Claims

[Claim 1]

An antibody which binds to a polypeptide comprising amino acid residues 39 to 165 of an amino acid sequence represented by SEQ ID NO: 2 and inhibits osteoclast formation and/or osteoclastic bone resorption, or a functional fragment of the antibody.

[Claim 2]

The antibody or a functional fragment of the antibody according to claim 1, characterized in that:

a heavy chain sequence contains a variable region having CDRH1, CDRH2, and CDRH3, and the CDRH1 comprises an amino acid sequence represented by SEQ ID NO: 44, the CDRH2 comprises any one of amino acid sequences represented by SEQ ID NO: 45 and SEQ ID NO: 97, and the CDRH3 comprises an amino acid sequence represented by SEQ ID NO: 46; and

a light chain sequence contains a variable region having CDRL1, CDRL2, and CDRL3, and the CDRL1 comprises an amino acid sequence represented by SEQ ID NO: 47, the CDRL2 comprises an amino acid sequence represented by SEQ ID NO: 48, and the CDRL3 comprises an amino acid sequence represented by SEQ ID NO: 49.

[Claim 3]

The antibody or a functional fragment of the antibody according to claim 2, characterized by containing a heavy chain variable region sequence comprising amino acid residues 20 to

140 of an amino acid sequence represented by SEQ ID NO: 41 and a light chain variable region sequence comprising amino acid residues 21 to 132 of an amino acid sequence represented by SEQ ID NO: 43.

[Claim 4]

The functional fragment of the antibody according to any one of claims 1 to 3 which is selected from the group consisting of Fab, F(ab')2, Fab' and Fv.

[Claim 5]

The antibody according to any one of claims 1 to 3, characterized by being an scFv.

[Claim 6]

The antibody or a functional fragment of the antibody according to any one of claims 1 to 4, characterized in that the antibody is a chimeric antibody.

[Claim 7]

The antibody or a functional fragment of the antibody according to claim 6, characterized by comprising a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 41 and a light chain sequence comprising amino acid residues 21 to 237 of an amino acid sequence represented by SEQ ID NO: 43.

[Claim 8]

The antibody or a functional fragment of the antibody according to any one of claims 1 to 4, and 6, characterized

in that the antibody is humanized.

[Claim 9]

The antibody according to claim 7 or 8, wherein the heavy chain has a constant region of a human immunoglobulin G2 heavy chain and the light chain has a constant region of a human immunoglobulin κ light chain.

[Claim 10]

An antibody which inhibits osteoclast formation and/or osteoclastic bone resorption or a functional fragment of the antibody, wherein the antibody contains:

(a) a heavy chain variable region selected from the group consisting of the following amino acid sequences:

a1) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 51;

a2) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 53;

a3) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 55;

a4) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 57;

a5) an amino acid sequence comprising amino acid residues

20 to 140 of an amino acid sequence represented by SEQ ID NO: 59;

a6) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 99;

a7) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 101;

a8) an amino acid sequence having a homology of at least 95% with any one of the amino acid sequences selected from a1) to a7);

a9) an amino acid sequence having a homology of at least 99% with any one of the amino acid sequences selected from a1) to a7); and

a10) an amino acid sequence including a substitution, deletion, or addition of one to several amino acid residues in any one of the amino acid sequences selected from a1) to a7); and

(b) a light chain variable region selected from the group consisting of the following amino acid sequences:

b1) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 61;

b2) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO:

63;

b3) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 65;

b4) an amino acid sequence comprising amino acid residues 21 to 132 of an amino acid sequence represented by SEQ ID NO: 67;

b5) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 69;

b6) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 71;

b7) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 103;

b8) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 105;

b9) an amino acid sequence having a homology of at least 95% with any one of the amino acid sequences selected from b1) to b8);

b10) an amino acid sequence having a homology of at least 99% with any one of the amino acid sequences selected from b1) to b8); and

b11) an amino acid sequence including a substitution, deletion, or addition of one to several amino acid residues in any one of the amino acid sequences selected from b1) to b8).

[Claim 11]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 51 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 61.

[Claim 12]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 53 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 63.

[Claim 13]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 55 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 138 of an amino acid sequence represented by SEQ ID NO: 65.

[Claim 14]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 55 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 132 of an amino acid sequence represented by SEQ ID NO: 67.

[Claim 15]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by

SEQ ID NO: 57 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 16]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 59 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 71.

[Claim 17]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 18]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 101 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 19]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 103.

[Claim 20]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by

SEQ ID NO: 99 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 105.

[Claim 21]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 51 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 61.

[Claim 22]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 53 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 63.

[Claim 23]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 55 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 65.

[Claim 24]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 55 and a light chain sequence comprising amino acid residues 21 to 237 of an amino acid sequence represented by SEQ ID NO: 67.

[Claim 25]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 57 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 26]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 59 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 71.

[Claim 27]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence comprising amino acid residues 20 to 466 of an

amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 28]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence comprising amino acid residues 20 to 466 of an amino acid sequence represented by SEQ ID NO: 101 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 29]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence comprising amino acid residues 20 to 466 of an amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 103.

[Claim 30]

The antibody or a functional fragment of the antibody according to claim 10, characterized by containing a heavy chain sequence comprising amino acid residues 20 to 466 of an amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 105.

[Claim 31]

A pharmaceutical composition, characterized by comprising at least one of the antibodies or functional fragments of the antibodies according to claims 1 to 30.

[Claim 32]

The pharmaceutical composition according to claim 31, characterized by being a therapeutic and/or preventive agent for abnormal bone metabolism.

[Claim 33]

A pharmaceutical composition for treating and/or preventing abnormal bone metabolism, characterized by comprising at least one of the antibodies or functional fragments of the antibodies according to claims 1 to 30 and at least one member selected from the group consisting of bisphosphonates, active vitamin D_3, calcitonin and derivatives thereof, hormones such as estradiol, SERMs (selective estrogen receptor modulators), ipriflavone, vitamin K_2 (menatetrenone), calcium preparations, PTH (parathyroid hormone), nonsteroidal anti-inflammatory agents, soluble TNF receptors, anti-TNF-α antibodies or functional fragments of the antibodies, anti-PTHrP (parathyroid hormone-related protein) antibodies or functional fragments of the antibodies, IL-1 receptor antagonists, anti-IL-6 receptor antibodies or functional fragments of the antibodies, anti-RANKL antibodies or functional fragments of the antibodies, and OCIF (osteoclastogenesis inhibitory factor).

[Claim 34]

The pharmaceutical composition according to claim 32 or 33, wherein the abnormal bone metabolism is selected from the group consisting of osteoporosis, bone destruction accompanying rheumatoid arthritis, cancerous hypercalcemia, bone destruction accompanying multiple myeloma or cancer metastasis to bone, giant cell tumor, osteopenia, tooth loss due to periodontitis, osteolysis around a prosthetic joint, bone destruction in chronic osteomyelitis, Paget's disease of bone, renal osteodystrophy, and osteogenesis imperfecta.

[Claim 35]

The pharmaceutical composition according to claim 34, characterized in that the abnormal bone metabolism is osteoporosis, bone destruction accompanying rheumatoid arthritis, or bone destruction accompanying cancer metastasis to bone.

[Claim 36]

The pharmaceutical composition according to claim 35, characterized in that the abnormal bone metabolism is osteoporosis.

[Claim 37]

The pharmaceutical composition according to claim 36, characterized in that the osteoporosis is postmenopausal osteoporosis, senile osteoporosis, secondary osteoporosis due to the use of a therapeutic agent such as a steroid or an

immunosuppressant, or osteoporosis accompanying rheumatoid arthritis.

[Claim 38]

Use of an antibody according to claims 1 to 30, or a functional fragment thereof, for the manufacture of a medicament for treating and/or preventing abnormal bone metabolism.

[Claim 39]

Use of an antibody according to claims 1 to 30, or a functional fragment thereof, for the manufacture of a medicament for treating and/or preventing abnormal bone metabolism, characterized by simultaneously or successively administering the antibody or functional fragments and at least one member selected from the group consisting of bisphosphonates, active vitamin D_3, calcitonin and derivatives thereof, hormones such as estradiol, SERMs (selective estrogen receptor modulators), ipriflavone, vitamin K_2 (menatetrenone), calcium preparations, PTH (parathyroid hormone), nonsteroidal anti-inflammatory agents, soluble TNF receptors, anti-TNF-α antibodies or functional fragments of the antibodies, anti-PTHrP (parathyroid hormone-related protein) antibodies or functional fragments of the antibodies, IL-1 receptor antagonists, anti-IL-6 receptor antibodies or functional fragments of the antibodies, anti-RANKL antibodies or functional fragments of the antibodies, and OCIF (osteoclastogenesis inhibitory factor).

[Claim 40]

The use according to claim 38 or 39, characterized in that the abnormal bone metabolism is osteoporosis, bone

destruction accompanying rheumatoid arthritis, or bone destruction accompanying cancer metastasis to bone.

[Claim 41]

The use according to claim 40, characterized in that the abnormal bone metabolism is osteoporosis.

[Claim 42]

The use according to claim 41, characterized in that the osteoporosis is postmenopausal osteoporosis, senile osteoporosis, secondary osteoporosis due to the use of a therapeutic agent such as a steroid or an immunosuppressant, or osteoporosis accompanying rheumatoid arthritis.

[Claim 43]

A polynucleotide encoding the antibody according to any one of claims 3, 7, and 10 to 30.

[Claim 44]

The polynucleotide according to claim 43, characterized by containing a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 40 and a nucleotide sequence comprising nucleotides 61 to 396 of

a nucleotide sequence represented by SEQ ID NO: 42.

[Claim 45]

The polynucleotide according to claim 44, characterized by containing a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 40 and a nucleotide sequence comprising nucleotides 61 to 711 of a nucleotide sequence represented by SEQ ID NO: 42.

[Claim 46]

The polynucleotide according to claim 43, characterized by containing:

(a) a polynucleotide selected from the group consisting of the following nucleotide sequences:

a1) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 50;

a2) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 52;

a3) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 54;

a4) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 56;

a5) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 58;

a6) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 98;

a7) a nucleotide sequence comprising nucleotides 58 to

420 of a nucleotide sequence represented by SEQ ID NO: 100;

a8) a nucleotide sequence of a polynucleotide which hybridizes to a polynucleotide comprising a nucleotide sequence complementary to any one of the nucleotide sequences selected from a1) to a7) under stringent conditions; and

a9) a nucleotide sequence including a substitution, deletion, or addition of one to several nucleotides in any one of the nucleotide sequences selected from a1) to a7); and

(b) a polynucleotide selected from the group consisting of the following nucleotide sequences:

b1) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 60;

b2) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 62;

b3) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 64;

b4) a nucleotide sequence comprising nucleotides 61 to 396 of a nucleotide sequence represented by SEQ ID NO: 66;

b5) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 68;

b6) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 70;

b7) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 102;

b8) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 104;

b9) a nucleotide sequence of a polynucleotide which hybridizes to a polynucleotide comprising a nucleotide sequence complementary to any one of the nucleotide sequences selected from b1) to b8) under stringent conditions; and

b10) a nucleotide sequence including a substitution, deletion, or addition of one to several nucleotides in any one of the nucleotide sequences selected from b1) to b8).

[Claim 47]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 50, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 60.

[Claim 48]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 52, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 62.

[Claim 49]

The polynucleotide according to claim 46, characterized

by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 54, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 64.

[Claim 50]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 54, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 396 of a nucleotide sequence represented by SEQ ID NO: 66.

[Claim 51]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 56, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 52]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 58, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to

399 of a nucleotide sequence represented by SEQ ID NO: 70.

[Claim 53]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 54]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 100, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 55]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 102.

[Claim 56]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide

sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 104.

[Claim 57]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 50, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 60.

[Claim 58]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 52, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 62.

[Claim 59]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 54, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 64.

[Claim 60]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 54, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 711 of a nucleotide sequence represented by SEQ ID NO: 66.

[Claim 61]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 56, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 62]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 58, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 70.

[Claim 63]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1398 of a nucleotide

sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 64]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1398 of a nucleotide sequence represented by SEQ ID NO: 100, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 65]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1398 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 102.

[Claim 66]

The polynucleotide according to claim 46, characterized by containing a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1398 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 104.

[Claim 67]

A vector, comprising any one of the polynucleotides according to claims 43 to 66.

[Claim 68]

A transformed host cell, comprising any one of the polynucleotides according to claims 43 to 66.

[Claim 69]

A transformed host cell, comprising the vector according to claim 67.

[Claim 70]

A method of producing the antibody according to any one of claims 3, 7, and 10 to 30, comprising culturing the host cell according to claim 68 or 69, and purifying an antibody from the resulting culture product.

CLAIMS

[Claim 1]

An isolated antibody which binds to a polypeptide comprising amino acid residues 39 to 165 of an amino acid sequence represented by SEQ ID NO: 2 and inhibits osteoclast formation and/or osteoclastic bone resorption, or a functional fragment of the antibody, wherein the antibody contains a heavy chain variable region sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 41 and a light chain variable region sequence comprising amino acid residues 21 to 132 of an amino acid sequence represented by SEQ ID NO: 43.

[Claim 2]

The functional fragment of the isolated antibody according claim 1 which is selected from the group consisting of Fab, F(ab')2, Fab' and Fv.

[Claim 3]

The isolated antibody according to claim 1, wherein the antibody is an scFv.

[Claim 4]

The isolated antibody or a functional fragment of the isolated antibody according to any one of claims 1 to 3, wherein the antibody is a chimeric antibody.

[Claim 5]

The isolated antibody or a functional fragment of the isolated antibody according to claim 4, wherein the antibody or functional fragment thereof comprises a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 41 and a light chain sequence comprising amino acid residues 21 to 237 of an amino acid sequence represented by SEQ ID NO: 43.

[Claim 6]

The isolated antibody or a functional fragment of the isolated antibody according to any one of claims 1, 2 or 4, wherein the antibody is humanized.

[Claim 7]

The isolated antibody according to claim 5 or claim 6, wherein the heavy chain has a constant region of a human immunoglobulin G2 heavy chain and the light chain has a constant region of a human immunoglobulin κ light chain.

[Claim 8]

An isolated antibody which inhibits osteoclast formation and/or osteoclastic bone resorption or a functional fragment of the antibody, wherein the antibody contains:

(a) a heavy chain variable region selected from the group consisting of the following amino acid sequences:

a1) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 51;

a2) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 53;

a3) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 55;

a4) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 57;

a5) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 59;

a6) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by

SEQ ID NO: 99;

a7) an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 101;

a8) an amino acid sequence having a homology of at least 95% with any one of the amino acid sequences selected from a1) to a7);

a9) an amino acid sequence having a homology of at least 99% with any one of the amino acid sequences selected from a1) to a7); and

a10) an amino acid sequence including a substitution, deletion, or addition of one amino acid residue in any one of the amino acid sequences selected from a1) to a7); and

(b) a light chain variable region selected from the group consisting of the following amino acid sequences:

b1) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 61;

b2) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 63;

b3) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 65;

b4) an amino acid sequence comprising amino acid residues 21 to 132 of an amino acid sequence represented by SEQ ID NO: 67;

b5) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 69;

b6) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 71;

b7) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 103;

b8) an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 105;

b9) an amino acid sequence having a homology of at least 95% with any one of the amino acid sequences selected from b1) to b8);

b10) an amino acid sequence having a homology of at least 99% with any one of the amino acid sequences selected from b1) to b8); and

b11) an amino acid sequence including a substitution, deletion, or addition of one amino acid residue in any one of the amino acid sequences selected from b1) to b8).

[Claim 9]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 51 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 61.

[Claim 10]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 53

and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 63.

[Claim 11]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 55 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 65.

[Claim 12]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 55 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 132 of an amino acid sequence represented by SEQ ID NO: 67.

[Claim 13]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 57

and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 14]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 59 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 71.

[Claim 15]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 16]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 101

and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 17]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 103.

[Claim 18]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence containing a heavy chain variable region comprising an amino acid sequence comprising amino acid residues 20 to 140 of an amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence containing a light chain variable region comprising an amino acid sequence comprising amino acid residues 21 to 133 of an amino acid sequence represented by SEQ ID NO: 105.

[Claim 19]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 51 and a light chain sequence comprising amino acid residues 21 to 238 of

an amino acid sequence represented by SEQ ID NO: 61.

[Claim 20]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 53 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 63.

[Claim 21]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 55 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 65.

[Claim 22]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 55 and a light chain sequence comprising amino acid residues 21 to 237 of an amino acid sequence represented by SEQ ID NO: 67.

[Claim 23]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 57 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 24]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence comprising amino acid residues 20 to 470 of an amino acid sequence represented by SEQ ID NO: 59 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 71.

[Claim 25]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence comprising amino acid residues 20 to 466 of an amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 26]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence comprising amino acid residues 20 to 466 of an amino acid sequence represented by SEQ ID NO: 101 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 69.

[Claim 27]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence comprising amino acid residues 20 to 466 of an amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 103.

[Claim 28]

The isolated antibody or a functional fragment of the isolated antibody according to claim 8, wherein the antibody or functional fragment thereof contains a heavy chain sequence comprising amino acid residues 20 to 466 of an amino acid sequence represented by SEQ ID NO: 99 and a light chain sequence comprising amino acid residues 21 to 238 of an amino acid sequence represented by SEQ ID NO: 105.

[Claim 29]

A pharmaceutical composition, wherein said pharmaceutical composition comprises at least one of the antibodies or functional fragments of the antibodies according to claims 1 to 28.

[Claim 30]

The pharmaceutical composition according to claim 29, wherein said pharmaceutical composition is a therapeutic and/or preventive agent for abnormal bone metabolism.

[Claim 31]

A pharmaceutical composition for treating and/or preventing abnormal bone metabolism, which comprises at least one of the antibodies or functional fragments of the antibodies according to claims 1 to 28 and at least one member selected from the group consisting of bisphosphonates, active vitamin D_3, calcitonin and derivatives thereof, hormones, SERMs (selective estrogen receptor modulators), ipriflavone, vitamin K_2 (menatetrenone), calcium preparations, PTH (parathyroid hormone), nonsteroidal anti-inflammatory agents, soluble TNF receptors, anti-TNF-α antibodies or functional fragments of the antibodies, anti-PTHrP (parathyroid hormone-related protein) antibodies or functional fragments of the antibodies, IL-1 receptor antagonists, anti-IL-6 receptor antibodies or functional fragments of the antibodies, anti-RANKL antibodies or functional fragments of the antibodies,

and OCIF (osteoclastogenesis inhibitory factor).

[Claim 32]

The pharmaceutical composition according to claim 30 or 31, wherein the abnormal bone metabolism is selected from the group consisting of osteoporosis, bone destruction accompanying rheumatoid arthritis, cancerous hypercalcemia, bone destruction accompanying multiple myeloma or cancer metastasis to bone, giant cell tumor, osteopenia, tooth loss due to periodontitis, osteolysis around a prosthetic joint, bone destruction in chronic osteomyelitis, Paget's disease of bone, renal osteodystrophy, and osteogenesis imperfecta.

[Claim 33]

The pharmaceutical composition according to claim 32, wherein the abnormal bone metabolism is osteoporosis, bone destruction accompanying rheumatoid arthritis, or bone destruction accompanying cancer metastasis to bone.

[Claim 34]

The pharmaceutical composition according to claim 33, wherein the abnormal bone metabolism is osteoporosis.

[Claim 35]

The pharmaceutical composition according to claim 34, wherein the osteoporosis is postmenopausal osteoporosis, senile osteoporosis, secondary osteoporosis due to the use of a therapeutic agent, or osteoporosis accompanying rheumatoid arthritis.

[Claim 36]

Use of an antibody according to any one of claims 1 to 28 or a functional fragment thereof for the manufacture of a medicament for treating and/or preventing abnormal bone metabolism.

[Claim 37]

Use of an antibody according to any one of claims 1 to 28 or a functional fragment threof for the manufacture of a

medicament for treating and/or preventing abnormal bone metabolism, wherein said medicament is for simultaneous or successive administration with at least one member selected from the group consisting of bisphosphonates, active vitamin D_3, calcitonin and derivatives thereof, hormones, SERMs (selective estrogen receptor modulators), ipriflavone, vitamin K_2 (menatetrenone), calcium preparations, PTH (parathyroid hormone), nonsteroidal anti-inflammatory agents, soluble TNF receptors, anti-TNF-α antibodies or functional fragments of the antibodies, anti-PTHrP (parathyroid hormone-related protein) antibodies or functional fragments of the antibodies, IL-1 receptor antagonists, anti-IL-6 receptor antibodies or functional fragments of the antibodies, anti-RANKL antibodies or functional fragments of the antibodies, and OCIF (osteoclastogenesis inhibitory factor).

[Claim 38]

The use according to claim 36 or 37, wherein the abnormal bone metabolism is osteoporosis, bone destruction accompanying rheumatoid arthritis, or bone destruction accompanying cancer metastasis to bone.

[Claim 39]

The use according to claim 38, wherein the abnormal bone metabolism is osteoporosis.

[Claim 40]

The use according to claim 39, wherein the osteoporosis is postmenopausal osteoporosis, senile osteoporosis, secondary osteoporosis due to the use of a therapeutic agent, or osteoporosis accompanying rheumatoid arthritis.

[Claim 41]

The pharmaceutical composition according to claims 31 to 35, or the use according to claim 37, wherein the

hormones are estradiol.

[Claim 42]

The pharmaceutical composition according to claim 35 or the use according to claim 40 wherein the therapeutic agent is a steroid or an immunosuppressant.

[Claim 43]

An isolated polynucleotide encoding the antibody according to any one of claims 1, 5, and 8 to 28.

[Claim 44]

The isolated polynucleotide according to claim 43, wherein said polynucleotide contains a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 40 and a nucleotide sequence comprising nucleotides 61 to 396 of a nucleotide sequence represented by SEQ ID NO: 42.

[Claim 45]

The isolated polynucleotide according to claim 44, wherein said polynucleotide contains a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 40 and a nucleotide sequence comprising nucleotides 61 to 711 of a nucleotide sequence represented by SEQ ID NO: 42.

[Claim 46]

The isolated polynucleotide according to claim 43, wherein said polynucleotide contains:

(a) a polynucleotide selected from the group consisting of the following nucleotide sequences:

a1) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 50;

a2) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 52;

a3) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 54;

a4) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 56;

a5) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 58;

a6) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 98;

a7) a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 100;

a8) a nucleotide sequence of a polynucleotide which hybridizes to a polynucleotide comprising a nucleotide sequence complementary to any one of the nucleotide sequences selected from a1) to a7) under stringent conditions; and

a9) a nucleotide sequence including a substitution, deletion, or addition of one nucleotide in any one of the nucleotide sequences selected from a1) to a7); and

(b) a polynucleotide selected from the group consisting of the following nucleotide sequences:

b1) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 60;

b2) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 62;

b3) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 64;

b4) a nucleotide sequence comprising nucleotides 61 to 396 of a nucleotide sequence represented by SEQ ID NO: 66;

b5) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 68;

b6) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 70;

b7) a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 102;

b8) a nucleotide sequence comprising nucleotides 61 to

399 of a nucleotide sequence represented by SEQ ID NO: 104;

b9) a nucleotide sequence of a polynucleotide which hybridizes to a polynucleotide comprising a nucleotide sequence complementary to any one of the nucleotide sequences selected from b1) to b8) under stringent conditions; and

b10) a nucleotide sequence including a substitution, deletion, or addition of one nucleotide in any one of the nucleotide sequences selected from b1) to b8).

[Claim 47]

The polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 50, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 60.

[Claim 48]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 52, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 62.

[Claim 49]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 54, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 64.

[Claim 50]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 54, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 396 of a nucleotide sequence represented by SEQ ID NO: 66.

[Claim 51]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 56, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 52]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 58, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 70.

[Claim 53]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 54]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 100, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 55]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 102.

[Claim 56]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 420 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 399 of a nucleotide sequence represented by SEQ ID NO: 104.

[Claim 57]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 50, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 60.

[Claim 58]

The isolated polynucleotide according to claim 46,

wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 52, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 62.

[Claim 59]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 54, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 64.

[Claim 60]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 54, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 711 of a nucleotide sequence represented by SEQ ID NO: 66.

[Claim 61]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 56, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 62]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide

comprising a nucleotide sequence comprising nucleotides 58 to 1410 of a nucleotide sequence represented by SEQ ID NO: 58, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 70.

[Claim 63]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1398 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 64]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1398 of a nucleotide sequence represented by SEQ ID NO: 100, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 68.

[Claim 65]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58 to 1398 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 102.

[Claim 66]

The isolated polynucleotide according to claim 46, wherein said polynucleotide contains a polynucleotide comprising a nucleotide sequence comprising nucleotides 58

to 1398 of a nucleotide sequence represented by SEQ ID NO: 98, and a polynucleotide comprising a nucleotide sequence comprising nucleotides 61 to 714 of a nucleotide sequence represented by SEQ ID NO: 104.

[Claim 67]

A vector, comprising any one of the polynucleotides according to claims 43 to 66.

[Claim 68]

A transformed host cell, comprising any one of the polynucleotides according to claims 43 to 66.

[Claim 69]

A transformed host cell, comprising the vector according to claim 67.

[Claim 70]

A method of producing the antibody according to any one of claims 1, 5, and 8 to 28, comprising culturing the host cell according to claim 68 or 69, and purifying an antibody from the resulting culture product.