acid numbers 31 to 35 of SEQ ID NO: 2, CDR2 consisting of the amino acid sequence of the amino acid numbers 50 to 66 of SEQ ID NO: 2, and CDR3 consisting of the amino acid sequence of the amino acid numbers 99 to 111 of SEQ ID NO: 2;

the light chain variable region comprises CDR1 consisting of the amino acid sequence of the amino acid numbers 24 to 39 of SEQ ID NO: 4, CDR2 consisting of the amino acid sequence of the amino acid numbers 55 to 61 of SEQ ID NO: 4, and CDR3 consisting of the amino acid sequence of the amino acid numbers 94 to 102 of SEQ ID NO: 4; and

the one heavy chain variable region and the one light chain variable region constitute one antigen-binding site, and the antibody or the antigen-binding fragment comprises four antigen-binding sites.

[Claim 2] The anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 1, selected from (1) or (2) below:

(1) an anti-human Tie2 antibody or an antigen-binding fragment thereof, comprising four heavy chain variable regions and four light chain variable regions, in which

the heavy chain variable region consists of the amino acid sequence of the amino acid numbers 1 to 122 of SEQ ID NO: 2,

the light chain variable region consists of the amino acid sequence of the amino acid numbers 1 to 113 of SEQ ID NO: 4, and

the one heavy chain variable region and the one light chain variable region constitute one antigen-binding site, and the antibody or the antigen-binding fragment comprises four antigen-binding sites; and

(2) an anti-human Tie2 antibody or an antigen-binding fragment thereof wherein the antibody or the antigen-binding fragment thereof has undergone pyroglutamylation at the N terminal of the heavy chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof of (1).

[Claim 3] The anti-human Tie2 antibody according to claim 1, wherein

the antibody comprises two heavy chains and four light chains;

each heavy chain comprises two structures consisting of a heavy chain variable region comprising CDR1 consisting of the amino acid sequence of the amino acid numbers 31 to 35 of SEQ ID NO: 2, CDR2 consisting of the amino acid sequence of the amino acid numbers 50 to 66 of SEQ ID NO: 2, and CDR3 consisting of the amino acid sequence of the amino acid numbers 99 to 111 of SEQ ID NO: 2 and a CH1 region, a CH2 region, and a CH3 region, and the carboxy terminus (C terminus) of one of the structures is linked to the amino terminus (N terminus) of the other structure through a linker; and

each light chain comprises a light chain variable region comprising CDR1 consisting of the amino acid sequence of the amino acid numbers 24 to 39 of SEQ ID NO: 4, CDR2 consisting of the amino acid sequence of the amino acid numbers 55 to 61 of SEQ ID NO: 4, and CDR3 consisting of the amino acid sequence of the amino acid numbers 94 to 102 of SEQ ID NO: 4, and a light chain constant region.

[Claim 4] The anti-human Tie2 antibody according to claim 3, selected from (1) or (2) below:

(1) an anti-human Tie2 antibody comprising two heavy chains and four light chains, in which

each heavy chain comprises two structures consisting of a heavy chain variable region consisting of the amino acid sequence of the amino acid numbers 1 to 122 of SEQ ID NO: 2 and a CH1 region, a CH2 region, and a CH3 region, and the C terminus of one of the structures is linked to the N terminus of the other structure through a linker; and

each light chain comprises a light chain variable region consisting of the amino acid sequence of the amino acid numbers 1 to 113 of SEQ ID NO: 4, and a light chain constant region; and

(2) an anti-human Tie2 antibody wherein the antibody has undergone pyroglutamylation at the N terminal of the heavy chain variable region of the anti-human Tie2 antibody of (1).

[Claim 5] The anti-human Tie2 antibody according to claim 4, selected from (1) or (2) below:

(1) an anti-human Tie2 antibody comprising two heavy chains consisting of the amino acid sequence shown by SEQ ID NO: 2 and four light chains consisting of the

amino acid sequence shown by SEQ ID NO: 4; or

(2) an anti-human Tie2 antibody comprising two heavy chains consisting of the amino acid sequence shown by SEQ ID NO: 2 in which glutamic acid of the amino acid number 1 of SEQ ID NO: 2 is modified to pyroglutamic acid and/or lysine of the amino acid number 679 of SEQ ID NO: 2 is deleted and four light chains consisting of the amino acid sequence shown by SEQ ID NO: 4.

[Claim 6] The anti-human Tie2 antibody according to claim 5, comprising two heavy chains consisting of the amino acid sequence shown by SEQ ID NO: 2 and four light chains consisting of the amino acid sequence shown by SEQ ID NO: 4.

[Claim 7] The anti-human Tie2 antibody according to claim 5, comprising two heavy chains consisting of the amino acid sequence of the amino acid numbers 1 to 678 of SEQ ID NO: 2 and four light chains consisting of the amino acid sequence shown by SEQ ID NO: 4.

[Claim 8] A tetravalent anti-human Tie2 antibody or an antigen-binding fragment thereof, binding to the same human Tie2 epitope as the anti-human Tie2 antibody according to claim 5.

[Claim 9] The tetravalent anti-human Tie2 antibody or the antigen-binding fragment thereof according to Claim 8, wherein the human Tie2 epitope is the human Tie2 epitope containing the amino acid of the amino acid numbers 192, 195 and 197 of Accession No. NP_000450.2.

[Claim 10] A polynucleotide selected from the group consisting of (a) and (b):
(a) a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 2(1); and
(b) a polynucleotide comprising a base sequence encoding the light chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 2(1).

[Claim 11] A polynucleotide selected from the group consisting of (a) and (b):
(a) a polynucleotide comprising a base sequence encoding the heavy chain of the

anti-human Tie2 antibody according to claim 6; and
(b) a polynucleotide comprising a base sequence encoding the light chain of the anti-human Tie2 antibody according to claim 6.

[Claim 12] An expression vector comprising:
(i) a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 2(1), and/or
(ii) a polynucleotide comprising a base sequence encoding the light chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 2(1).

[Claim 13] An expression vector comprising:
(i) a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Tie2 antibody according to claim 6, and/or
(ii) a polynucleotide comprising a base sequence encoding the light chain of the anti-human Tie2 antibody according to claim 6.

[Claim 14] A host cell transformed with an expression vector selected from the group consisting of (a) to (d) below:

(a) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 2(1), and a polynucleotide comprising a base sequence encoding the light chain variable region of the antibody or an antigen-binding fragment thereof;

(b) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-human Tie2 antibody or the antigen-biding fragment thereof according to claim 2(1) and an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain variable region of the antibody or an antigen-binding fragment thereof;

(c) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 2(1); and

(d) a host cell transformed with an expression vector comprising a

polynucleotide comprising a base sequence encoding the light chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 2(1).

[Claim 15] A host cell transformed with an expression vector selected from the group consisting of (a) to (d) below:

(a) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Tie2 antibody according to claim 6 and a polynucleotide comprising a base sequence encoding the light chain of the antibody;

(b) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Tie2 antibody according to claim 6 and an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain of the antibody;

(c) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Tie2 antibody according to claim 6; and

(d) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain of the anti-human Tie2 antibody according to claim 6.

[Claim 16] A method for producing an anti-human Tie2 antibody or an antigen-binding fragment thereof, comprising culturing host cell(s) selected from the group consisting of (a) to (c) below to express a tetravalent anti-human Tie2 antibody or an antigen-binding fragment thereof:

(a) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 2(1) and a polynucleotide comprising a base sequence encoding the light chain variable region of the antibody or the antigen-binding fragment thereof;

(b) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 2(1) and an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain variable region of the antibody or the antigen-binding fragment thereof; and

(c) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain variable region of the anti-human Tie2 antibody or the antigen-binding fragment thereof according to claim 2(1) and a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain variable region of the antibody or the antigen-binding fragment thereof.

[Claim 17] A method for producing an anti-human Tie2 antibody, comprising culturing host cell(s) selected from the group consisting of (a) to (c) below to express an anti-human Tie2 antibody:

(a) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Tie2 antibody according to claim 6 and a polynucleotide comprising a base sequence encoding the light chain of the antibody;

(b) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Tie2 antibody according to claim 6 and an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain of the antibody; and

(c) a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the heavy chain of the anti-human Tie2 antibody according to claim 6 and a host cell transformed with an expression vector comprising a polynucleotide comprising a base sequence encoding the light chain of the anti-human Tie2 antibody.

[Claim 18] A pharmaceutical composition comprising the anti-human Tie2 antibody according to claim 6 and/or the anti-human Tie2 antibody according to claim 7, and a pharmaceutically acceptable excipient.

[Claim 19] The pharmaceutical composition according to claim 18, which is a pharmaceutical composition for preventing or treating diabetic macular edema, diabetic retinopathy, or critical limb ischemia.

[Claim 20] The anti-human Tie2 antibody according to claim 5, for preventing or treating diabetic macular edema, diabetic retinopathy, or critical limb ischemia.

[Claim 21] Use of the anti-human Tie2 antibody according to claim 5 for manufacture of a pharmaceutical composition for preventing or treating diabetic macular edema, diabetic retinopathy, or critical limb ischemia.