Expanded View Figures

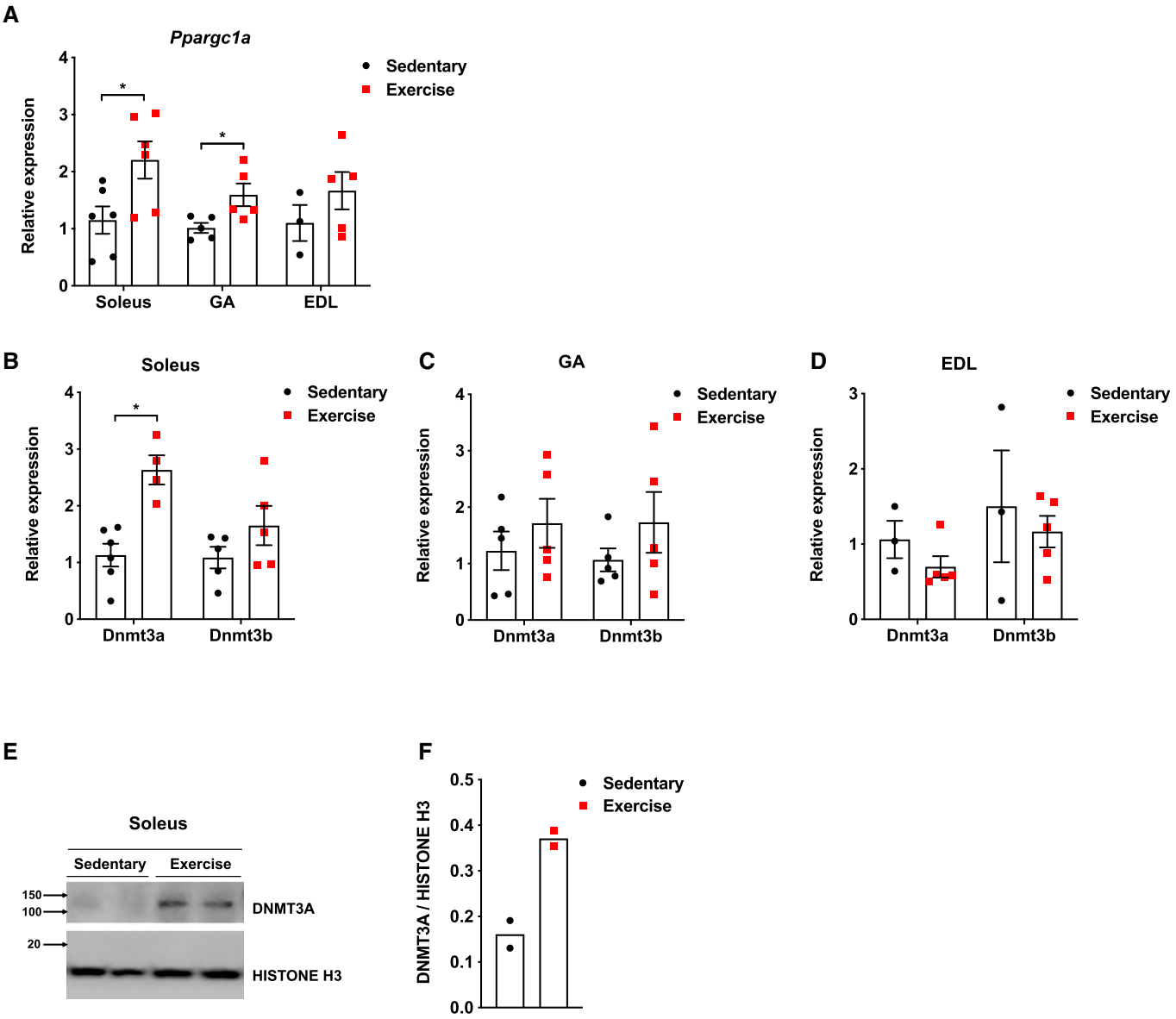

Figure EV1. *Dnmt3a* levels are upregulated in soleus and GA muscles after a bout of endurance exercise.

A *Ppargc1a* was measured in various muscle types from C57BL/6J mice at rest and after a bout of low-intensity exercise (n = 6 Soleus, n = 5 GA, n = 3 EDL Sedentary and n = 5 EDL exercise, means ± SEM, *P < 0.05, two-tailed Student's t-test).

B–D Transcript levels of genes encoding *de novo* DNMTs were measured in soleus (B), GA (C), and EDL (D) from C57BL/6J mice at rest and after a bout of low-intensity exercise (B: n = 6 Sedentary and n = 4 Exercise for Dnmt3a measurement and n = 5 for Dnmt3b measurement, C: n = 5, D: n = 3 Sedentary and n = 5 Exercise. means ± SEM, *P < 0.05, two-tailed Student's t-test).

E, F (E) Soleus DNMT3A protein level in the nuclear fraction from (A) was measured by immunoblotting and (F) normalizing to Histone H3 using ImageJ.

Source data are available online for this figure.

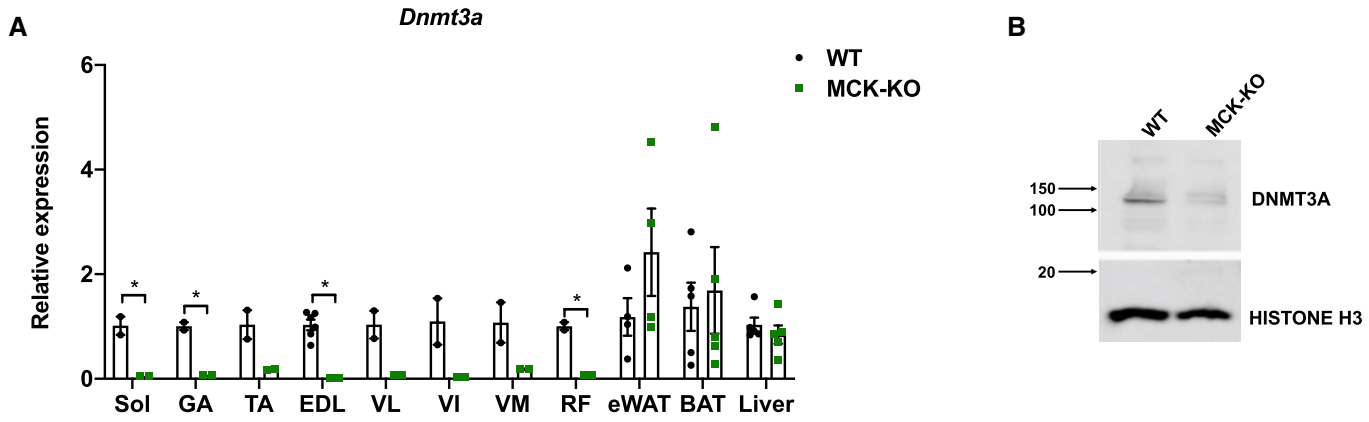

Figure EV2. Establishment of muscle-specific knockout of Dnmt3a using MCK-Cre.

A *Dnmt3a* mRNA expression measured in various tissues from WT and MCK-KO by qPCR analysis ($n = 2$ for soleus, GA, TA, VL, VI, VM, and RF $n = 5$ for EDL, BAT, Liver, $n = 4$ for eWAT, means ± SEM, $^*P < 0.05$, two-tailed Student's *t*-test). eWAT (epididymal white adipose tissue), Quad (quadriceps), Sol (soleus), TA (tibialis anterior), VL (vastus lateralis), VI (vastus intermedius), VM (vastus medialis), RF (rectus femoris).

B DNMT3A protein expression was assessed by immunoblotting using nuclear extract from WT and MCK-KO soleus muscle.

Source data are available online for this figure.

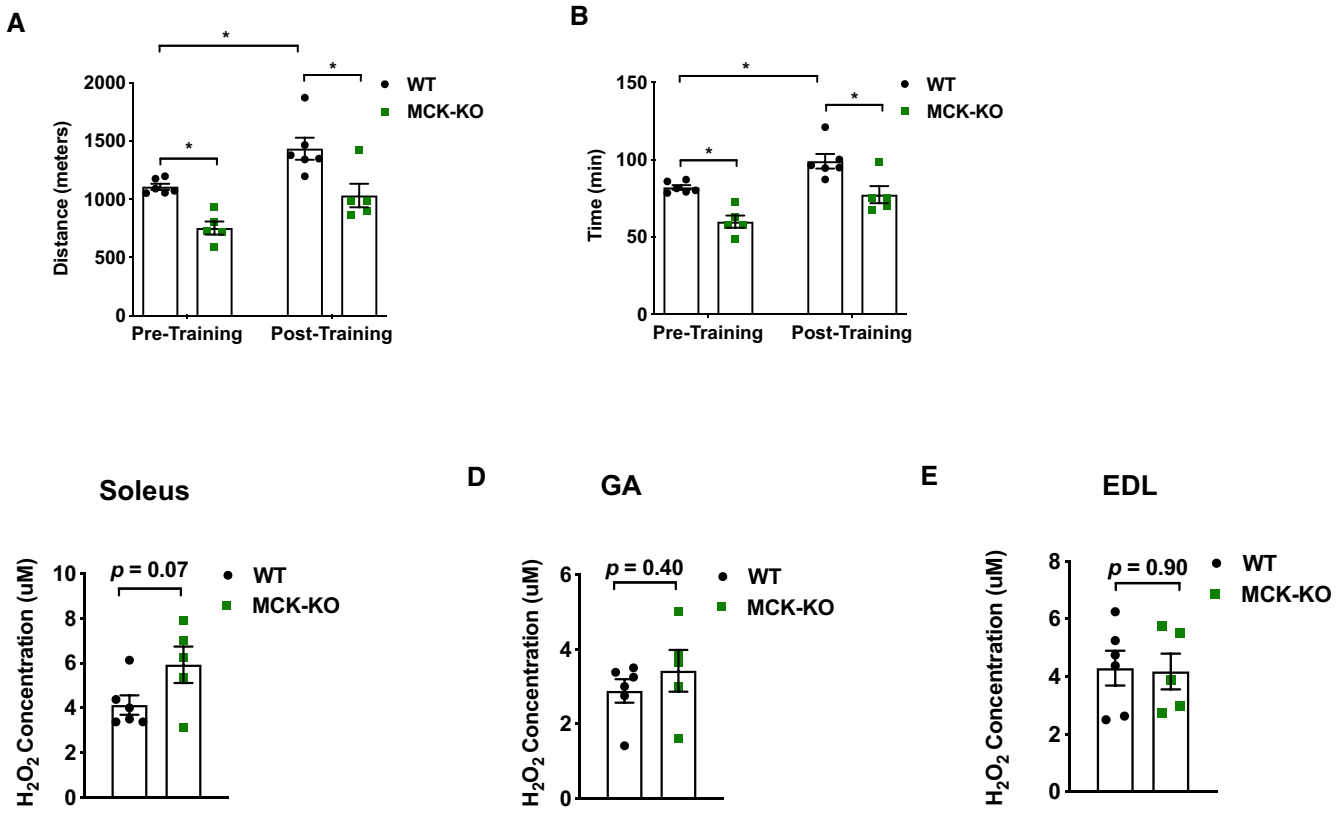

Figure EV3. Response to an exercise training of MCK-*Dnmt3a* KO mice.

A, B Exercise capacity of MCK-KO and WT from the low-intensity regimen accomplished during initial (pretraining) and final exercise testing (post-training) following 4 weeks of treadmill training (n = 6 WT, n = 5 MCK-KO, means ± SEM, *P < 0.05, two-tailed Student's t-test and two-way ANOVA followed by Bonferroni *post hoc* testing).

C–E Hydrogen peroxide (H_2O_2) levels were measured in WT and MCK-KO after 4 weeks of treadmill training in soleus (C), GA (D) and EDL (E). (n = 6 WT, n = 5 MCK-KO means ± SEM, two-tailed Student's t-test).

Source data are available online for this figure.

Figure EV4. type="main"›*Dnmt3a*-KO soleus and GA muscles display a decreased trend in oxidative capacity at 5 weeks of age following exercise.

A–F Succinate dehydrogenase staining and quantification was performed in WT and MCK-KO after a bout of low-intensity exercise for 50 min in soleus (A, B) GA (C, D) and EDL (E, F; 10×, 20× magnifications), and the staining intensity was quantified using ImageJ (n = 6, means ± SEM, two-tailed Student's t-test).

Source data are available online for this figure.

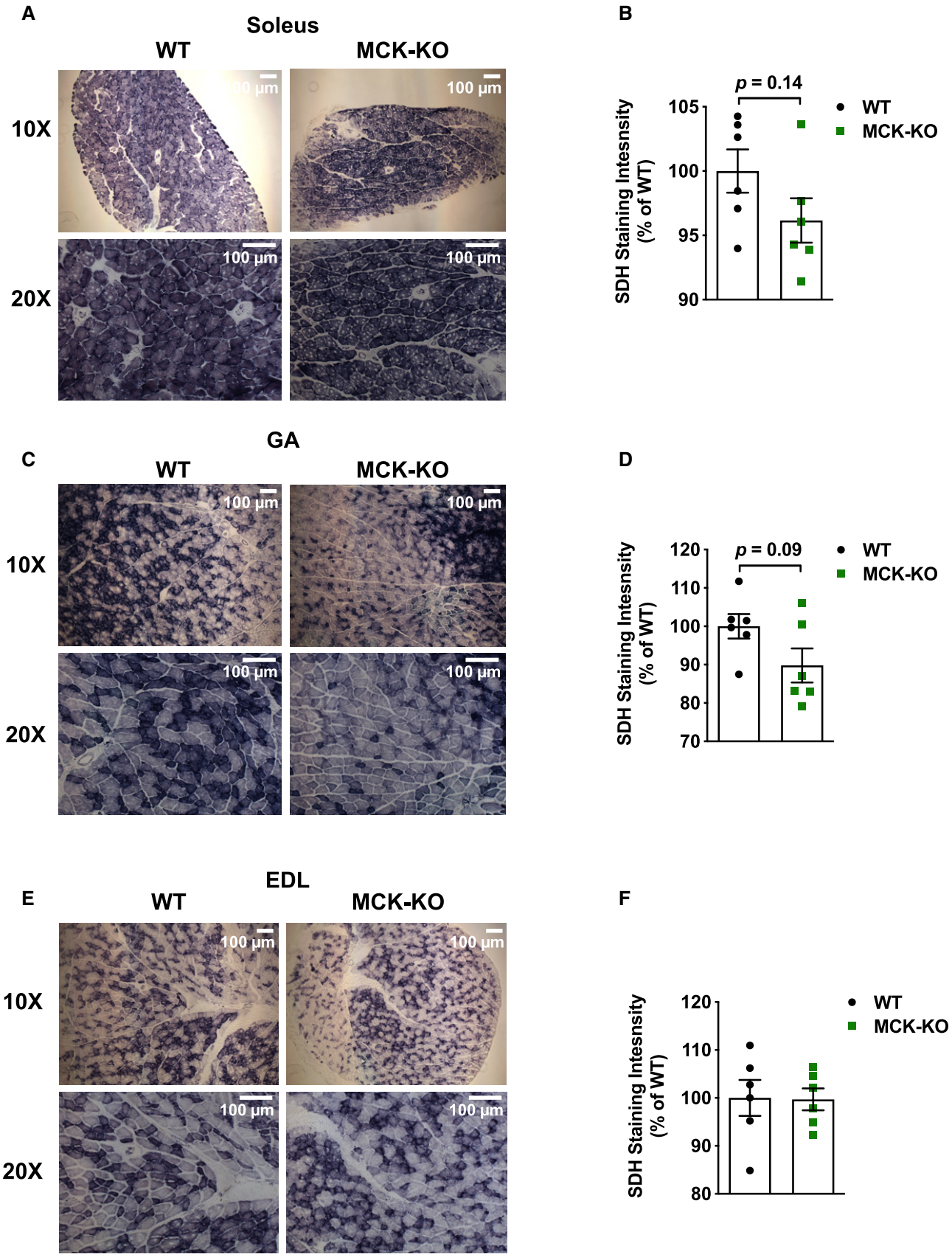

Figure EV4.

Figure EV5. Distribution of MHC isoforms is unchanged in Dnmt3a KO muscles.

A–F Cross sections and quantification of WT and MCK-KO soleus (A, B), GA (C, D), and EDL (E, F) stained with antibodies that are MHC fiber-specific (type I [blue], IIA [green], IIB [red], and IIX [unstained]). ($n = 3$, data are expressed as means ± SEM, two-tailed Student's *t*-test).

G The mRNA expression of muscle subtype-specific MHC isoforms was measured in WT and MCK-KO soleus muscles ($n = 6$, $^*P < 0.05$, means ± SEM, two-tailed Student's *t*-test).

Source data are available online for this figure.

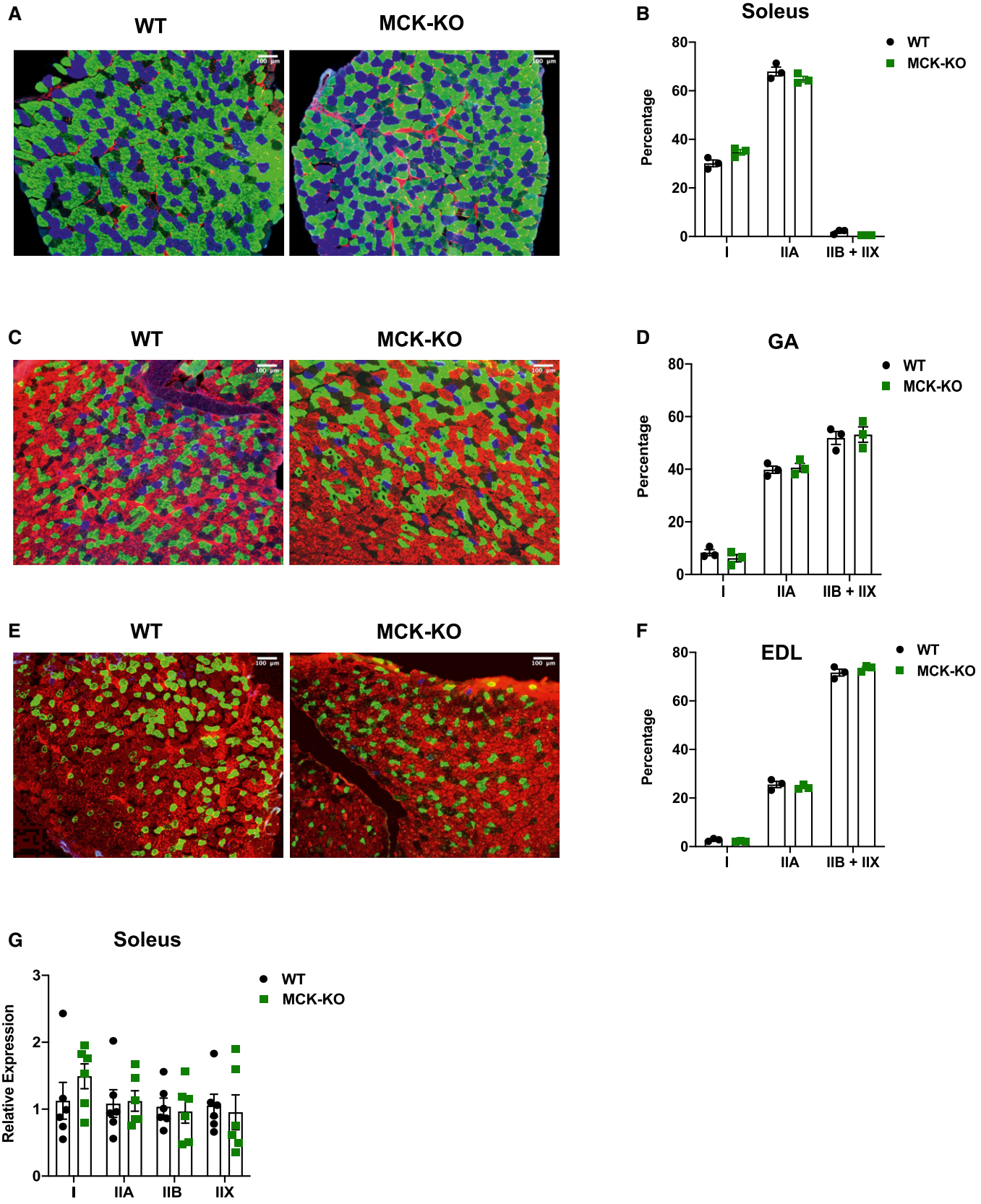
A
WT
MCK-KO
B
Soleus
WT
MCK-KO
Percentage
I
IIA
IIB + IIX
C
WT
MCK-KO
D
GA
WT
MCK-KO
Percentage
I
IIA
IIB + IIX
E
WT
MCK-KO
F
EDL
WT
MCK-KO
Percentage
I
IIA
IIB + IIX
G
Soleus
WT
MCK-KO
Relative Expression
I
IIA
IIB
IIX

Figure EV5.