Solution to Problem

[0038] The disclosure provides anti-myostatin antibodies and methods of using the same. The disclosure also provides proteins containing a variant Fc region and methods of using the same. In one aspect, the present disclosure refers to an antibody that binds to latent myostatin, wherein the antibody comprises:

(i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 114,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 58,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(ii) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 114,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 116,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 121,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(iii) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 57,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 117,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(iv) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 57,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 118,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(v) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 57,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 119,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(vi) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 114,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 118,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(vii) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 114,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 58,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 123,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and

HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or
(viii) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 115,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 58,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 123,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or
(ix) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 114,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 58,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 124,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 125, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or
(x) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 115,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 120,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 123,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74. In another example, the present disclosure refers to an isolated antibody that binds to latent myostatin, comprising (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) the VH sequence of (a) and the VL sequence of (b).

[0039] In some examples, an isolated anti-myostatin antibody of the present disclosure binds to latent myostatin. In further examples, the antibody binds to an epitope within a fragment consisting of amino acids 21-100 of myostatin propeptide (SEQ ID NO: 78). In some examples, an isolated anti-myostatin antibody of the present disclosure inhibits activation of myostatin. In further examples, the antibody blocks the release of mature myostatin from latent myostatin. In further examples, the antibody blocks the proteolytic release of mature myostatin. In further examples, the antibody blocks the spontaneous release of mature myostatin. In further examples, the antibody does not bind to mature myostatin. In further examples, the antibody binds to the same epitope as an antibody described in Table 13. In further examples, the antibody binds to the same epitope as an antibody comprising a VH and a VL pair described in Table 13. In further examples, the antibody binds to the same epitope as an antibody described in Table 2a. In further examples, the antibody binds to the same epitope as an antibody comprising a VH and a VL pair described in Table 2a. In further examples, the antibody binds to the same epitope as an antibody described in Table 11a. . In further examples, the antibody binds to the same epitope as an antibody comprising a VH and a VL pair described in Table 11a. In further

examples, the antibody binds to the same epitope as an antibody described in Table 2a, 11a, or 13. In further examples, the antibody binds to the same epitope as an antibody comprising a VH and a VL pair described in Table 2a, 11a, or 13.

[0040] In some examples, an isolated anti-myostatin antibody of the present disclosure binds to latent myostatin with higher affinity at neutral pH than at acidic pH. In some examples, the anti-myostatin antibody binds to latent myostatin with higher affinity at pH7.4 than at pH5.8. In some examples, an isolated anti-myostatin antibody of the present disclosure binds to a polypeptide fragment consisting of amino acids 21-100 of myostatin propeptide (SEQ ID NO: 78) with higher affinity at pH7.4 than at pH5.8. In some examples, the antibody binds to the same myostatin epitope as an antibody described in Table 13 with a higher affinity at neutral pH than at acidic pH. In additional examples, an anti-myostatin antibody binds to the same epitope as an antibody described in Table 13 with a higher affinity at pH7.4 than at pH5.8. In further examples, the antibody binds to the same epitope as an antibody comprising a VH and a VL pair described in Table 13 with a higher affinity at pH7.4

CLAIMS

[Claim 1]

An antibody that binds to latent myostatin, wherein the antibody comprises:

(i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 114,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 58,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(ii) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 114,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 116,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 121,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(iii) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 57,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 117,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(iv) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 57,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 118,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(v) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 57,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 119,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(vi) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 114,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 118,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 122,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(vii) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 114,

HVR-H2 comprising the amino acid sequence of SEQ ID NO: 58,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 123,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(viii) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 115,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 58,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 123,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(ix) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 114,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 58,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 124,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 125, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74; or

(x) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 115,
HVR-H2 comprising the amino acid sequence of SEQ ID NO: 120,
HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63,
HVR-L1 comprising the amino acid sequence of SEQ ID NO: 123,
HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71, and
HVR-L3 comprising the amino acid sequence of SEQ ID NO: 74.

[Claim 2]
An isolated nucleic acid encoding the antibody of claim 1.

[Claim 3]
A host cell comprising the nucleic acid of claim 2.

[Claim 4]
A method of producing an anti-myostatin antibody comprising culturing the host cell of claim 3 so that the antibody is produced.

[Claim 5]
A pharmaceutical formulation comprising the antibody of claim 1 and a pharmaceutically acceptable carrier.