Beehler et al. studied the effect of the proteasome inhibitor Velcade (also known as PS-341 and bortezomib) in denervated skeletal muscle in rats. Rats were given vehicle or Velcade (3 mg/kg po) daily for 7 days beginning immediately after induction of muscle atrophy by crushing the sciatic nerve. At the end of the study, the rats were euthanized and the soleus and extensor digitorum longus (EDL) muscles were harvested. In vehicle-treated rats, denervation caused a 33.5 +/- 2.8% and 16.2 +/- 2.7% decrease in the soleus and EDL muscle wet weights (% atrophy), respectively, compared to muscles from the contralateral (innervated) limb. Velcade significantly reduced denervation-induced atrophy to 17.1 +/- 3.3% in the soleus ($P < 0.01$), a 51.6% reduction in atrophy associated with denervation, with little effect on the EDL (9.8 +/- 3.2% atrophy). Histology showed a preservation of muscle mass and preservation of normal cellular architecture after Velcade treatment. Ubiquitin mRNA levels in denervated soleus muscle at the end of the study were significantly elevated 120 +/- 25% above sham control levels and were reduced to control levels by Velcade. In contrast, testosterone proprionate (3 mg/kg sc) did not alleviate denervation-induced skeletal muscle atrophy but did prevent castration-induced levator ani atrophy, while Velcade was without effect. These results show that proteasome inhibition attenuates denervation-induced muscle atrophy in vivo in soleus muscles. However, this mechanism may not be operative in all types of atrophy [1].

1)

Beehler BC, Sleph PG, Benmassaoud L, Grover GJ. Reduction of skeletal muscle atrophy by a proteasome inhibitor in a rat model of denervation. Exp Biol Med (Maywood). 2006 Mar;231(3):335-41. PubMed PMID: 16514182.