

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

[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 or functional fragment thereof comprises:

a heavy chain sequence containing 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 containing 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, and

wherein the antibody is not the antibody produced by hybridoma FERM BP-10999.

[Claim 2]

The antibody or a functional fragment of the antibody according to claim 1, which 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 3]

The functional fragment of the isolated antibody

according to claim 1 or claim 2 which is selected from the group consisting of Fab, F(ab')₂, Fab' and Fv.

[Claim 4]

The isolated antibody according to claim 1 or claim 2, wherein the antibody is an scFv.

[Claim 5]

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 6]

The isolated antibody or a functional fragment of the isolated antibody according to claim 5, 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 7]

The isolated antibody or a functional fragment of the isolated antibody according to any one of claims 1 to 3, or 5, wherein the antibody is humanized.

[Claim 8]

The isolated antibody according to claim 6 or claim 7, 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 9]

A pharmaceutical composition, wherein said pharmaceutical composition comprises at least one of the antibodies or functional fragments of the antibodies according to any one of claims 1 to 8.

[Claim 10]

The pharmaceutical composition according to claim 9, wherein said pharmaceutical composition is a therapeutic

and/or preventive agent for abnormal bone metabolism.

[Claim 11]

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 any one of claims 1 to 8 and at least one member selected from the group consisting of bisphosphonates, active vitamin D₃, calcitonin and derivatives thereof, hormones, SERMs (selective estrogen receptor modulators), ipriflavone, vitamin K₂ (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 12]

The pharmaceutical composition according to claim 10 or claim 11, 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 13]

The pharmaceutical composition according to claim 12, wherein the abnormal bone metabolism is osteoporosis, bone destruction accompanying rheumatoid arthritis, or bone

destruction accompanying cancer metastasis to bone.

[Claim 14]

The pharmaceutical composition according to claim 13, wherein the abnormal bone metabolism is osteoporosis.

[Claim 15]

The pharmaceutical composition according to claim 14, wherein the osteoporosis is postmenopausal osteoporosis, senile osteoporosis, secondary osteoporosis due to the use of a therapeutic agent, or osteoporosis accompanying rheumatoid arthritis.

[Claim 16]

Use of an antibody according to any one of claims 1 to 8 or a functional fragment thereof for the manufacture of a medicament for treating and/or preventing abnormal bone metabolism

[Claim 17]

Use of an antibody according to any one of claims 1 to 8 or a functional fragment thereof 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 D₃, calcitonin and derivatives thereof, hormones, SERMs (selective estrogen receptor modulators), ipriflavone, vitamin K₂ (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 18]

The use according to claim 16 or claim 17, wherein the abnormal bone metabolism is osteoporosis, bone destruction accompanying rheumatoid arthritis, or bone destruction accompanying cancer metastasis to bone.

[Claim 19]

The use according to claim 18, wherein the abnormal bone metabolism is osteoporosis.

[Claim 20]

The use according to claim 19, wherein the osteoporosis is postmenopausal osteoporosis, senile osteoporosis, secondary osteoporosis due to the use of a therapeutic agent, or osteoporosis accompanying rheumatoid arthritis.

[Claim 21]

The pharmaceutical composition according to any one of claims 11 to 15, or the use according to claim 17, wherein the hormones are estradiol.

[Claim 22]

The pharmaceutical composition according to claim 15 or the use according to claim 20 wherein the therapeutic agent is a steroid or an immunosuppressant.

[Claim 23]

An isolated polynucleotide encoding the antibody according to claim 2 or claim 6.

[Claim 24]

The isolated polynucleotide according to claim 23, 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 25]

The isolated polynucleotide according to claim 24, 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 26]

A vector, comprising any one of the polynucleotides according to any one of claims 23 to 25.

[Claim 27]

A transformed host cell, comprising any one of the polynucleotides according to any one of claims 23 to 25.

[Claim 28]

A transformed host cell, comprising the vector according to claim 26.

[Claim 29]

A method of producing the antibody according to claim 2 or claim 6, comprising culturing the host cell according to claim 27 or claim 28, and purifying an antibody from the resulting culture product.

[Claim 30]

An antibody or functional fragment thereof according to any one of claims 1 to 8, or a pharmaceutical composition according to any one of claims 9 to 15, 21 or 22, or a method according to claim 29, or use according to any one of claims 16 to 22, or a polynucleotide according to any one of claims 23 to 25, or a vector according to claim 26, or a transformed host cell according to claim 27 or 28 substantially as hereinbefore defined.