Supplemental Methods

Sybr Green primers used in Figure 3 are also described previously (1).

Cacna1s For primer:	5'-tccagct actgccatgctgat-3'
Cacna1s Rev primer	5'-tcgacttcctctggttccat-3
Cacnb1 For primer	5'-ctttgcctttgagctagacc-3'
Cacnb1 Rev primer	5'-gcacgtgctctgtcttctta-3'
Cacng1 For primer	5'-catctgcgcatttctgtcct-3'
Cacng1 Rev primer	5'-atcat acgcttcaccgactg-3'
Ryr1 For primer	5'-gtt atcgtcattctgctggc-3'
Ryr1 Rev primer	5'-gcctattccacagatgaagc-3'
Atp2a1 For primer	5'-tggctcatggtcctcaagat-3'
Atp2a1 Rev primer	5'-cctcagctttggctgaagat-3'
Atp2a2 For primer	5'-agcttggagcaggtcaagaa-3'
Atp2a2 Rev primer	5'-gctctacaaaggctgtaatcg-3'
Casq1For primer	5'-actcagagaaggatgcagct-3'
Casq1 Rev primer	5'-ctctacagggtcttctagga-3'
Casq2 For primer	5'-gtgtcttcagacaaggtctc-3'
Casq2 Rev primer	5'-acccttcagaacatacaggc-3'

.

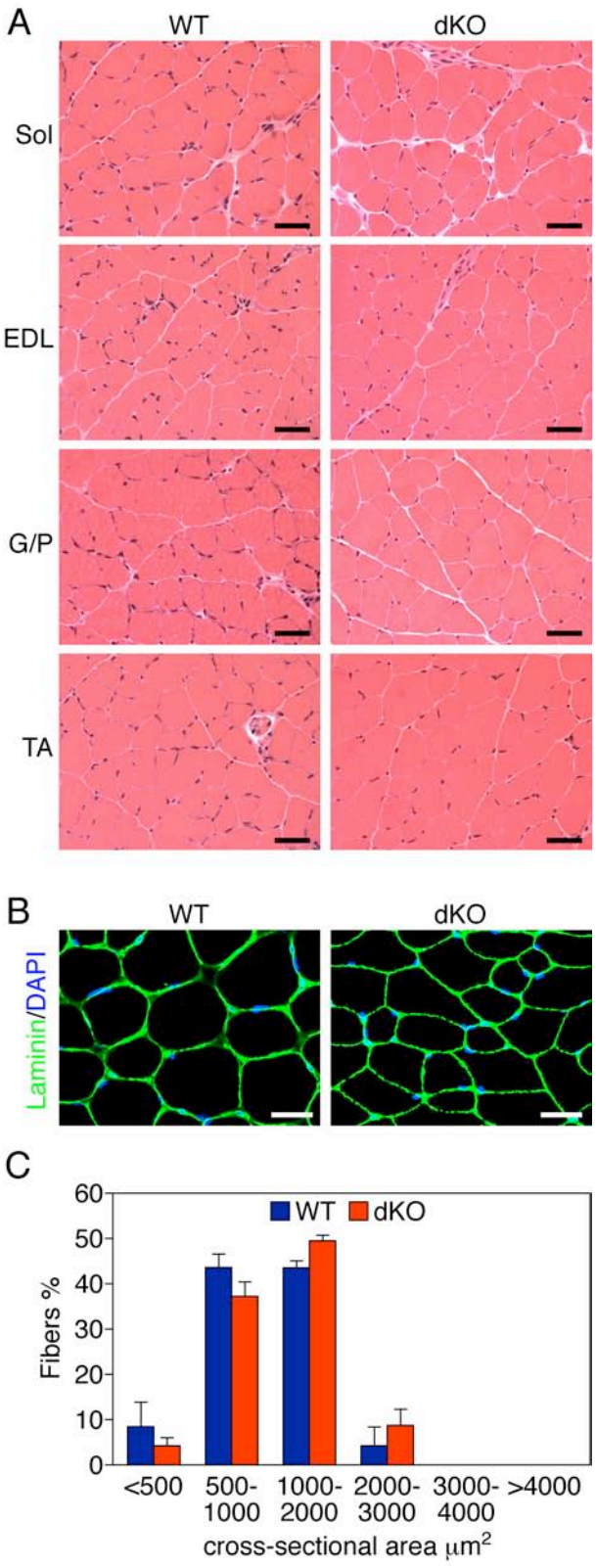
Sybr Green primer used in Figure 8 are also described previously (2).

MHC-1 For primer	5'-CCTTGGCACCAATGTCCCGGCTC-3'
MHC-1 Rev primer	5'-GAAGCGCAATGCAGAGTCGGTG-3'
MHC-IIa For primer	5'-ATGAGCTCCGACGCCGAG-3'
MHC-IIa Rev primer	5'-TCTGTTAGCATGAACTGGTAGGCG-3'
MHC-IIx For primer	5'-AAGGAGCAGGACACCAGCGCCCA-3'
MHC-IIx Rev primer	5'-ATCTCTTTGGTCACTTTCCTGCT-3'
MHC-IIb For primer	5'-GTGATTTCTCCTGTCACCTCTC-3'
MHC-IIb Rev primer	5'-GGAGGACCGCAAGAACGTGCTGA-3'

Reference:

1. Al-Qusairi, L., Weiss, N., Toussaint, A., Berbey, C., Messaddeq, N., Kretz, C., Sanoudou, D., Beggs, A.H., Allard, B., Mandel, J.L., et al. 2009. T-tubule disorganization and defective excitation-contraction coupling in muscle fibers lacking myotubularin lipid phosphatase. *Proc Natl Acad Sci U S A* **106**:18763-18768.
2. Oh, M., Rybkin, II, Copeland, V., Czubryt, M.P., Shelton, J.M., van Rooij, E., Richardson, J.A., Hill, J.A., De Windt, L.J., Bassel-Duby, R., et al. 2005. Calcineurin is necessary for the maintenance but not embryonic development of slow muscle fibers. *Mol Cell Biol* **25**:6629-6638.

Supplemental Figures

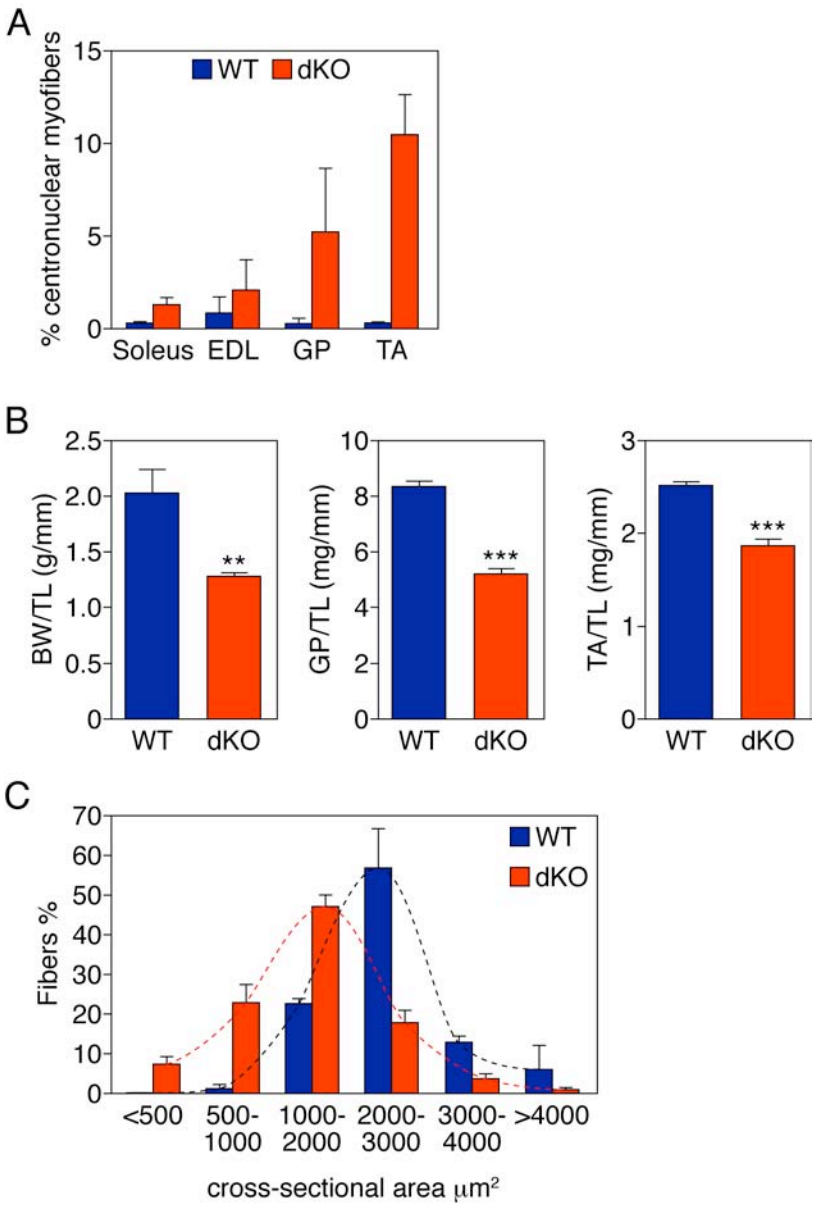


Supplemental Figure 1. **dKO mice have normal muscle appearance at four weeks of age.**

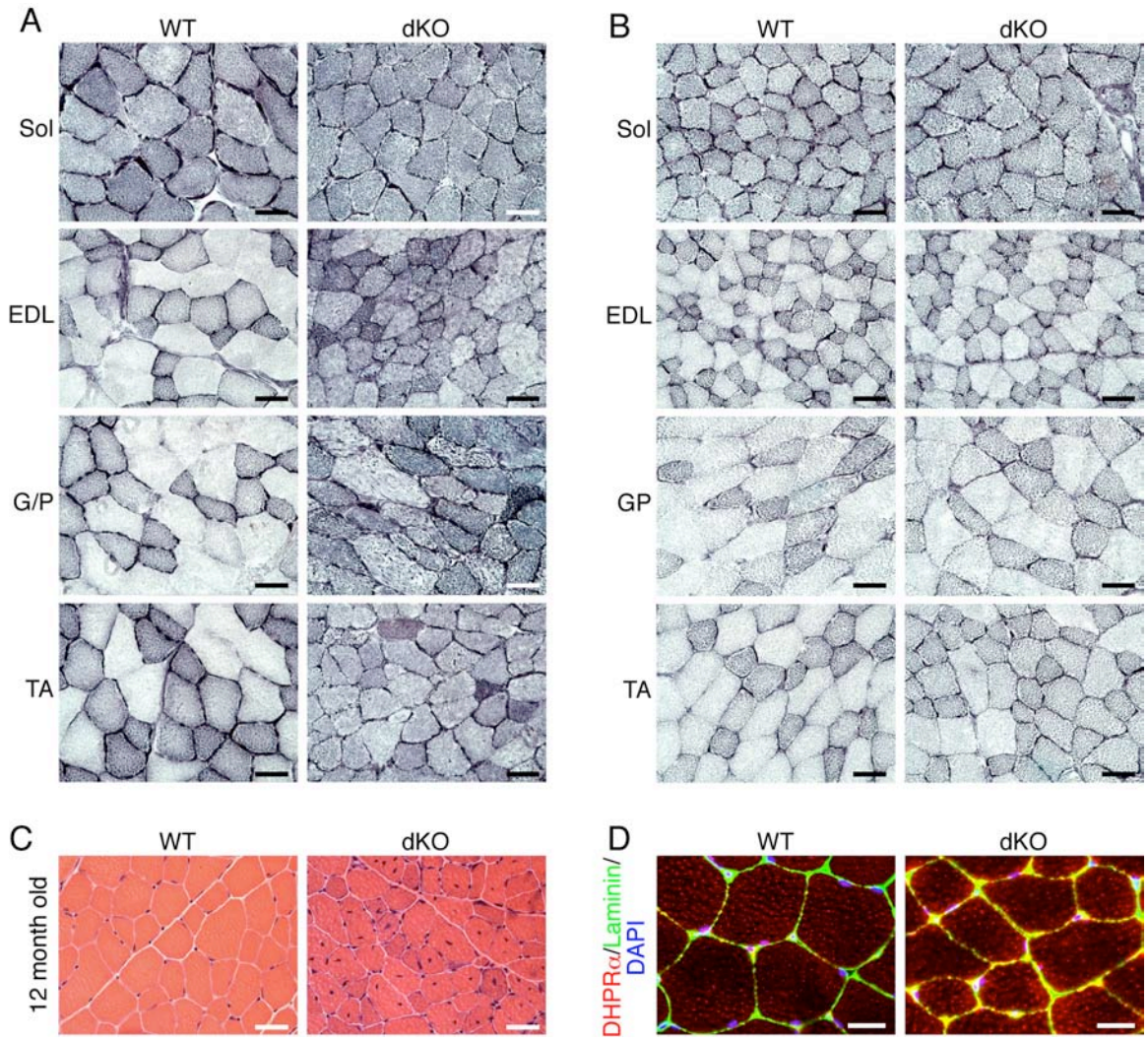
(A) H&E staining of soleus, EDL, G/P and TA muscles from WT and dKO mice at 4 weeks of age. Scale bar = 40 μm.

(B) TA muscle from WT and dKO mice at 4 weeks of age was immunostained with antibody against laminin. DAPI stain was used to detect nuclei and showed no centralized nuclei. Size bar: 30 μm.

(C) Cross-sectional areas of TA muscle fibers of WT and dKO mice at 4 weeks of age was determined using ImageJ program. n=3 WT and dKO. More than 300 TA fibers from each mouse were examined.



Supplemental Figure 2. Characterization of dKO mice.
(A) Percentage of centronuclear fibers in various muscle groups of WT and dKO mice at 6-8 weeks of age. n=3 for WT and n=6 for dKO. Error bars represent SEM.
(B) Measurements of body mass (BW) and muscle mass relative to tibia length (TL) ratios from WT and dKO mice at 12 weeks of age. ** represents $p < 0.01$; *** represents $p < 0.001$.
(C) Cross-sectional areas of TA muscle fibers were determined from WT and dKO mice at 3 months of age. n=5 for WT and n=7 for dKO.



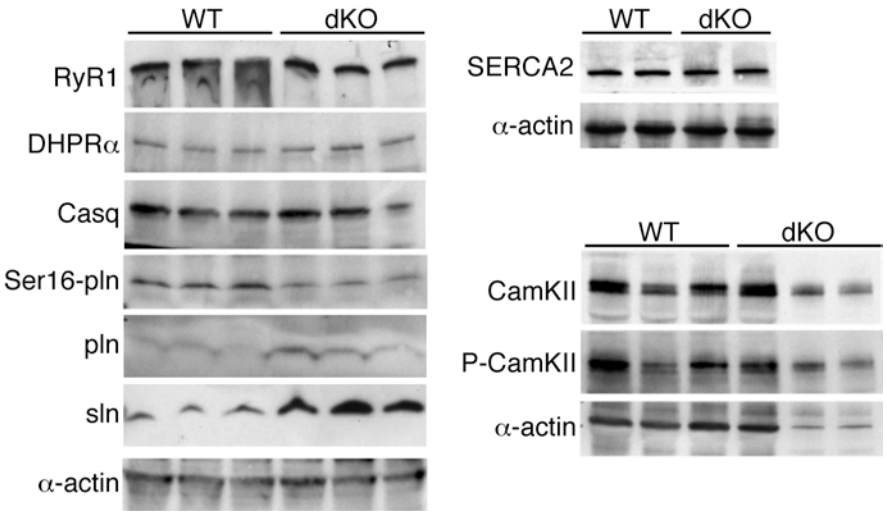
Supplemental Figure 3. Analysis of dKO muscles by NADH-TR, H&E and immunohistochemistry.

(A) NADH-TR staining of soleus, EDL, G/P, and TA muscles of WT and dKO mice at 12 weeks of age. Scale bar = 40 μm.

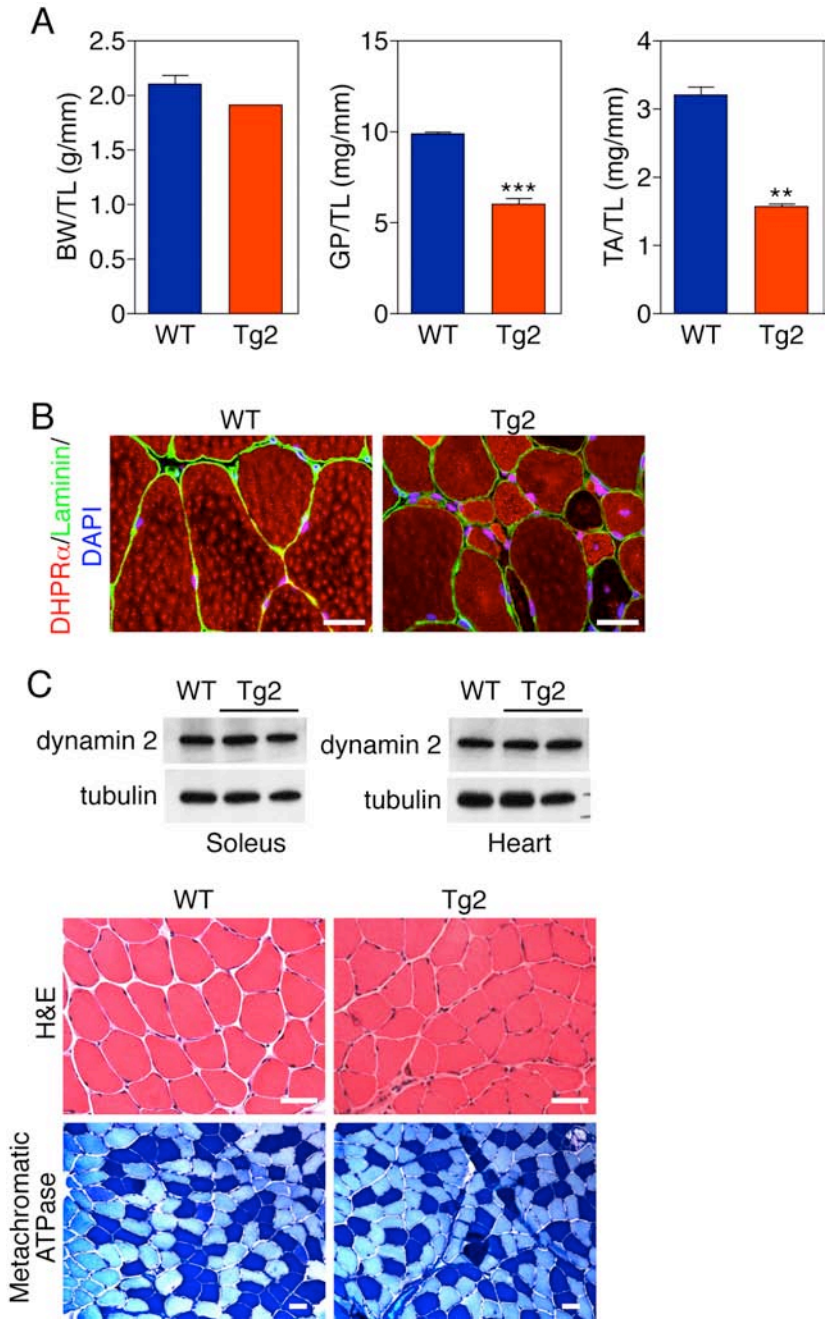
(B) NADH-TR staining of soleus, EDL, G/P, and TA muscles of WT and dKO mice at 4 weeks of age. Scale bar = 40 μm.

(C) H&E staining of TA muscle of WT and dKO mice at 12 months of age. Scale bar = 40 um.

(D) Immunostaining of TA muscle from WT and dKO mice at 4 weeks using antibody against DHPRα to detect T-tubule distributions. There is no apparent difference in the T-tubule staining pattern between WT and dKO muscle at this age. Size bar: 30 μm.



Supplemental Figure 4. Western blot analysis of WT and dKO TA muscle on proteins related to SR and T-tubules.
Western blot analysis was performed on protein lysates from 3 month-old WT dKO TA muscle. Antibodies were used to detect expression of RyR1, DPHRα, Calsequestrin (Casq), SERCA2, Phospholamban (pln), phosphorylated Phospholamban at Serine 16 (Ser16-pln), Sarcolipin (sln), CamKII, and phosphorylated CamKII. α-actin was detected as a loading control.

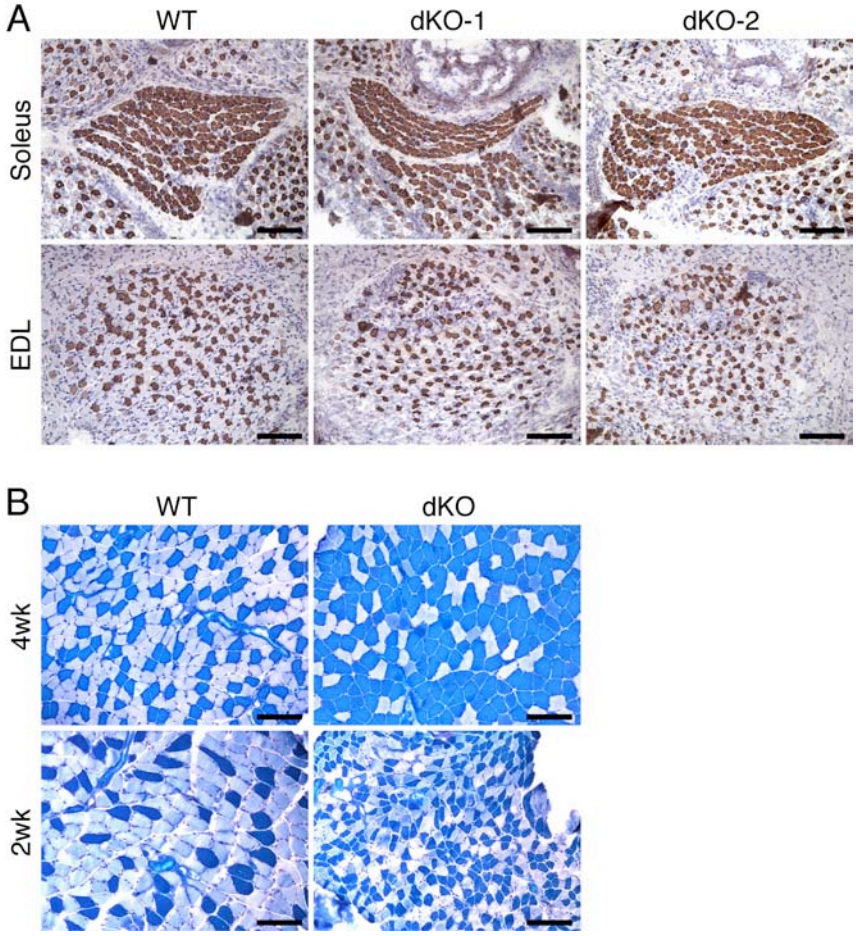


Supplemental Figure 5. Analysis of MCK-Dnm2 transgenic mice.

(A) Measurements of body mass (BW) and muscle mass of WT and MCK-Dnm2 Tg mice at 11 weeks of age. ** represents $p < 0.01$; *** represents $p < 0.001$. n=3 for WT and Tg2 mice.

(B) Immunostaining of TA muscle from WT and Tg2 mice at 11 weeks of age using antibody against DHPRα to detect T-tubule distributions. Size bar: 30 μm.

(C) Top panel: western blot analysis showing expression of dynamin 2 protein in Tg2 soleus muscle and heart at 11 weeks of age. Bottom panel: histological analysis of soleus muscle of WT and Tg2 mice at 11 weeks of age. Soleus muscle sections were stained with H&E and Metachromatic ATPase to show Type I myofibers (dark blue).



Supplemental Figure 6. Fiber type analysis of WT and dKO muscles.
(A) Immunohistochemistry of soleus and EDL muscles from WT and dKO mice at postnatal day 1 using antibody against MHC-I. Scale bar = 100 μm.
(B) Metachromatic ATPase staining of soleus muscle from WT and dKO mice at 4 and 2 weeks. Scale bar = 100 μm.