



Supplemental Figure 4. Effect of myostatin on capillaries and endothelial cell proliferation.

(a-d) Investigations were done after a 4 months treatment of wild-type and *mdx* mice with either sActRIIB-Fc or PBS (controls). Plots in (a-d) depict capillarization of wild-type *EDL* ($n=1625$ fibers from PBS treated muscles ($n=3$) and $n=2752$ fibers from sActRIIB-Fc treated muscles ($n=4$)) and *mdx* *EDL* muscle ($n=2609$ fibers from PBS treated muscles ($n=3$) and $n=2137$ fibers from sActRIIB-Fc treated muscles ($n=3$)). Histograms in (a) and (c) depict the distribution of muscle fibers according to the number of capillaries per muscle fiber. Diagrams in (b) and (d) depict the capillary domain (average fiber area serviced per capillary [μm^2]). Values are depicted as means \pm SEM. p-Values were calculated using the non-parametric *U*-Test (e) Cultures of human umbilical vein endothelial cells (HUVEC) were treated for 24 h with recombinant myostatin at concentrations of 0.06, 0.10 and 0.33 $\mu\text{g/ml}$. At low concentration (0.06 $\mu\text{g/ml}$), myostatin inhibited cell proliferation as the doubling time of cells in culture increased. Higher myostatin concentrations caused large variability of doubling time which was caused by cytotoxicity. All values are statistically significant relative to the control.