Myostatin inhibition attenuates atrophy and loss of muscle function in mice with cancer cachexia

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Cancer cachexia describes the progressive skeletal muscle wasting and weakness in many cancer patients. Cancer cachexia impairs mobility, causes severe fatigue, and accounts for >20% of cancer-related deaths. We tested the hypothesis that antibody-directed myostatin inhibition would attenuate the atrophy and loss of function in skeletal muscles of tumour-bearing mice. Twelve week old C57BL/6 mice received a subcutaneous injection of saline (Control) or 7.5×10^5 Lewis Lung Carcinoma (LLC) tumour cells. One week later, mice began once-weekly injections of saline (Control, n=12; LLC, n=9) or a mouse chimera of anti-human myostatin antibody (PF-354, 10 mg/kg/week, Pfizer Global Research and Development, Groton; USA; LLC+PF-354, n=11), which continued for 5 weeks. Compared with controls, LLC mice had an 8-10% lower muscle mass ($P<0.05$) which was prevented with PF-354 ($P>0.20$). Peak tetanic *in situ* force production of *tibialis anterior* (TA) muscles of LLC mice was reduced by 8% ($P<0.05$), but this deficit was attenuated with PF-354 treatment ($P>0.05$). PF-354 increased the cross-sectional area (CSA) of Type IIx/b fibres in TA muscle from LLC mice by 12% ($P<0.05$), but there was no difference between groups in CSA of Type IIa fibres ($P=0.56$). Apoptosis in cross-sections of TA muscle from LLC mice was increased by 140% ($P<0.05$), but this increase was prevented with PF-354 treatment ($P>0.05$). Antibody-directed myostatin inhibition attenuated the skeletal muscle atrophy and loss of muscle force-producing capacity in a murine model of cancer cachexia, in part by reducing apoptosis. These findings highlight the therapeutic potential of myostatin inhibition for cancer cachexia.