

[CLAIMS]

[Claim 1]

Use of an antibody that binds to latent myostatin in the manufacture of a medicament for treatment of a muscle wasting disease, wherein the antibody inhibits activation of myostatin.

[Claim 2]

Use of an antibody that binds to latent myostatin in the manufacture of a medicament for increasing mass of muscle tissue, wherein the antibody inhibits activation of myostatin.

[Claim 3]

Use of an antibody that binds to latent myostatin in the manufacture of a medicament for increasing strength of muscle tissue, wherein the antibody inhibits activation of myostatin.

[Claim 4]

Use of an antibody that binds to latent myostatin in the manufacture of a medicament for reducing body fat accumulation, wherein the antibody inhibits activation of myostatin.

[Claim 5]

The use according to any one of claims 1 to 4, wherein the antibody blocks the release of mature myostatin from latent myostatin.

[Claim 6]

The use according to claim 5, wherein the antibody blocks the proteolytic release of mature myostatin.

[Claim 7]

The use according to claims 5, wherein the antibody blocks the spontaneous release of mature myostatin.

[Claim 8]

The use according to any one of claims 1 to 7, wherein the antibody does not bind to mature myostatin.

[Claim 9]

The use according to any one of claims 1 to 8, wherein the antibody binds to an epitope within a fragment consisting of amino acids 21-100 of myostatin propeptide (SEQ ID NO: 78).

[Claim 10]

The use according to any one of claims 1 to 9, wherein the antibody binds to the same epitope as an antibody described in Tables 2a, 11a, and 13.

[Claim 11]

The use according to any one of claims 1 to 10, wherein the antibody binds to latent myostatin with higher affinity at neutral pH than at acidic pH.

[Claim 12]

The use according to any one of claims 1 to 11, wherein the antibody is a monoclonal antibody.

[Claim 13]

The use according to any one of claims 1 to 12, wherein the antibody is a human, humanized, or chimeric antibody.

[Claim 14]

The use according to any one of claims 1 to 13, wherein the antibody is an antibody fragment that binds to myostatin.

[Claim 15]

The use according to any one of claims 1 to 14, wherein the antibody comprises (a) HVR-H3 comprising the amino acid sequence GVPAX₁SX₂GGDX₃, wherein X₁ is Y or H, X₂ is T or H, X₃ is L or K (SEQ ID NO: 128), (b) HVR-L3 comprising the amino acid sequence AGGYGGGX₁YA, wherein X₁ is L or R (SEQ ID NO: 131), and (c) HVR-H2 comprising the amino acid sequence IISX₁AGX₂X₃YX₄X₅X₆WAKX₇, wherein X₁ is Y or H, X₂ is S or K, X₃ is T, M or K, X₄ is Y or K, X₅ is A, M or E, X₆ is S or E, X₇ is G or K (SEQ ID NO: 127).

[Claim 16]

The use according to any one of claims 1 to 14, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence X₁X₂DIS, wherein X₁ is S or H, X₂ is Y, T, D or E (SEQ ID NO: 126), (b) HVR-H2 comprising the amino acid sequence IISX₁AGX₂X₃YX₄X₅X₆WAKX₇, wherein X₁ is Y or H, X₂ is S or K, X₃ is T, M or K, X₄ is Y or K, X₅ is A, M or E, X₆ is S or E, X₇ is G or K (SEQ ID NO: 127), and (c) HVR-H3 comprising the amino acid sequence GVPAX₁SX₂GGDX₃, wherein X₁ is Y or H, X₂ is T or H, X₃ is L or K (SEQ ID NO: 128).

[Claim 17]

The use according to claim 16, wherein the antibody further comprises (a) HVR-L1 comprising the amino acid sequence X₁X₂SQX₃VX₄X₅X₆NWLS, wherein X₁ is Q or T, X₂ is S or T, X₃ is S or E, X₄ is Y or F, X₅ is D or H, X₆ is N, D, A or E (SEQ ID NO: 129), (b) HVR-L2 comprising the amino acid sequence WAX₁TLAX₂, wherein X₁ is S or E, X₂ is S, Y, F or W (SEQ ID NO: 130), and (c) HVR-L3 comprising the amino acid sequence AGGYGGGX₁YA, wherein X₁ is L or R (SEQ ID NO: 131).

[Claim 18]

The use according to any one of claims 1 to 14, wherein the antibody comprises (a) HVR-L1 comprising the amino acid sequence X₁X₂SQX₃VX₄X₅X₆NWLS, wherein X₁ is Q or T, X₂ is S or T, X₃ is S or E, X₄ is Y or F, X₅ is D or H, X₆ is N, D, A or E (SEQ ID NO: 129), (b) HVR-L2 comprising the amino acid sequence WAX₁TLAX₂, wherein

X₁ is S or E, X₂ is S, Y, F or W (SEQ ID NO: 130), and (c) HVR-L3 comprising the amino acid sequence AGGYGGGX₁YA, wherein X₁ is L or R (SEQ ID NO: 131).

[Claim 19]

The use according to claim 16, wherein the antibody further comprises a heavy chain variable domain framework FR1 comprising the amino acid sequence of any one of SEQ ID NOs: 132-134; FR2 comprising the amino acid sequence of any one of SEQ ID NOs: 135-136; FR3 comprising the amino acid sequence of SEQ ID NO: 137; and FR4 comprising the amino acid sequence of SEQ ID NO: 138.

[Claim 20]

The use according to claim 18, wherein the antibody further comprises a light chain variable domain framework FR1 comprising the amino acid sequence of SEQ ID NO: 139; FR2 comprising the amino acid sequence of any one of SEQ ID NOs: 140-141; FR3 comprising the amino acid sequence of any one of SEQ ID NOs: 142-143; and FR4 comprising the amino acid sequence of SEQ ID NO: 144.

[Claim 21]

The use according to any one of claims 1 to 14, wherein the antibody comprises (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of any one of SEQ ID NOs: 13, 16-30, 32-34, and 86-95; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of any one of SEQ ID NOs: 15, 31, 35-38, and 96-99; or (c) a VH sequence as in (a) and a VL sequence as in (b).

[Claim 22]

The use according to claim 21, wherein the antibody comprises a VH sequence of any one of SEQ ID NOs: 13, 16-30, 32-34, and 86-95.

[Claim 23]

The use according to claim 21, wherein the antibody comprises a VL sequence of any one of SEQ ID NOs: 15, 31, 35-38, and 96-99.

[Claim 24]

Use of an antibody in the manufacture of a medicament for treating a muscle wasting disease, wherein the antibody comprises a VH sequence of any one of SEQ ID NOs: 13, 16-30, 32-34, and 86-95 and a VL sequence of any one of SEQ ID NOs: 15, 31, 35-38, and 96-99.

[Claim 25]

Use of an antibody in the manufacture of a medicament for increasing mass of muscle tissue, wherein the antibody comprises a VH sequence of any one of SEQ ID NOs: 13, 16-30, 32-34, and 86-95 and a VL sequence of any one of SEQ ID NOs: 15, 31, 35-38, and 96-99.

[Claim 26]

Use of an antibody in the manufacture of a medicament for increasing strength of muscle tissue, wherein the antibody comprises a VH sequence of any one of SEQ ID

NOs: 13, 16-30, 32-34, and 86-95 and a VL sequence of any one of SEQ ID NOs: 15, 31, 35-38, and 96-99.

[Claim 27]

Use of an antibody in the manufacture of a medicament for reducing body fat accumulation, wherein the antibody comprises a VH sequence of any one of SEQ ID NOs: 13, 16-30, 32-34, and 86-95 and a VL sequence of any one of SEQ ID NOs: 15, 31, 35-38, and 96-99.

[Claim 28]

The use according to any one of claims 1 to 27, wherein the antibody is a full length IgG antibody.