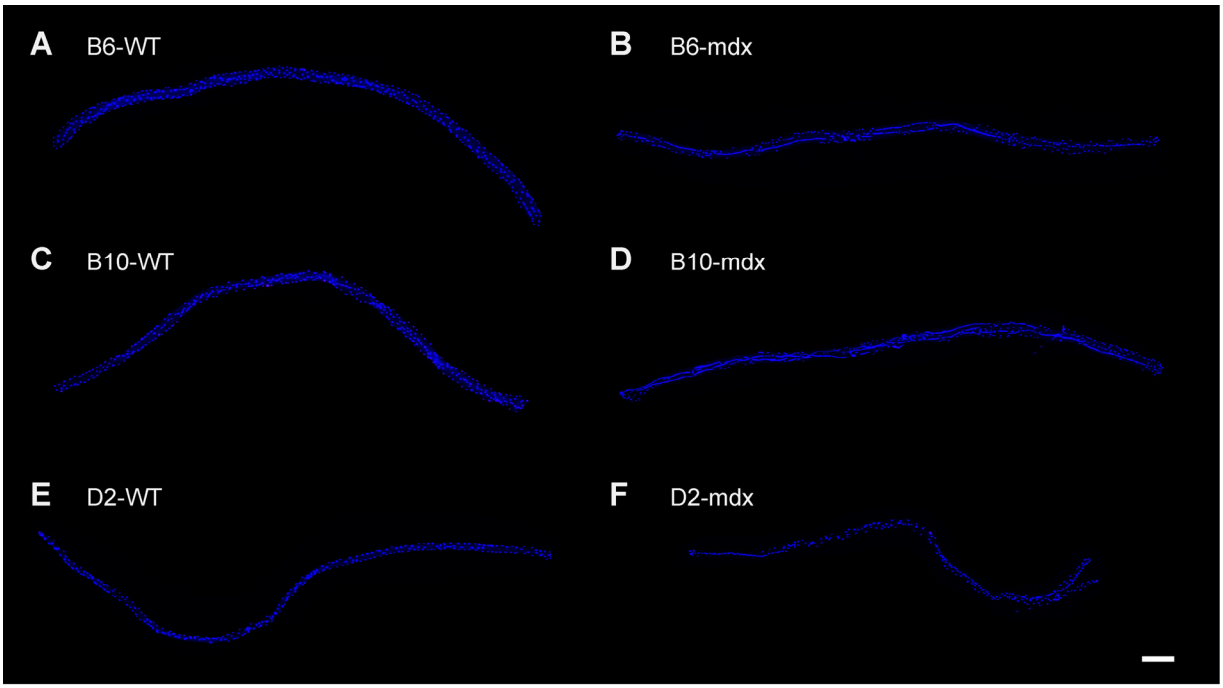


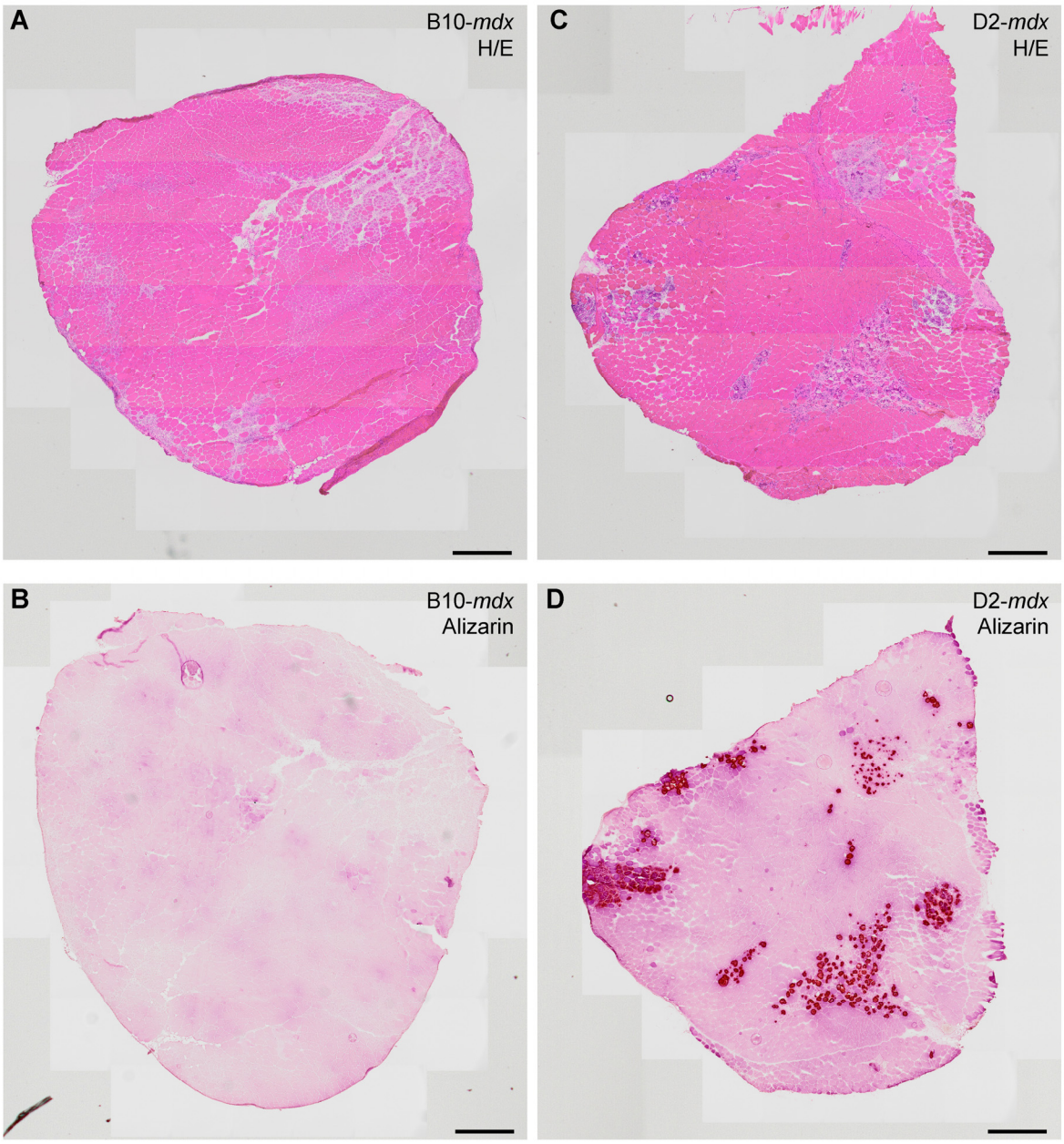
G

Genotype, Age	Genotype, Age	*Adjusted p-value*
B6-WT, 4 wk	B6-WT, 8 wk	0.004
B6-WT, 8 wk	B6-WT, 14 wk	0.0001
B6-WT, 14 wk	D2-WT, 14 wk	0.12
B6-WT, 14 wk	B10-WT, 14 wk	0.003
B10-WT, 14 wk	D2-WT, 14 wk	0.006
B6-WT, 4 wk	B6-*mdx*, 4 wk	0.001
B6-WT, 8 wk	B6-*mdx*, 8 wk	0.001
B6-WT, 14 wk	B6-*mdx*, 14 wk	<0.0001
B6-*mdx*, 4 wk	B6-*mdx*, 8 wk	0.0006
B6-*mdx*, 8 wk	B6-*mdx*, 14 wk	0.004
B6-*mdx*, 14 wk	B10-*mdx*, 14 wk	0.98
B6-*mdx*, 14 wk	D2-*mdx*, 14 wk	0.001
B10-*mdx*, 14 wk	D2-*mdx*, 14 wk	0.0002
B6-WT, 14 wk	B6-*mdx*, 14 wk	<0.0001
B10-WT, 14 wk	B10-*mdx*, 14 wk	<0.0001
D2-WT, 14 wk	D2-*mdx*, 14 wk	<0.0001

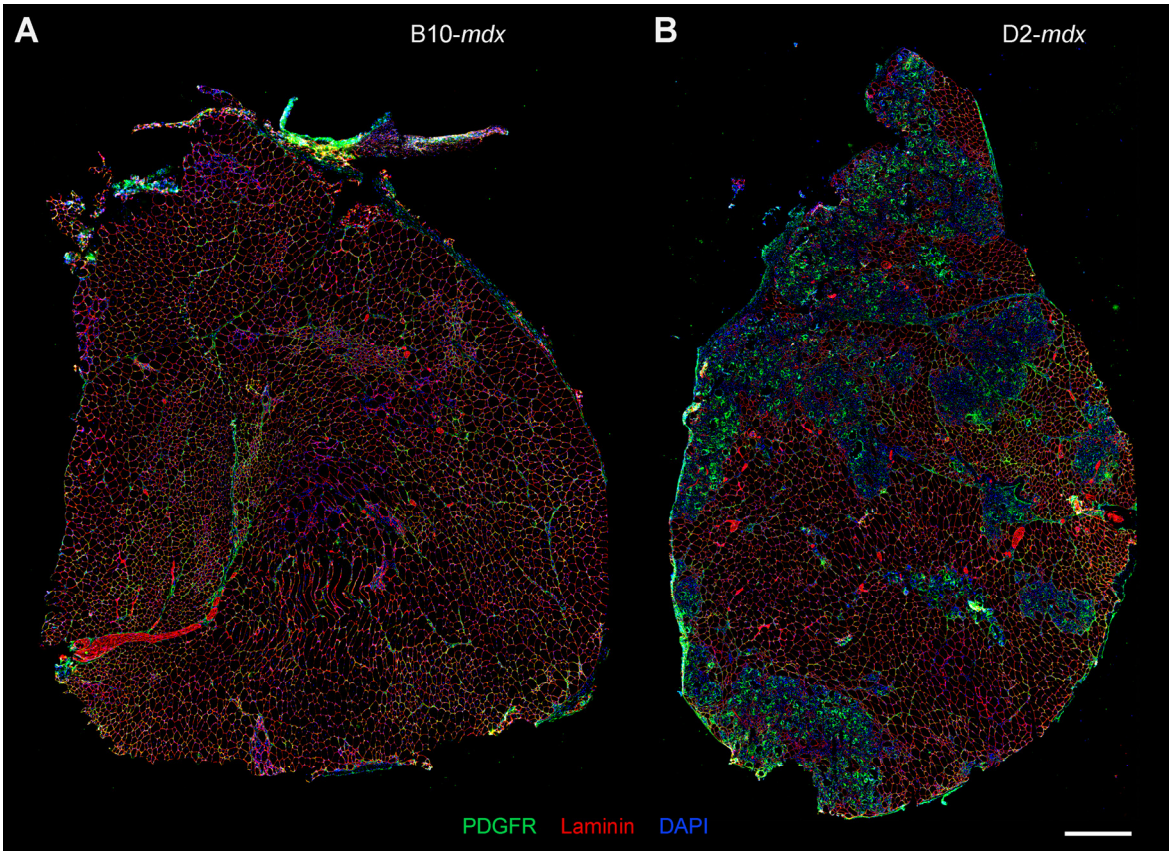
H

Genotype, Age	Kolmogorov-Smirnov Normality Test
B6-WT, 4 wk	Yes, p>0.1000
B6-WT, 8 wk	*No, p=0.0262*
B6-WT, 14 wk	Yes, p>0.1000
B6-*mdx*, 4 wk	Yes, p>0.1000
B6-*mdx*, 8 wk	Yes, p>0.1000
B6-*mdx*, 14 wk	Yes, p>0.1000
B10-WT, 14 wk	Yes, p>0.1000
B10-*mdx*, 14 wk	Yes, p=0.0512
D2-WT, 14 wk	Yes, p>0.1000
D2-*mdx*, 14 wk	Yes, p>0.1000

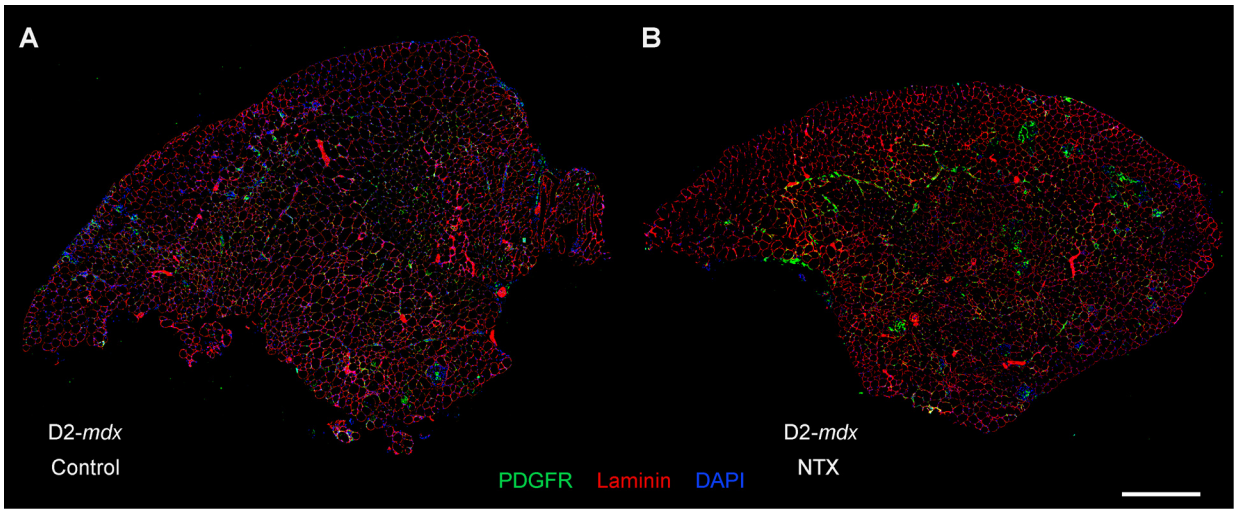
Supplemental Figure 1. Myonuclear incorporation in single EDL myofibers from B6-*mdx*, B10-*mdx*, and D2-*mdx* mice, and their corresponding genotype controls. (**A** to **F**) DAPI nuclear staining of isolated, single EDL muscle fiber depicting nuclear density and fiber branching for 14-week-old B6-WT, B6-*mdx*, B10-WT, B10-*mdx*, D2-WT and D2-*mdx* strains. Scale bar, 200μm. (**G**) Statistical analysis using linear regression models clustered on mouse with Tukey post-hoc multiple comparison adjustment. (**H**) Assessment of data normality was calculated using the Kolmogorov-Smirnov normality test.



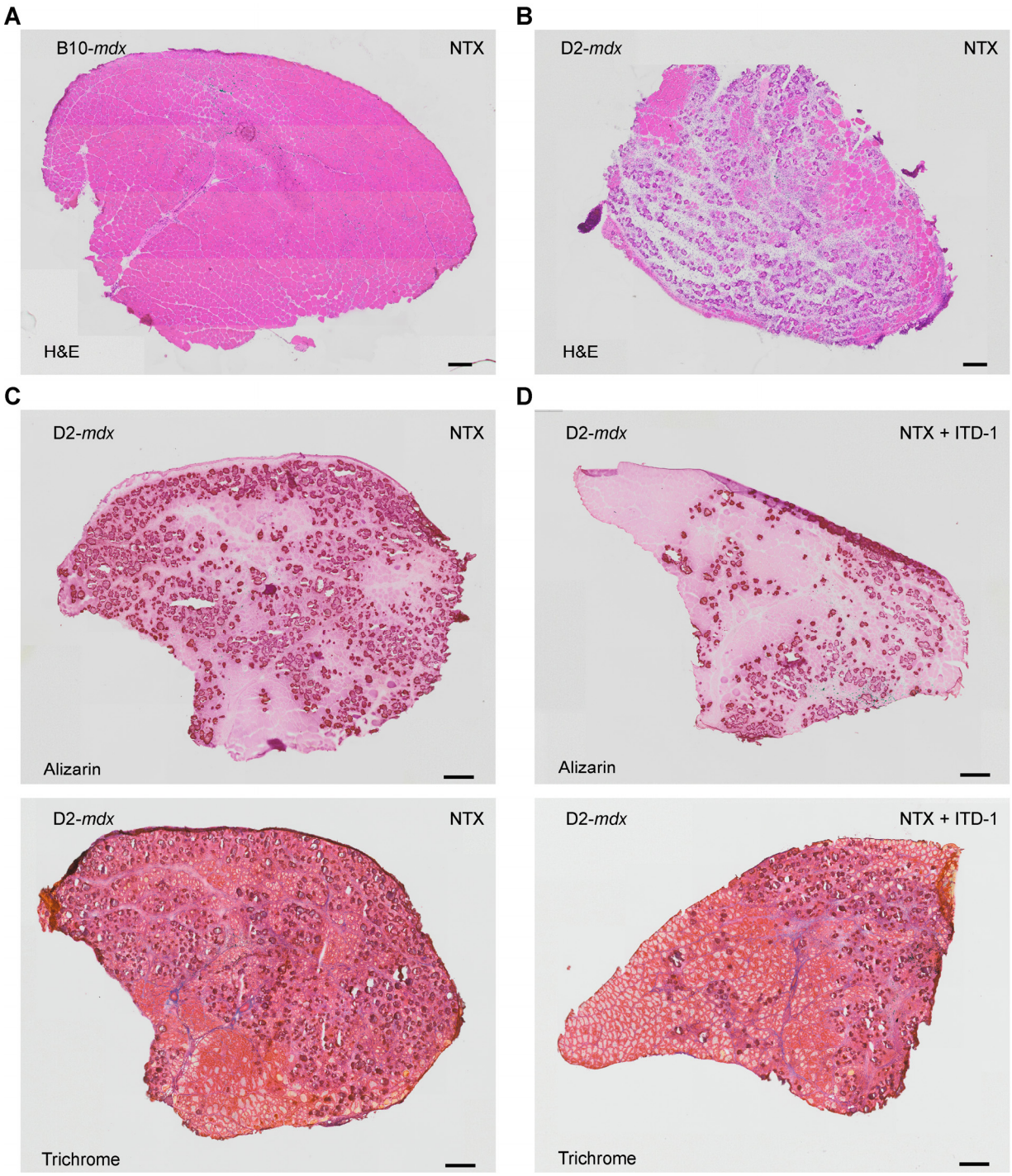
Supplemental Figure 2. Histology of whole muscle sections showing widespread inflammation, degeneration, and calcification in muscles from D2-*mdx* mice. (**A** and **C**) H&E staining of triceps muscle sections from B10-*mdx* and D2-*mdx* mice, respectively, at 38d of age. (**B** and **D**) Alizarin red staining of triceps muscle sections from B10-*mdx* and D2-*mdx* mice, respectively, at 38d of age. Alternate images from those shown in main figures were chosen for whole cross-sectional representation in supplemental panels; upper and lower panels correspond to serial cross-sections. Scale bar, 500μm.



Supplemental Figure 3. Increased expansion of PDGFRα^+ FAPs in response to spontaneous injury in D2-*mdx* muscle. (**A** and **B**) Immunostaining for PDGFRα^+ cells in whole muscle cross-sections from triceps at 38 days of age in B10-*mdx* (**A**) and D2-*mdx* (**B**) mice. Note higher accumulation of PDGFRα^+ cells in muscles from D2-*mdx* mice showing increased presence of fibroadipogenic precursors (FAPs). Scale bar, 500µm.



Supplemental Figure 4. Increased expansion of PDGFRα^+ FAPs in response to notexin-induced injury in D2-*mdx* mice. (**A** and **B**) Immunostaining for PDGFRα^+ cells in whole muscle cross-sections from TA of D2-*mdx* mice analyzed 14 days post NTX-injury; NTX administered at 24 days of age and mice were euthanized at 38 days of age (**B**). Uninjured, contralateral TA muscles (no NTX) were used as controls (**A**). Alternate images from those shown in main figures were chosen for whole cross-sectional representation in supplemental panels. Scale bar, 500μm.



Supplemental Figure 5. Histopathological analysis of fibro-calcification in dystrophic muscle after NTX injury and ITD-1 treatment. (**A** and **B**) H&E staining of NTX-injured TAs from B10-*mdx* (**A**) and D2-*mdx* dissected 5 days post-injury (**B**). Tattoo dye (green). (**C** and **D**) Alizarin red and trichrome staining of corresponding TA muscle sections from D2-*mdx* mice after NTX injury with (**D**) or without (**C**) 3 intramuscular injections of ITD-1. Alternate images from those shown in main figures were chosen for whole cross-sectional representation in supplemental panels; upper and lower panels correspond to serial cross-sections. Scale bar, 200μm.