## SUPPLEMENTAL DATA

**Supplemental Figure 1.** Correlation of SDH staining with fiber types in skeletal muscle. SDH stainings (left panels) and myosin heavy chain (MHC) immunofluorescences (right panels) for the four different skeletal muscle MHC isoforms reveal strong SDH activity in the predominantly oxidative fiber types I and IIb. IIx fibers revealed a slight trace of positive SDH staining, while IIb fibers remained completely negative. Scale bar  $50\mu$ m.

Supplemental Figure 2: Reduction in gastrocnemius muscle cross sectional area.

**Supplemental Figure 3: CS2** inhibits baseline NFAT-luc reporter activity in C2C12 cells in a dose-dependent manner.

**Supplemental Figure 4:**  $\alpha$ -actinin2 and  $\alpha$ -actinin3 bind to CS2 and reveal an unaltered expression in *CS2* KO mice. (**A** and **B**) CS2 binds to  $\alpha$ -actinin-2 and  $\alpha$ -actinin-3. Both  $\alpha$ -actinin-2 (**A**) and  $\alpha$ -actinin-3 (**B**) co-immunoprecipitated with HA-CS2 (lanes 2 and 3), while no signal was detected with the vector alone (lane 1). (**C**) Western blot analyses for  $\alpha$ -actinin-2 (upper panel) and -3 (lower panel) of "fast" gastrocnemius muscle homogenates from WT and *CS2* KO mice, respectively. (**D**) Western blot analyses for  $\alpha$ -actinin-2 (upper panel) and -3 (lower panel) of "slow" soleus muscle homogenates from WT and *CS2* KO mice.



Supp. Fig. 1







 $\alpha$ -actinin3

 $\alpha$ -actinin3