

CLAIMS

1. Use of a composition in the preparation of a medicament for treating or preventing a disease associated with impaired neurological signaling between a neuron and a target tissue in a human subject, wherein the disease is spinal muscular atrophy (SMA), spinal cord injury (SCI), muscular atrophy, muscular dystrophy, amyotrophic lateral sclerosis (ALS), or myasthenia gravis; and wherein the composition comprises an antibody, or an antigen binding fragment thereof, that specifically binds pro/latent-myostatin and blocks release of mature myostatin, wherein the antibody or antigen binding fragment is in an amount effective to treat or prevent the disease.
2. The use of claim 1, wherein the antibody or antigen binding fragment is in an amount effective to increase the level of latent myostatin in a circulation serum sample, as compared to the level of latent myostatin in a control serum sample.
3. The use of claim 1, wherein the disease is SMA or SCI.
4. The use of claim 1, wherein the muscular atrophy is associated with a defect in motor neurons, SMA, ALS, or myasthenia gravis.
5. The use of claim 4, wherein the defect in motor neurons comprises a genetic mutation.
6. The use of claim 1, wherein the muscle atrophy comprises glucocorticoid-induced muscle atrophy.
7. The use of claim 1 or 3, wherein the subject is in an acute phase of SCI, a sub-acute phase of SCI, or a chronic phase of SCI.
8. The use of claim 1, 3, or 7, wherein the SCI is partial/incomplete SCI.
9. The use of claim 1, 3, 7, or 8, wherein the SCI is associated with a metabolic disorder.
10. The use of claim 9, wherein the metabolic disorder is or comprises insulin resistance, inflammation, abnormal lipid metabolism, or an increase in intramuscular fat infiltration.
11. The use of any one of claims 1-10, wherein the composition further comprises a second therapeutic agent.

12. The use of claim 11, wherein the second therapeutic agent comprises a neuroprotective therapy or a gene therapy.
13. The use of claim 12, wherein the neuroprotective therapy comprises a stem cell therapy.
14. The use of any one of claims 1-13, wherein the antibody or antigen binding fragment comprises:
- a) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 24 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 30;
 - b) a heavy chain variable region comprising a CDRH1 sequence comprising SEQ ID NO: 1, a CDRH2 sequence comprising SEQ ID NO: 4, and a CDRH3 sequence comprising SEQ ID NO: 10 or 66; and a light chain variable region comprising a CDRL1 sequence comprising SEQ ID NO: 12, a CDRL2 sequence comprising SEQ ID NO: 18, and a CDRL3 sequence comprising SEQ ID NO: 22 or 67;
 - c) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 25 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 31;
 - d) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 26 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 32;
 - e) a heavy chain variable region comprising a CDRH1 sequence comprising SEQ ID NO: 1, a CDRH2 sequence comprising SEQ ID NO: 6, and a CDRH3 sequence comprising SEQ ID NO: 11; and a light chain variable region comprising a CDRL1 sequence comprising SEQ ID NO: 14, a CDRL2 sequence comprising SEQ ID NO: 20, and a CDRL3 sequence comprising SEQ ID NO: 23;
 - f) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 27 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 33;
 - g) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 28 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 34;
 - h) a heavy chain variable region comprising a CDRH1 sequence comprising SEQ ID NO: 1, a CDRH2 sequence comprising SEQ ID NO: 8, and a CDRH3 sequence comprising SEQ ID NO: 11; and a light chain variable region comprising a CDRL1 sequence comprising SEQ ID NO: 16, a CDRL2 sequence comprising SEQ ID NO: 20, and a CDRL3 sequence comprising SEQ ID NO: 23;
 - i) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 29 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 35;

j) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 73 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 74;

k) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 98 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 99;

l) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 88 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 89;

m) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 78 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 79;

n) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 83 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 84;

o) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 93 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 94;

p) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 103 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 104;

q) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 108 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 109; or

r) a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 113 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 114.

15. The use of any one of claims 1-14, wherein the antibody or antigen binding fragment comprises:

a) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 24 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30;

b) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 25 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 31;

c) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 26 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 32;

d) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 27 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 33;

- e) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 28 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 34;
- f) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 35;
- g) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 73 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 74;
- h) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 98 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 99;
- i) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 88 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 89;
- j) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 78 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 79;
- k) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 83 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 84;
- l) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 93 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 94;
- m) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 103 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 104;
- n) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 108 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 109; or
- o) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 113 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 114.

16. The use of any one of claims 1-14, wherein the antibody or antigen binding fragment comprises a heavy chain variable region comprising a CDRH1 sequence comprising SEQ ID NO: 1, a CDRH2 sequence comprising SEQ ID NO: 4, and a CDRH3 sequence comprising SEQ ID NO: 66; and a light chain variable region comprising a CDRL1 sequence comprising SEQ ID NO: 12, a CDRL2 sequence comprising SEQ ID NO: 18, and a CDRL3 sequence comprising SEQ ID NO: 67.

17. The use of claim 16, wherein the antibody or antigen binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 25 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 31.

18. The use of claim 16 or 17, wherein the antibody or antigen binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 50, and a light chain comprising an amino acid sequence of SEQ ID NO: 51.