Claims

[Claim 1]

An antibody having the following properties (i) and (ii) or a functional fragment of the antibody:

(i) specifically binding to GPR20, and

(ii) having internalization ability that permits cellular uptake after binding to GPR20, wherein the antibody has competitive inhibitory activity, for binding to GPR20, against any one antibody selected from the group consisting of the following antibodies (a) to (c):

(a) an antibody having a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 475 of SEQ ID NO: 2 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 233 of SEQ ID NO: 7,

(b) an antibody having a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 475 of SEQ ID NO: 12 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 233 of SEQ ID NO: 17, and

(c) an antibody having a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 475 of SEQ ID NO: 22 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 233 of SEQ ID NO: 27.

[Claim 2]

The antibody or the functional fragment of the antibody according to claim 1, which comprises CDRH1, CDRH2 and CDRH3 in any one combination selected from the group consisting of the following combinations (a) to (c), and CDRL1, CDRL2 and CDRL3 in any one combination selected from the group consisting of the following combinations (d) to (h):

(a) CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 4, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 5, and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 6,

(b) CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 14, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 15, and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 16,

(c) CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 24, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 25, and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 26,

(d) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 9, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 10, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 11,

(e) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 9, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 92, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 11,

(f) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 9, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 93, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 11,
(g) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 19, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 20, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 21, and
(h) CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 29, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 30, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 31.

[Claim 3]

The antibody or the functional fragment of the antibody according to claim 1 or 2, which comprises CDRH1, CDRH2 and CDRH3, and CDRL1, CDRL2 and CDRL3 in any one combination selected from the group consisting of the following combinations (a) to (e):
(a) CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 4, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 5, and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 6, and CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 9, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 10, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 11,
(b) CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 4, CDRH2 consisting of the amino acid sequence

shown in SEQ ID NO: 5, and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 6, and CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 9, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 92, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 11,

(c) CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 4, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 5, and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 6, and CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 9, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 93, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 11,

(d) CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 14, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 15, and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 16, and CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 19, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 20, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 21, and

(e) CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 24, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 25, and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 26, and CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 29, CDRL2 consisting of the amino acid sequence shown in

SEQ ID NO: 30, and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 31.

[Claim 4]

The antibody or the functional fragment of the antibody according to any one of claims 1 to 3, which has any one heavy chain variable region selected from the group consisting of the following variable regions (a) to (c), and any one light chain variable region selected from the following variable regions (d) to (h):

a heavy chain variable region selected from the group consisting of

(a) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 3,

(b) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 13, and

(c) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 23,

(d) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 8,

(e) a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 62,

(f) a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 64,

(g) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 18, and

(h) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 28.

[Claim 5]

The antibody or the functional fragment of the antibody according to any one of claims 1 to 4, which comprises a heavy chain variable region and a light chain variable region in any one combination selected from the group consisting of the following combinations (a) to (e):

(a) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 3, and a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 8,

(b) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 3, and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 62,

(c) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 3, and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 64,

(d) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 13, and a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 18, and

(e) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 23, and a light chain

variable region consisting of the amino acid sequence shown in SEQ ID NO: 28.

[Claim 6]

The antibody or the functional fragment of the antibody according to any one of claims 1 to 5, wherein the constant region is a human-derived constant region.

[Claim 7]

The antibody or the functional fragment of the antibody according to claim 6, which comprises a heavy chain consisting of the amino acid sequence shown in SEQ ID NO: 44 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 45.

[Claim 8]

The antibody or the functional fragment of the antibody according to any one of claims 1 to 7, which is humanized.

[Claim 9]

The antibody or the functional fragment of the antibody according to claim 8, which has a heavy chain variable region consisting of any one amino acid sequence selected from the group consisting of the following amino acid sequences (a) to (h), and a light chain variable region consisting of any one amino acid sequence selected from the group consisting of the following amino acid sequences (i) to (o):

(a) the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 48,

(b) the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 50,

(c) the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 52,

(d) the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 54,

(e) the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 56,

(f) the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 44,

(g) an amino acid sequence having a homology of at least 95% or more to the sequence of a framework region other than at each CDR sequence in the sequences of (a) to (f),

(h) an amino acid sequence comprising a deletion, substitution or addition of one or several amino acids in the sequence of a framework region other than at each CDR sequence in the sequences of (a) to (g),

(i) the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 58,

(j) the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 60,

(k) the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 62,

(l) the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 64,

(m) the amino acid sequence at amino acid positions 21 to 128 in SEQ ID NO: 45,

(n) an amino acid sequence having a homology of at least 95% or more to the sequence of a framework region other than at each CDR sequence in the sequences of (i) to (m), and

(o) an amino acid sequence comprising a deletion, substitution or addition of one or several amino acids in the sequence of a framework region other than at each CDR sequence in the sequences of (i) to (n).

[Claim 10]

The antibody or the functional fragment of the antibody according to claim 9, which comprises a heavy chain variable region and a light chain variable region in any one combination selected from the group consisting of the following combinations (a) to (t):

(a) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 48 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 58,

(b) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 48 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 60,

(c) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 48 and a light chain variable region consisting of

the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 62,

(d) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 48 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 64,

(e) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 50 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 58,

(f) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 50 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 60,

(g) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 50 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 62,

(h) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 50 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 64,

(i) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 52 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 58,

(j) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 52 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 60,

(k) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 52 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 62,

(l) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 52 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 64,

(m) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 54 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 58,

(n) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 54 and a light chain variable region consisting of

the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 60,

(o) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 54 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 62,

(p) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 54 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 64,

(q) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 56 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 58,

(r) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 56 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 60,

(s) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 56 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 62, and

(t) a heavy chain variable region consisting of the amino acid sequence at amino acid positions 20 to 142 in SEQ ID NO: 56 and a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 64.

[Claim 11]

The antibody or the functional fragment of the antibody according to claim 9 or 10, which comprises a heavy chain and a light chain in any one combination selected from the group consisting of the following combinations (a) to (x):

(a) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 48 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,

(b) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 48 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,

(c) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 48 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62,

(d) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 48 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64,

(e) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 50 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,
(f) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 50 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,
(g) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 50 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62,
(h) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 50 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64,
(i) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 52 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,
(j) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 52 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,
(k) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 52 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62,

(l) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 52 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64,
(m) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 54 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,
(n) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 54 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,
(o) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 54 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62,
(p) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 54 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64,
(q) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 56 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,
(r) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 56 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,

(s) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 56 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62,
(t) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 56 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64,
(u) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 44 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,
(v) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 44 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,
(w) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 44 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62; and
(x) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 44 and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64.

[Claim 12]

The functional fragment of the antibody according to any one of claims 1 to 11, wherein the functional

fragment is selected from the group consisting of Fab, F(ab)2, Fab' and Fv.

[Claim 13]

A polynucleotide encoding the antibody or the functional fragment of the antibody according to any one of claims 1 to 12.

[Claim 14]

The polynucleotide according to claim 13, which comprises polynucleotides in any one combination selected from the group consisting of the following combinations (a) to (e):

(a) polynucleotides encoding CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 4, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 5 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 6, and polynucleotides encoding CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 9, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 10 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 11,

(b) polynucleotides encoding CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 4, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 5 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 6, and polynucleotides encoding CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 9, CDRL2 consisting of the amino acid sequence shown in

SEQ ID NO: 92 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 11,

(c) polynucleotides encoding CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 4, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 5 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 6, and polynucleotides encoding CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 9, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 93 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 11,

(d) polynucleotides encoding CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 14, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 15 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 16, and polynucleotides encoding CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 19, CDRL2 consisting of the amino acid sequence shown in SEQ ID NO: 20 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 21, and

(e) polynucleotides encoding CDRH1 consisting of the amino acid sequence shown in SEQ ID NO: 24, CDRH2 consisting of the amino acid sequence shown in SEQ ID NO: 25 and CDRH3 consisting of the amino acid sequence shown in SEQ ID NO: 26, and polynucleotides encoding CDRL1 consisting of the amino acid sequence shown in SEQ ID NO: 29, CDRL2 consisting of the amino acid sequence shown in

SEQ ID NO: 30 and CDRL3 consisting of the amino acid sequence shown in SEQ ID NO: 31.

[Claim 15]

The polynucleotide according to claim 13 or 14, which comprises polynucleotides in any one combination selected from the group consisting of the following combinations (a) to (e):

(a) a polynucleotide encoding a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 3, and a polynucleotide encoding a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 8,

(b) a polynucleotide encoding a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 3, and a polynucleotide encoding a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 62,

(c) a polynucleotide encoding a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 3, and a polynucleotide encoding a light chain variable region consisting of the amino acid sequence at amino acid positions 21 to 129 in SEQ ID NO: 64,

(d) a polynucleotide encoding a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 13, and a polynucleotide encoding a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 18, and

(e) a polynucleotide encoding a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 23, and a polynucleotide encoding a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 28.

[Claim 16]

An expression vector comprising the polynucleotide according to any one of claims 13 to 15.

[Claim 17]

Host cells transformed with the expression vector according to claim 16.

[Claim 18]

The host cells according to claim 17, wherein the host cells are eukaryotic cells.

[Claim 19]

A method for producing an antibody of interest or a functional fragment of the antibody, which comprises a step of culturing the host cells according to claim 17 or 18, and a step of collecting an antibody of interest or a functional fragment of the antibody from the culture obtained by the aforementioned step.

[Claim 20]

An antibody or a functional fragment of the antibody obtained by the production method according to claim 19.

[Claim 21]

The functional fragment of the antibody according to claim 20, wherein the functional fragment is selected from the group consisting of Fab, F(ab)2, Fab' and Fv.

[Claim 22]

The antibody or the functional fragment of the antibody according to any one of claims 1 to 12, 20 and 21, which comprises one or two or more modifications selected from the group consisting of N-linked glycosylation, O-linked glycosylation, N-terminal processing, C-terminal processing, deamidation, isomerization of aspartic acid, oxidation of methionine, addition of a methionine residue to the N-terminus, amidation of a proline residue, and a heavy chain comprising a deletion of one or two amino acids at the carboxyl terminus.

[Claim 23]

The antibody according to claim 22, wherein one or two amino acids are deleted at the carboxyl terminus of a heavy chain thereof.

[Claim 24]

The antibody according to claim 23, wherein one amino acid is deleted at each of the carboxyl termini of both of the heavy chains thereof.

[Claim 25]

The antibody according to any one of claims 22 to 24, wherein a proline residue at the carboxyl terminus of a heavy chain thereof is further amidated.

[Claim 26]

The antibody or the functional fragment of the antibody according to any one of claims 1 to 12 and 20 to 24, wherein sugar chain modification is regulated in

order to enhance antibody-dependent cellular cytotoxic activity.

[Claim 27]

An antibody-drug conjugate comprising the antibody or the functional fragment of the antibody according to any one of claims 1 to 12 and 20 to 26 conjugated to a drug.

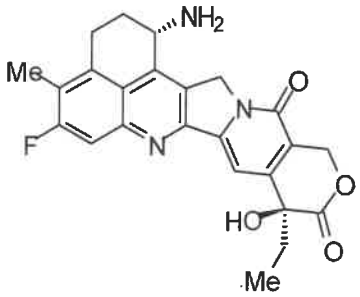
[Claim 28]

The antibody-drug conjugate according to claim 27, wherein the drug is an antitumor compound.

[Claim 29]

The antibody-drug conjugate according to claim 28, wherein the antitumor compound is an antitumor compound represented by the following formula:

[Formula 1]



[Claim 30]

The antibody-drug conjugate according to claim 29, wherein the antibody is conjugated to the antitumor compound via a linker having any structure selected from the group consisting of the following formulas (a) to (f):

(a) -(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-,

(b) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-,

(c) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-,

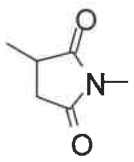
(d) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-,

(e) -(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-, and

(f) -(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-,

wherein the antibody is connected to the terminus of -(Succinimid-3-yl-N), the antitumor compound is connected to the carbonyl group of the -$(CH_2)n^2$-C(=O)- moiety with the nitrogen atom of the amino group at position 1 as a connecting position, GGFG represents an amino acid sequence consisting of glycine-glycine-phenylalanine-glycine linked through peptide bonds, and -(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 2]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

[Claim 31]

The antibody-drug conjugate according to any one of claims 27 to 30, wherein the linker is represented by any formula selected from the group consisting of the following formulas (a) to (c):

(a) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-,

(b) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-, and

(c) -(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-.

[Claim 32]

The antibody-drug conjugate according to any one of claims 27 to 31, wherein the linker is represented by the following formula (a) or (b):

(a) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-, and

(b) -(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-.

[Claim 33]

The antibody-drug conjugate according to any one of claims 27 to 32, wherein the linker is represented by the following formula (a):

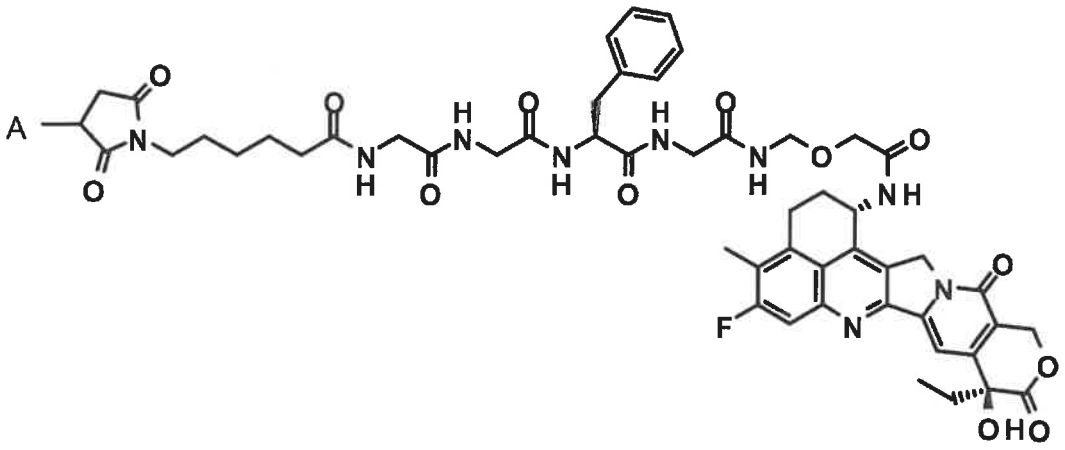
(a) -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-.

[Claim 34]

The antibody-drug conjugate according to any one of claims 27 to 33, wherein the antibody is conjugated to a

drug linker represented by the following formula [Formula 3] (wherein A represents a connecting position to the antibody) by a thioether bond:

[Formula 3]

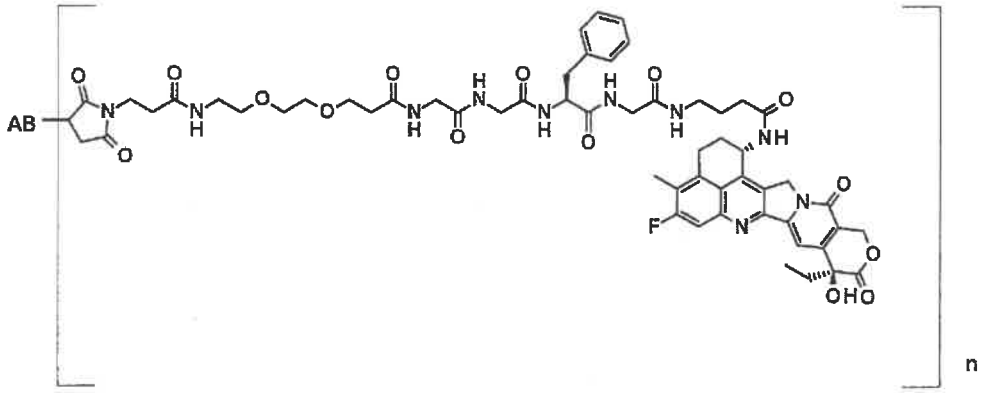


[Claim 35]

The antibody-drug conjugate according to any one of claims 27 to 33, which has a structure represented by the following formula [Formula 4],

wherein AB represents the antibody or the functional fragment of the antibody, n represents an average number of units of the drug-linker structure conjugated to the antibody per antibody, and the antibody is connected to the linker via a sulfhydryl group derived from the antibody:

[Formula 4]

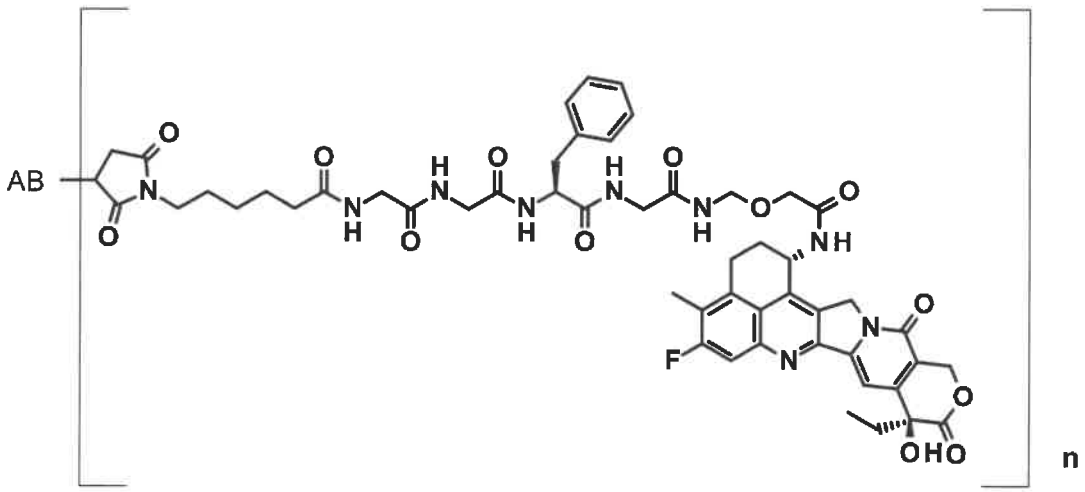


[Claim 36]

The antibody-drug conjugate according to any one of claims 27 to 34, which is represented by the following formula [Formula 5],

wherein AB represents the antibody or the functional fragment of the antibody, n represents an average number of units of the drug-linker structure conjugated to the antibody per antibody, and the antibody is connected to the linker via a sulfhydryl group derived from the antibody:

[Formula 5]



[Claim 37]

The antibody-drug conjugate according to any one of claims 34 to 36, wherein the antibody is an antibody comprising a heavy chain and a light chain in any one combination selected from the group consisting of the following combinations (a) to (x), or a functional fragment of the antibody:

(a) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 48, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,

(b) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 48, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,

(c) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 48, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62,

(d) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 48, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64,

(e) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 50, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,

(f) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 50, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,
(g) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 50, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62,
(h) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 50, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64,
(i) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 52, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,
(j) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 52, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,
(k) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 52, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62,
(l) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 52, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64,

(m) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 54, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,
(n) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 54, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,
(o) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 54, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62,
(p) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 54, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64,
(q) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 56, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,
(r) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 56, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,
(s) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 56, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62,

(t) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 474 in SEQ ID NO: 56, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64,
(u) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 44, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 58,
(v) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 44, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 60,
(w) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 44, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 62, and
(x) a heavy chain consisting of the amino acid sequence at amino acid positions 20 to 472 in SEQ ID NO: 44, and a light chain consisting of the amino acid sequence at amino acid positions 21 to 234 in SEQ ID NO: 64.

[Claim 38]

The antibody-drug conjugate according to claim 37, wherein the heavy chain of the antibody comprises one or two or more modifications selected from the group consisting of N-linked glycosylation, O-linked glycosylation, N-terminal processing, C-terminal processing, deamidation, isomerization of aspartic acid, oxidation of methionine, addition of a methionine residue

to the N-terminus, amidation of a proline residue, and a heavy chain comprising a deletion of one or two amino acids at the carboxyl terminus.

[Claim 39]

The antibody-drug conjugate according to any one of claims 27 to 38, wherein an average number of units of the selected one drug-linker structure conjugated per antibody is in a range of from 1 to 10.

[Claim 40]

The antibody-drug conjugate according to any one of claims 27 to 39, wherein an average number of units of the selected one drug-linker structure conjugated per antibody is in a range of from 2 to 8.

[Claim 41]

The antibody-drug conjugate according to any one of claims 27 to 40, wherein an average number of units of the selected one drug-linker structure conjugated per antibody is in a range of from 3 to 8.

[Claim 42]

The antibody-drug conjugate according to any one of claims 27 to 41, wherein an average number of units of the selected one drug-linker structure conjugated per antibody is in a range of from 7 to 8.

[Claim 43]

The antibody-drug conjugate according to any one of claims 27 to 42, wherein an average number of units of the selected one drug-linker structure conjugated per antibody is 8.

[Claim 44]

A pharmaceutical composition comprising any component selected from the antibodies or the functional fragments of the antibodies according to any one of claims 1 to 12 and 20 to 26 and the antibody-drug conjugates according to any one of claims 27 to 43, a salt of the component, or a hydrate of the component or the salt.

[Claim 45]

The pharmaceutical composition according to claim 44, which is an antitumor drug.

[Claim 46]

The pharmaceutical composition according to claim 45, wherein the tumor is a tumor expressing GPR20.

[Claim 47]

The pharmaceutical composition according to claim 45 or 46, wherein the tumor is gastrointestinal stromal tumor.

[Claim 48]

The pharmaceutical composition according to any one of claims 44 to 47, further comprising an additional antitumor drug.

[Claim 49]

Use of the antibodies or the functional fragments of the antibodies according to any one of claims 1 to 12 and 20 to 26, the antibody-drug conjugates according to any one of claims 27 to 43, salts of these components, and hydrates of these components or the salts for the

manufacture of a medicament for treating a tumor in an individual.

[Claim 50]

The use according to claim 49, wherein the tumor is gastrointestinal stromal tumor.

[Claim 51]

The use according to claim 49 or 50, wherein the tumor is a tumor that exhibits resistance to a tyrosine kinase inhibitor.

[Claim 52]

Use of a pharmaceutical composition comprising at least one component selected from the antibodies or the functional fragments of the antibodies according to any one of claims 1 to 12 and 20 to 26, the antibody-drug conjugates according to any one of claims 27 to 43, salts of these components, and hydrates of these components or the salts for the manufacture of a medicament for the treatment of a tumor by simultaneous, separate or continuous administration with at least one antitumor drug.

[Claim 53]

Use of at least one antitumor drug for the manufacture of a medicament for the treatment of a tumor by simultaneous, separate or continuous administration with a pharmaceutical composition comprising at least one component selected from the antibodies or the functional fragments of the antibodies according to any one of claims 1 to 12 and 20 to 26, the antibody-drug conjugates

according to any one of claims 27 to 42, salts of these components, and hydrates of these components or the salts.

[Claim 54]

The use according to claim 52 or 53, wherein the antitumor drug is a tyrosine kinase inhibitor.

[Claim 55]

The use according to claim 54, wherein the tyrosine kinase inhibitor is at least one selected from sunitinib, imatinib, and regorafenib.

[Claim 56]

The use according to any one of claims 49 to 55, wherein the tumor is gastrointestinal stromal tumor that exhibits resistance to a tyrosine kinase inhibitor.

[Claim 57]

A method for producing an antibody-drug conjugate, which comprises a step of culturing the host cells according to claim 17 or 18, a step of collecting an antibody of interest or a functional fragment of the antibody from the culture obtained by the aforementioned step, and a step of reacting the antibody or the functional fragment of the antibody obtained by the aforementioned step with a drug-linker intermediate compound.