

CLAIMS

[Claim 1]

An antibody that binds to human CDCP1 (CUB domain-containing protein 1), which has low binding property to human CD34-positive cells, or an antigen-binding fragment thereof,

wherein the antibody and the antigen-binding fragment comprise a heavy chain variable region and a light chain variable region,

wherein the amino acid sequences of CDRs (complementarity determining regions) 1 to 3 of the heavy chain variable region and the light chain variable region satisfy any of the following (A) to (K):

(A)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 25,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 26,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 27,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 29,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 30,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 31;

(B)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 33,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 34,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 35,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 37,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 38,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 39;

(C)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 41,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 42,

heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 43,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 45,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 46,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 47;
(D)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 49,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 50,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 51,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 53,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 54,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 55;
(E)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 57,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 58,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 59,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 61,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 62,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 63;
(F)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 65,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 66,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 67,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 69,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 70,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 71;
(G)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 73,

heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 74,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 75,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 77,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 78,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 79;
(H)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 81,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 82,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 83,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 85,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 86,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 87;
(I)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 89,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 90,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 91,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 93,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 94,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 95;
(J)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 97,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 98,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 99,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 101,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 102,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 103;
and

(K)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 105,

heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 106,

heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 107,

light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 109,

light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 110,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 111.
[Claim 2]

An antibody that binds to human CDCP1 (CUB domain-containing protein 1), which has low binding property to human CD34-positive cells, or an antigen-binding fragment thereof,

wherein the antibody and the antigen-binding fragment comprise a heavy chain variable region and a light chain variable region,

wherein the amino acid sequences of CDRs (complementarity determining regions) 1 to 3 of the heavy chain variable region and the light chain variable region satisfy either the following (L) or (M):

(L)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 49,

heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 50,

heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 51,

light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 53,

light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 54,

and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 55;

or

(M) the antibody satisfying the above (L), which has heavy chain and light chain variable regions, in which the amino acid at position 102 of the heavy chain and the

amino acid at positions 28 and 29 of the light chain according to Kabat definition are substituted with other amino acids.

[Claim 3]

An antibody that binds to human CDCP1 (CUB domain-containing protein 1), which has low binding property to human CD34-positive cells, or an antigen-binding fragment thereof,

wherein the antibody and the antigen-binding fragment comprise a heavy chain variable region and a light chain variable region,

wherein the amino acid sequences of CDRs (complementarity determining regions) 1 to 3 of the heavy chain variable region and the light chain variable region satisfy either the following (N) or (O):

(N)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 65,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 66,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 67,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 69,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 70,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 71;

or

(O) the antibody satisfying the above (N), which has a heavy chain variable region, in which the amino acids at position 54 and 55 of the heavy chain according to Kabat definition are substituted with other amino acids.

[Claim 4]

An antibody that binds to human CDCP1 (CUB domain-containing protein 1), which has low binding property to human CD34-positive cells, or an antigen-binding fragment thereof,

wherein the antibody and the antigen-binding fragment comprise a heavy chain variable region and a light chain variable region,

wherein the amino acid sequences of CDRs (complementarity determining regions) 1 to 3 of the heavy chain variable region and the light chain variable region satisfy either the following (P) or (Q):

(P)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 73,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 74,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 75,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 77,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 78,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 79;
or

(Q) the antibody satisfying the above (P), which has heavy chain and light chain variable regions, in which the amino acids at position 54 and 55 of the heavy chain and the amino acid at position 33 of the light chain according to Kabat definition are substituted with other amino acids.

[Claim 5]

An antibody that binds to human CDCP1 (CUB domain-containing protein 1), which has low binding property to human CD34-positive cells, or an antigen-binding fragment thereof,

wherein the antibody and the antigen-binding fragment comprise a heavy chain variable region and a light chain variable region,

wherein the amino acid sequences of CDRs (complementarity determining regions) 1 to 3 of the heavy chain variable region and the light chain variable region satisfy either the following (R) or (S):

(R)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 89,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 90,
heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 91,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 93,

light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 94,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 95;
or

(S) the antibody satisfying the above (R), which has heavy chain and light chain variable regions, in which the amino acids at positions 52a and 53 of the heavy chain and the amino acid at position 33 of the light chain according to Kabat definition are substituted with other amino acids.

[Claim 6]

An antibody that binds to human CDCP1 (CUB domain-containing protein 1), which has low binding property to human CD34-positive cells, or an antigen-binding fragment thereof,

wherein the antibody and the antigen-binding fragment comprise a heavy chain variable region and a light chain variable region,

wherein the amino acid sequences of CDRs (complementarity determining regions) 1 to 3 of the heavy chain variable region satisfy either following (T) or (U), and the amino acid sequences of CDRs 1 to 3 of the light chain variable region satisfy any of the following (t) to (v):

(T)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 49,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 50,
and

heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 113; or

(U)

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 183,

heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 50,
and

heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 113; and

(t)

light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 117,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 54,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 55;

(u)

light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 186,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 54,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 55;
and

(v)

light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 188,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 54,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 55.

[Claim 7]

An antibody that binds to human CDCP1 (CUB domain-containing protein 1),
which has low binding property to human CD34-positive cells, or an antigen-binding
fragment thereof,

wherein the antibody and the antigen-binding fragment comprise a heavy
chain variable region and a light chain variable region,

wherein the amino acid sequences of CDRs (complementarity determining
regions) 1 to 3 of the heavy chain variable region and the light chain variable region
satisfy:

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 73,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO:
147,

heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 75,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 149,

light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 78,
and
light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 79.
[Claim 8]

An antibody that binds to human CDCP1 (CUB domain-containing protein 1),
which has low binding property to human CD34-positive cells, or an antigen-binding
fragment thereof,

wherein the antibody and the antigen-binding fragment comprise a heavy chain
variable region and a light chain variable region,

wherein the amino acid sequences of CDRs (complementarity determining
regions) 1 to 3 of the heavy chain variable region and the light chain variable region
satisfy:

heavy chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 89,
heavy chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO:
151,

heavy chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 91,
light chain CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 93,
light chain CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 94,
and

light chain CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 95.
[Claim 9]

The antibody or the antigen-binding fragment thereof according to any one of
claims 1 to 8, wherein the concentration of a comparative antibody in the evaluation of
the binding property to human CD34-positive cells is any concentration of 10 ng/ml or
more.

[Claim 10]

The antibody or the antigen-binding fragment thereof according to any one of
claims 1 to 9, wherein the antibody is a humanized antibody.

[Claim 11]

The antibody or the antigen-binding fragment thereof according to any one of
claims 1 to 10, which binds to a substance having antitumor activity.

[Claim 12]

The antibody or the antigen-binding fragment thereof according to claim 11, wherein the substance having antitumor activity is an anticancer agent.

[Claim 13]

The antigen-binding fragment according to any one of claims 1 to 12, which is Fab, Fab', F(ab')₂, Fv, a single chain antibody, scFv, an scFv dimer, or dsFv.

[Claim 14]

A pharmaceutical composition, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 13.