SUPPLEMENTAL MATERIAL

Table S1. Primers used for qRT-PCR.

Target	Forward primer (5´ to 3´)	Reverse primer (5´ to 3´)
Tgfbr1	AAATTGCTCGACGCTGTTCT	CAACCGATGGATCAGAAGGT
Tgfbr3	CGGAGTACCTTCAACCCAAA	CTCGAGCAGGTCGTATGTCA
Tgfb1	TGAGTGGCTGTCTTTTGACG	AGCCCTGTATTCCGTCTCCT
Tgfb2	CGAGGAGTACTACGCCAAGG	GCGGACGATTCTGAAGTAGG
Tgfb3	GATGAGCACATAGCCAAGCA	TTTCCAGACCCAAGTTGGAC
Myh11	AGCCGGAAAGACAGAGAACA	CCAAAGCGAGAGGAGTTGTC
Tagln	GATGGAACAGGTGGCTCAAT	TTCCATCGTTTTTGGTCACA
Smtn	TCAGAGGCTTCTCCAACACTAAGAG	TTGGCTCTCGATTTGGGGTTGGTTG
Ctgf	AGCAGCTGGGAGAACTGTGT	GCTGCTTTGGAAGGACTCAC
Lox	GGGAGTGGCACAGCTGTCA	TCAGCCACTCTCCTCTGTGTGT
Loxl1	TGTGCAGCCTGGGAACTACA	TGGTGAAGTCAGACTCCAGAACA
Serpine1	GGGCATGCCTGACATGTTTA	TTGCAGTGCCTGTGCTACAGA
Mmp2	CCTGGACCCTGAAACCGTG	TCCCCATCATGGATTCGAGAA
Mmp9	GCGTCGTGATCCCCACTTAC	CAGGCCGAATAGGAGCGTC
Mmp12	TGGTACACTAGCCCATGCTTT	AGTCCACGTTTCTGCCTCATC
Eln	GCGTCTTGCTGATCCTCTTG	GGGAACTCCACCAGGAAGTC
Fbn1	AAGGGTACATCGGCACTCAC	CGTTGAGACAGCCACTTTCA
18S	GGCGTCCCCCAACTTCTTA	GGGCATCACAGACCTGTTATTG

Supplemental Figure Legends:

Figure S1. Pathologic sequelae of knockdown of TBRII in aortic SMC of MFS mice. Representative images of sections of ascending aortas of 16-week-old mice, 10 weeks after treatment with tamoxifen: **A**, **C**, **E**, sections from aortas of *Acta2*-Cre$^{0/0}$ *Fbn1*$^{+/+}$ mice (WT). **B**, **D**, **F**, sections from aortas of *Acta2*-Cre$^{+/0}$ *Fbn1*$^{C1039G/+}$ mice (MFS-TBRII$^{-/-}$). All mice were *Tgfbr2*$^{flox/flox}$. Sections were chosen to illustrate specific pathologic features, not to provide a formal comparison among the 3 groups in this experiment. For a formal comparison of all 3 groups of experimental mice (WT, MFS-TBRII$^{+/+}$, and MFS-TBRII$^{-/-}$), see Table 1. **B**, Arrow: penetrating aortic ulcer. **D**, Arrowheads: aortic intramural hematomas. **F**, arrowheads: Prussian blue stain. Dashed line indicates the boundary between media and adventitia. **A**–**F**, scale bars: 100 µm. **A**–**D**, Hematoxylin and eosin stain; **E**–**F**, Prussian blue stain with eosin counterstain. MFS = Marfan syndrome; TBRII = type II TGF-β receptor.

Figure S2. Abnormal elastic laminae in 16-week-old MFS and MFS-TBRII$^{-/-}$ mice. Representative images of sections of ascending aortas, 10 weeks after treatment with tamoxifen (**A**, **B**, and **D**) or vehicle (**C**). Hematoxylin and eosin-stained sections were illuminated with fluorescein wavelengths. Sections are from: **A**, an *Acta2*-Cre$^{0/0}$ *Fbn1*$^{+/+}$ mouse (WT); **B**, an *Acta2*-Cre$^{0/0}$ *Fbn1*$^{C1039G/+}$ mouse [MFS (T)]; **C**, an *Acta2*-Cre$^{+/0}$ *Fbn1*$^{C1039G/+}$ mouse [MFS (V)]; or **D**, an *Acta2*-Cre$^{+/0}$ *Fbn1*$^{C1039G/+}$ mouse (MFS-TBRII$^{-/-}$). All mice were *Tgfbr2*$^{flox/flox}$. Arrows: elastin breaks. **A** – **D**, scale bars: 100 µm. MFS = Marfan syndrome; (T) = tamoxifen; (V) = vehicle; TBRII = type II TGF-β receptor.

Figure S3. 16-week-old MFS mice develop aortic medial degeneration that is worsened by loss of SMC TBRII. **A**–**D**, images of representative sections of ascending aortas of 16-week-old mice, 10 weeks after treatment with tamoxifen or vehicle. Hematoxylin and eosin-stained sections were illuminated with fluorescein wavelengths. Sections are from: **A**, an *Acta2*-Cre$^{0/0}$ *Fbn1*$^{+/+}$ mouse (WT), **B**, a *Acta2*-Cre$^{0/0}$ *Fbn1*$^{C1039G/+}$ mouse [MFS (T)]; **C**, an *Acta2*-Cre$^{+/0}$ *Fbn1*$^{C1039G/+}$ mouse that

received vehicle [MFS (V)]; and **D**, an *Acta2*-Cre$^{+/0}$ *Fbn1*$^{C1039G/+}$ mouse (MFS-TBRII$^{-/-}$). All mice were *Tgfbr2*$^{flox/flox}$. Boxed areas in **A**, **B**, **C**, **and D** are enlarged in **E**, **F**, **G**, **H**, and **I,** with corresponding colored frames. **F, G**, arrows: moderate elastin damage; **H**, **I**, arrowheads: severe media damage leaving 0–1 elastic laminae intact. Scale bars: 100 μm. MFS = Marfan syndrome; (T) = tamoxifen; (V) = vehicle; TBRII = type II TGF-β receptor.

Figure S4. 8-week-old MFS mice do not have alterations in 3 TGF-β signaling pathways in the ascending aortic media. Protein was extracted from aortic media of 8-week-old *Acta2*-Cre$^{0/0}$ *Fbn1*$^{+/+}$ mice (WT) or *Acta2*-Cre$^{0/0}$ *Fbn1*$^{C1039G/+}$ mice (MFS). All mice were *Tgfbr2*$^{flox/flox}$ and were not injected either with tamoxifen or vehicle. **A**, Western blots were probed with antibodies to phospho-SMAD2, SMAD2, phospho-P38, P38, phospho-ERK1/2, ERK1/2, or β-actin. Each lane is from a single mouse. **B**, Densitometry of western blots shown in **A**. Levels of phosphorylated signaling proteins were normalized to the corresponding unphosphorylated proteins in the same samples. Data are from 3 mice per group; all are shown in **A**. Data are mean ± SEM; P>0.3 for all three; unpaired t tests. MFS = Marfan syndrome; AU = arbitrary units.

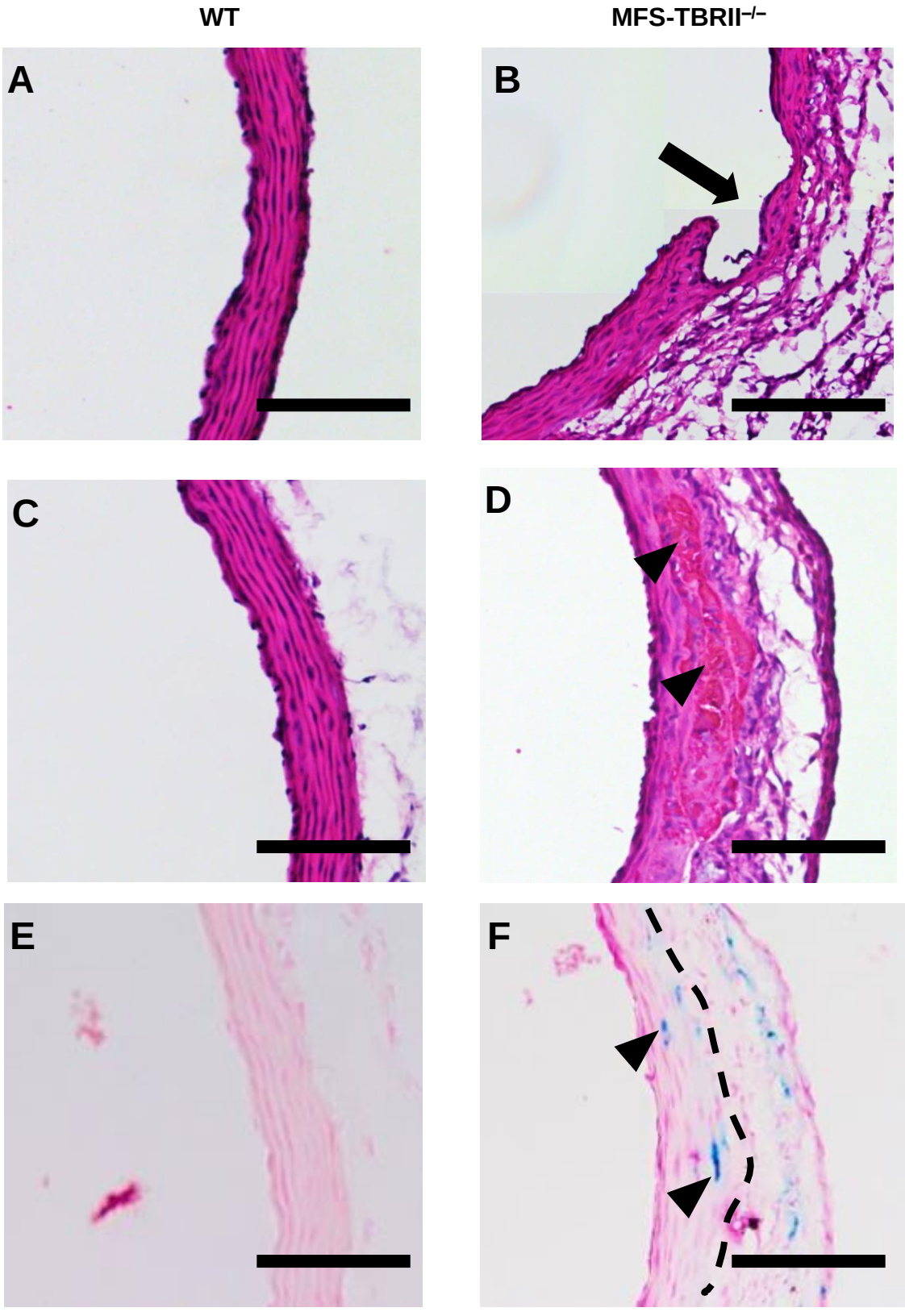

Figure S1

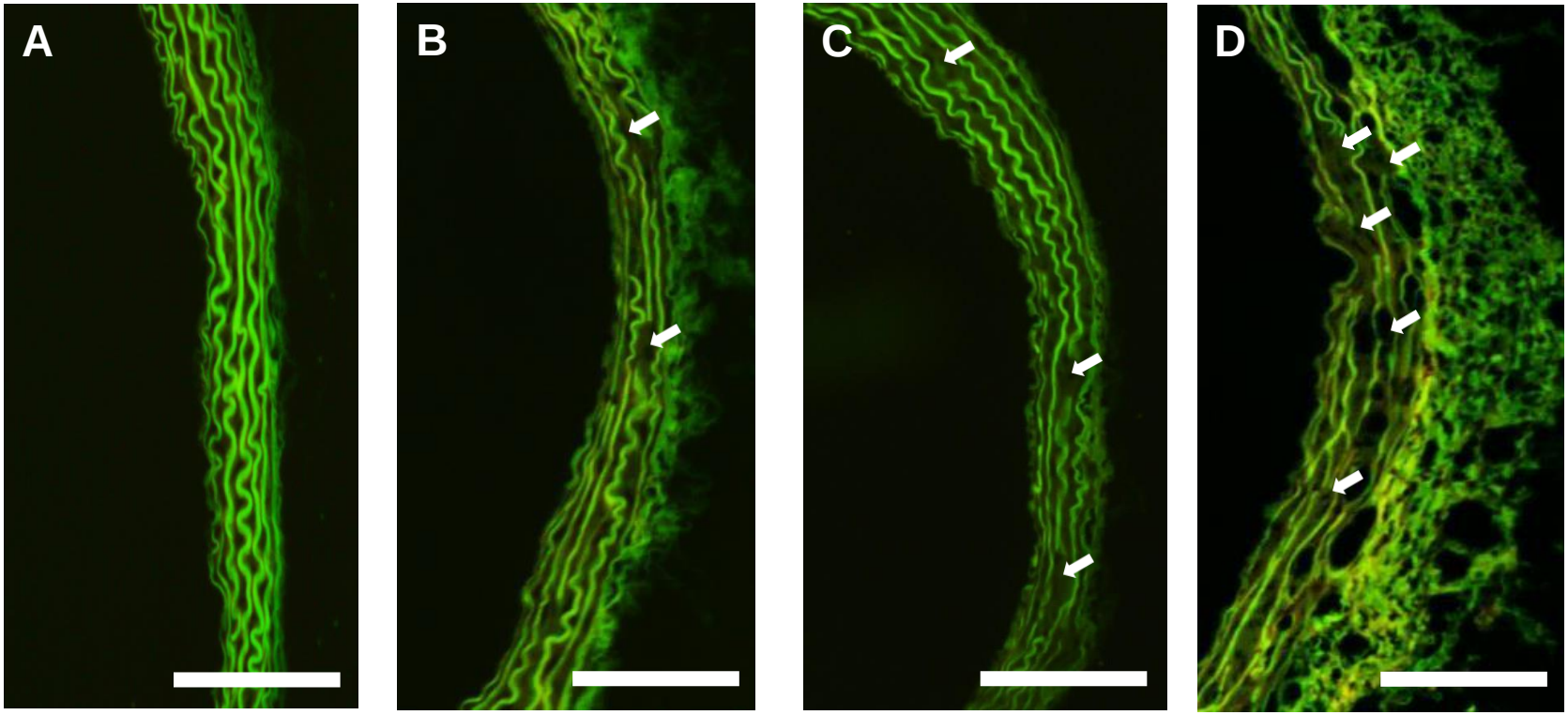

Figure S2

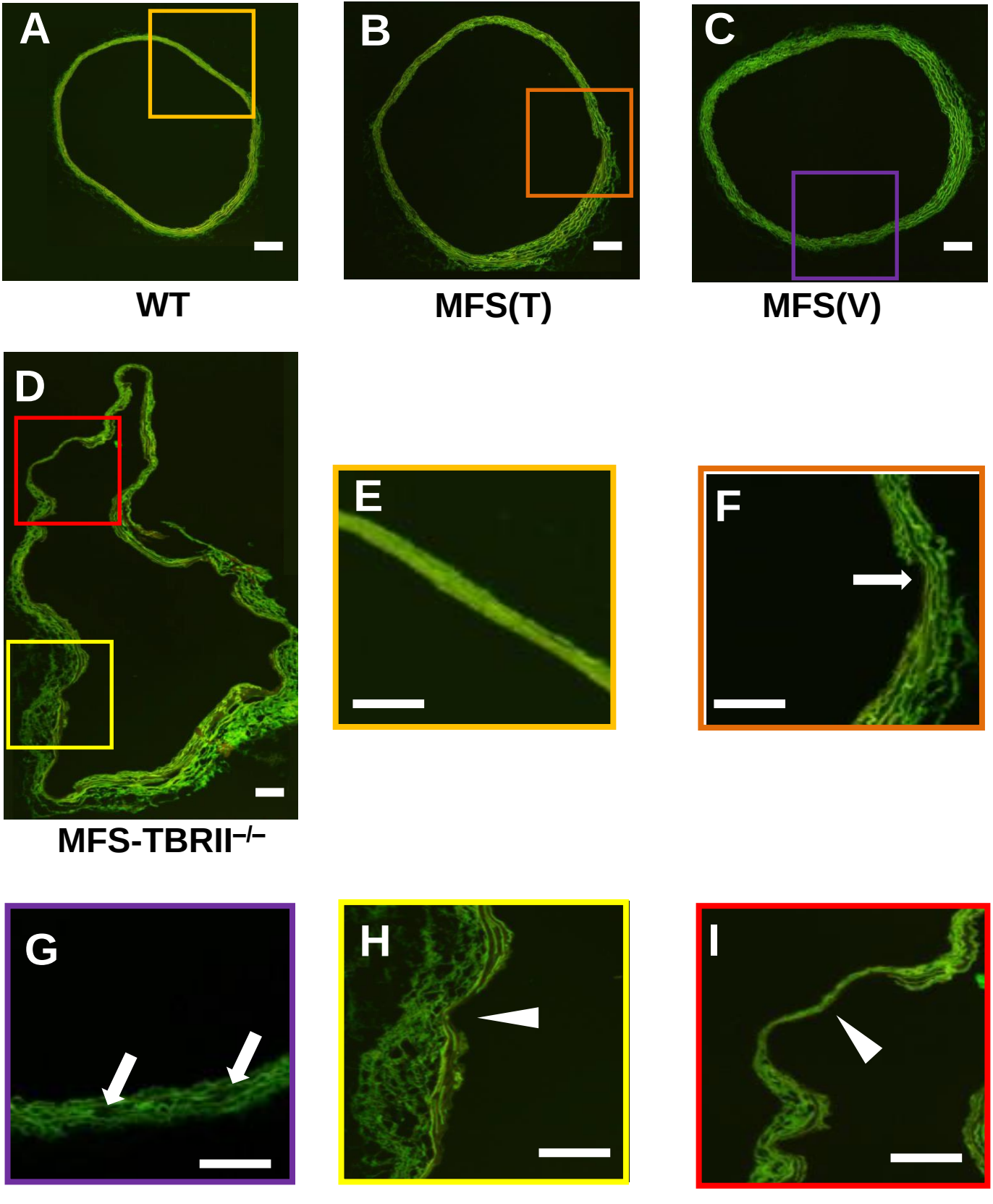

Figure S3

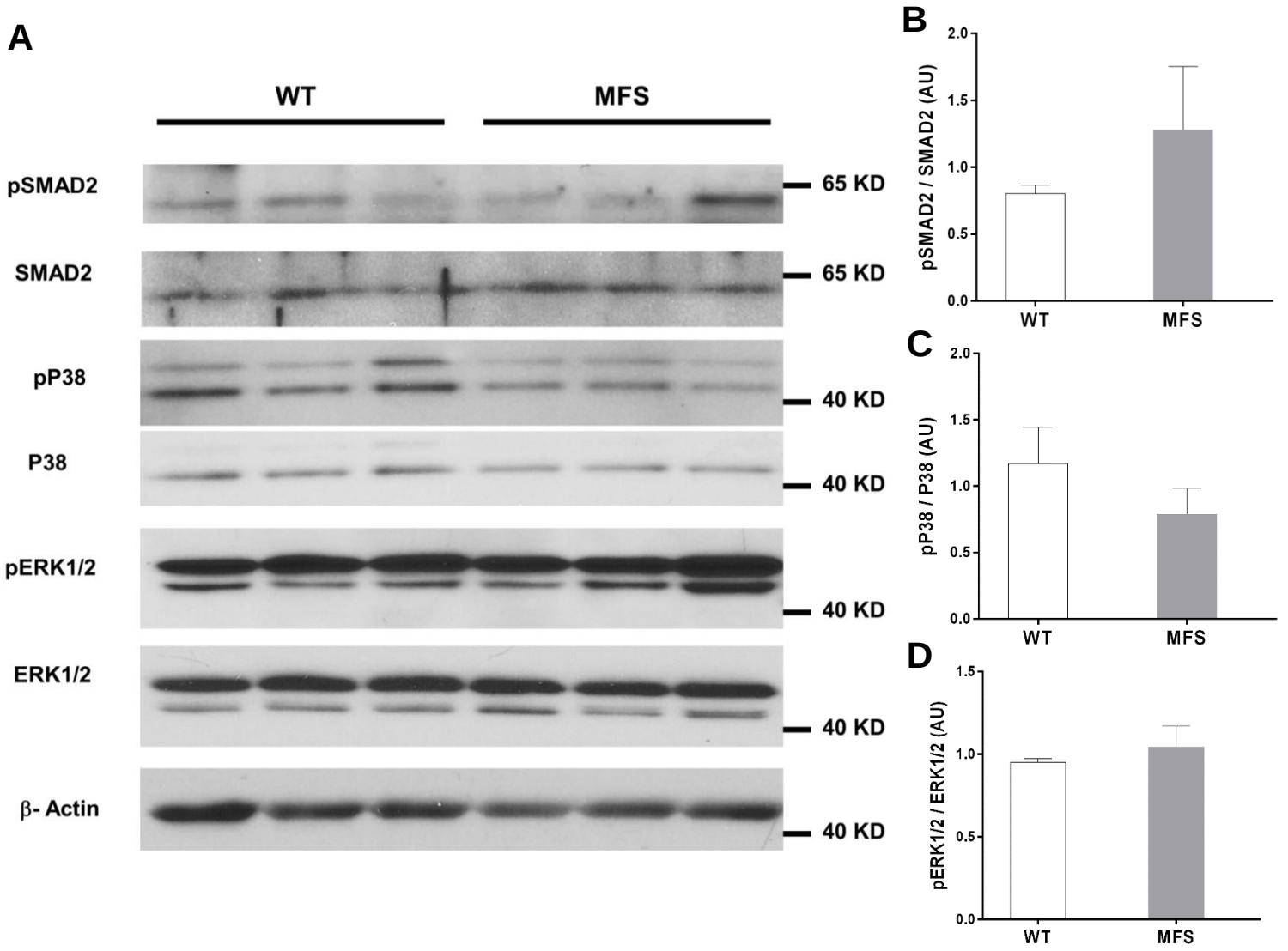
A
WT
MFS
pSMAD2
65 KD
SMAD2
65 KD
pP38
40 KD
P38
40 KD
pERK1/2
40 KD
ERK1/2
40 KD
β- Actin
40 KD
B
pSMAD2 / SMAD2 (AU)
2.0
1.5
1.0
0.5
0.0
WT
MFS
C
pP38 / P38 (AU)
2.0
1.5
1.0
0.5
0.0
WT
MFS
D
pERK1/2 / ERK1/2 (AU)
1.5
1.0
0.5
0.0
WT
MFS

Figure S4