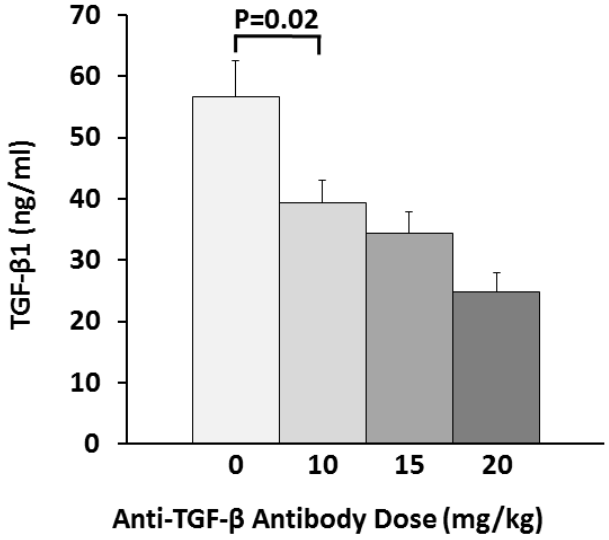
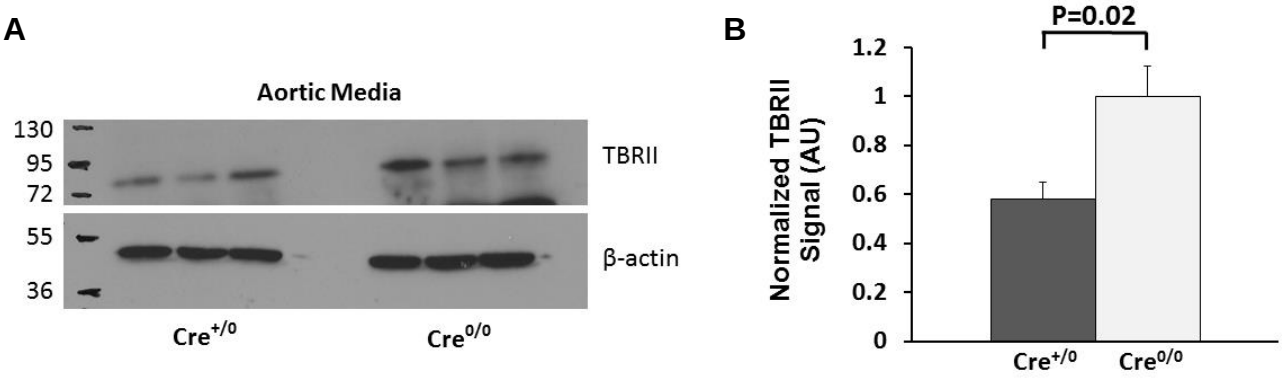
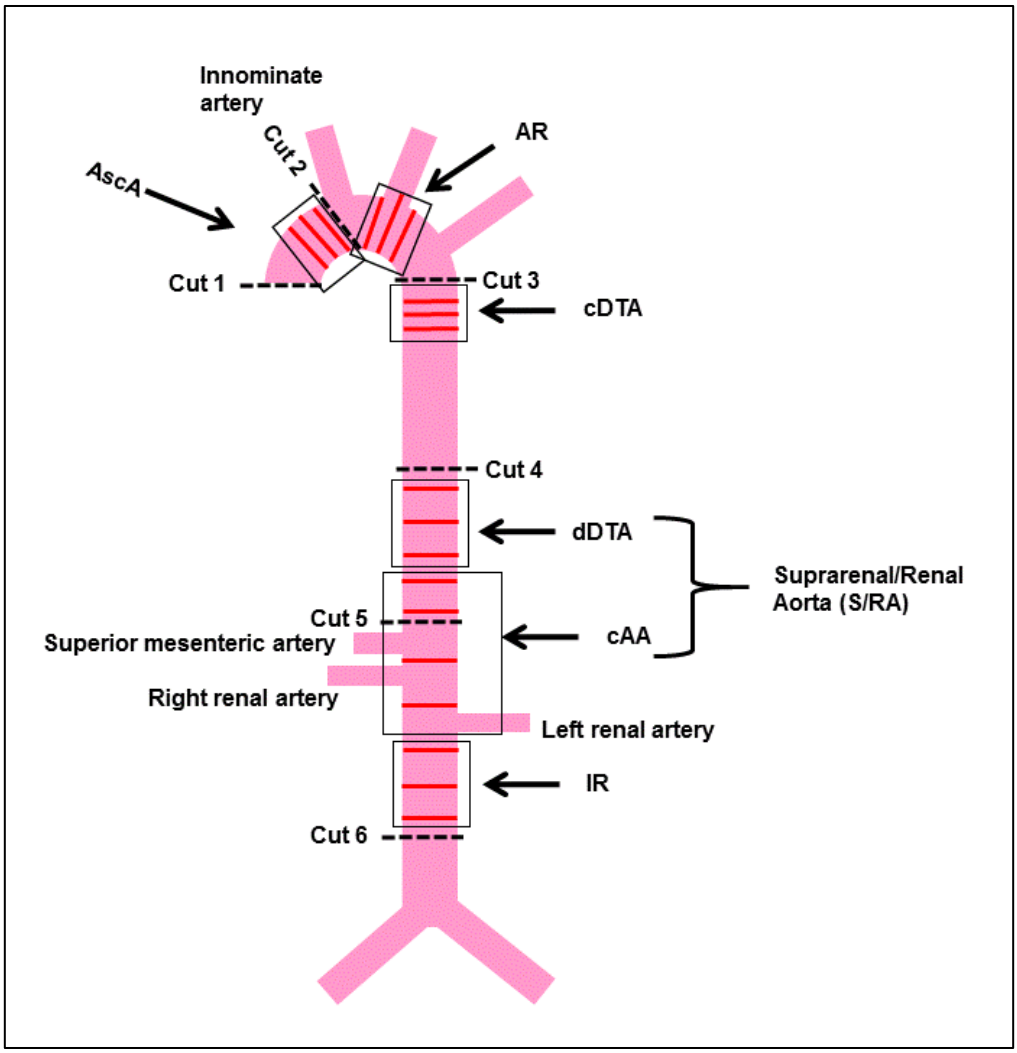


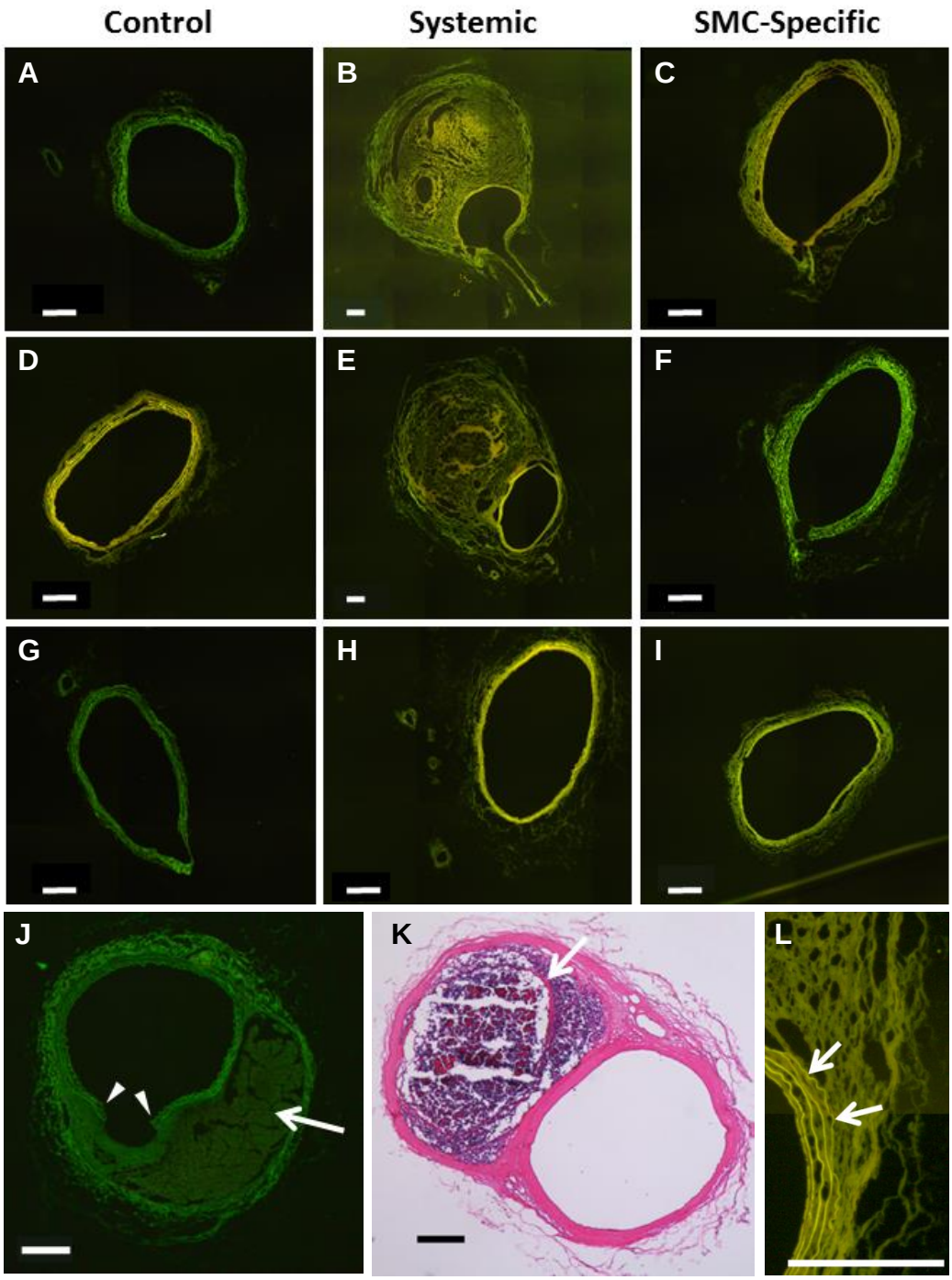
Supplemental Figure I. Mouse antibody clone 2G7 neutralizes TGF-β1 in vivo. Mice (n=4 per group, 2 male and 2 female) were injected three times (3 days apart) with saline alone (0) or with 10, 15, or 20 mg/kg anti-TGF-β antibody (clone 2G7). One day after the last injection serum was collected, TGF-β was activated by acidification of the serum and measured with an ELISA for active TGF-β1. Bar heights are means; variance is SEM. P value is from one-tailed t-test. The decrease in TGF-β1 was similar between males and females.



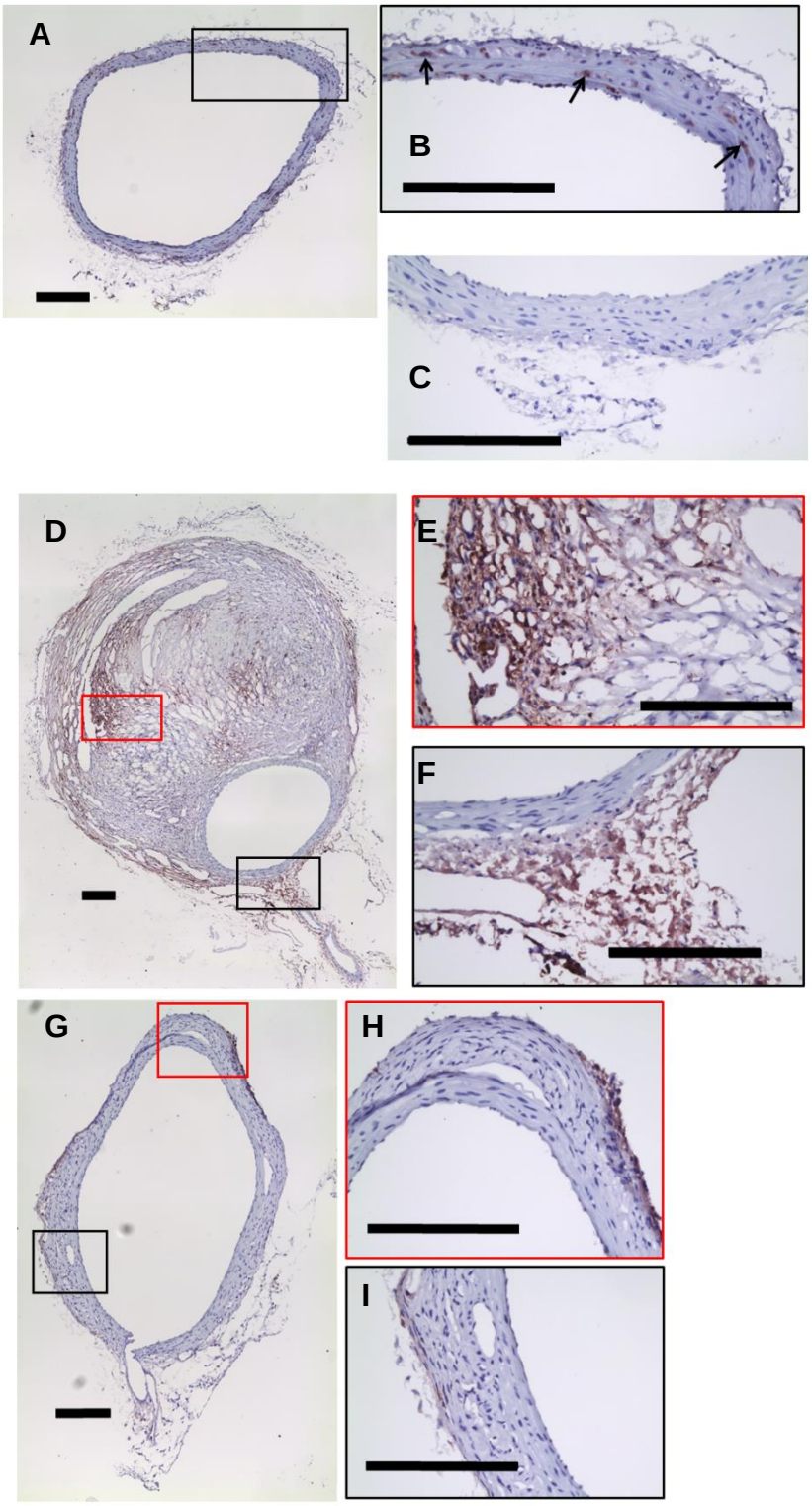
Supplemental Figure II. Knockdown of TBRII protein in aortic media. Tamoxifen was injected into *Acta2-Cre*ER$^{T2\ +/0}$ *Tgfbr2*$^{flox/flox}$ mice (Cre$^{+/0}$; n=6) and *Acta2-Cre*ER$^{T2\ 0/0}$ *Tgfbr2* $^{flox/flox}$ mice (Cre$^{0/0}$; n=6). Two weeks later, aortas were removed and protein extracted from the medial layer. (**A**) Western blots were probed with antibodies to TBRII and β-actin; each lane has protein isolated from a single mouse. Size markers are in kDa. (**B**) TBRII signal was quantified by densitometry of blot in (**A**) and of a second blot with 3 other mice per group, with normalization to β-actin signal in the same lane. Bar heights are means; variance is SEM. P value is from two-tailed t-test.



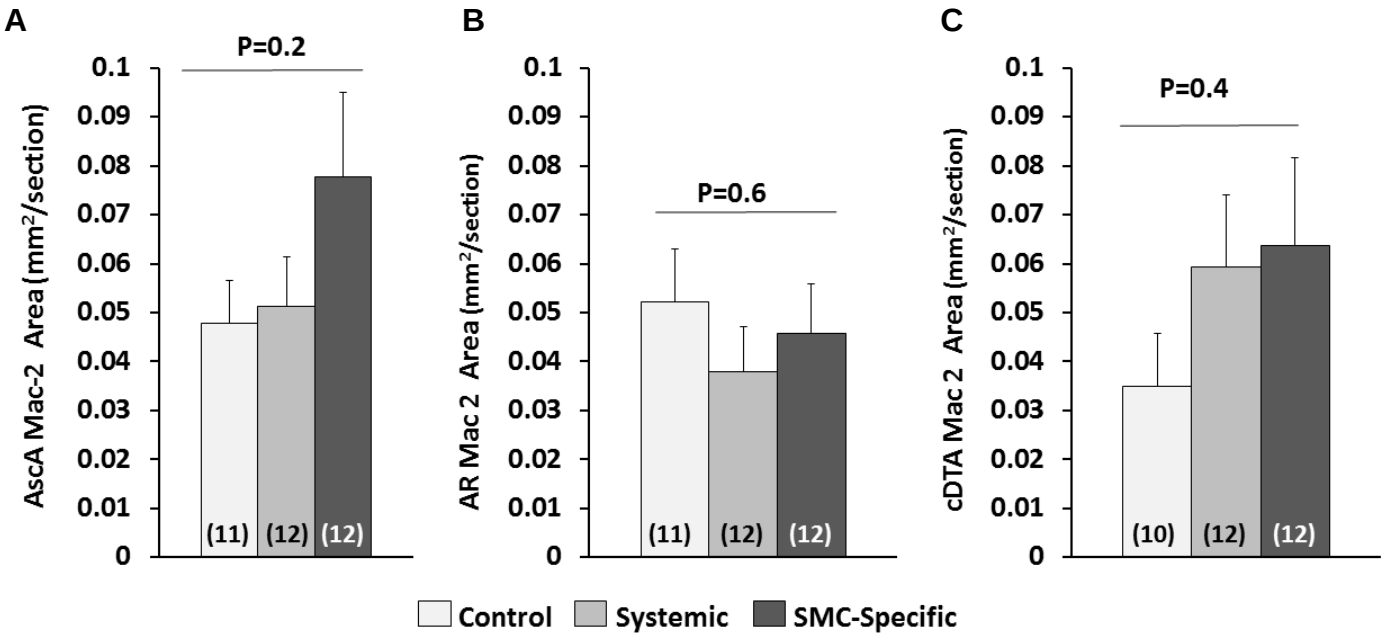
Supplemental Figure III. Protocol for sectioning aortas for histological analyses. As described in Methods, aortas were cut transversely at 6 locations (dashed lines). These 6 cuts yielded 5 segments that were embedded and sectioned and one segment that was discarded (distal infrarenal aorta; below Cut 6). Serial transverse sections were cut at 19 steps (red lines) within the 5 segments. The three most cranial segments included the ascending aorta (AscA), the aortic arch (AR), and the cranial descending thoracic aorta (cDTA). The two most caudal segments included: 1) the distal descending thoracic aorta (dDTA) and part of the cranial abdominal aorta (between Cuts 4 and 5); and 2) most of the remaining abdominal aorta including the proximal infrarenal aorta (between Cuts 5 and 6). As indicated, the 10 steps within these 2 most caudal segments were within the distal descending thoracic aorta (dDTA; 3 steps), the cranial abdominal aorta (cAA; 4 steps), or the infrarenal aorta (IR; 3 steps). Some analyses included step sections from both the dDTA and cAA; this combined area is referred to as the suprarenal/juxtarenal aorta.



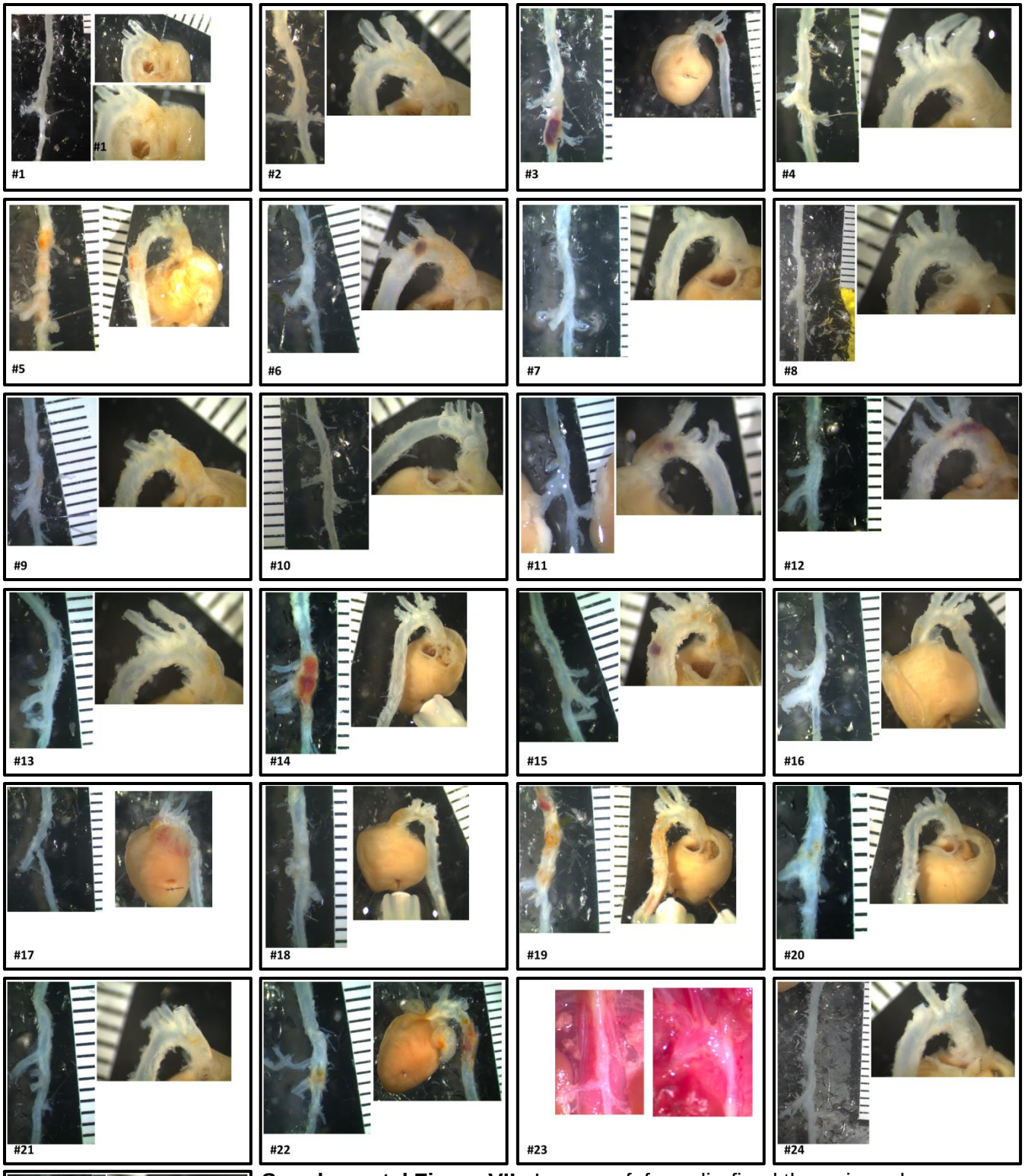
Supplemental Figure IV. Adventitial thickening, contained medial rupture, and thrombosis in abdominal aortas of mice with systemic TGF-β signaling blockade. Figure is for illustrative purposes. Formal comparisons of vascular dimensions and pathology among the 3 groups are in Figures 2 and 4. Images are of transverse sections of abdominal aortas of: (**A**, **D**, **G**) control mice (no TGF-β inhibition); (**B**, **E**, **H**, **J**, **K**, **L**) mice with systemic inhibition of TGF-β activity; and (**C**, **F**, **I**) mice with SMC-specific loss of TGF-β signaling. All mice also had 28 days of angiotensin II infusion. (**J**) Arrowheads indicate medial rupture. (**J**, **K**) arrows indicate thrombus (assumed due to medial rupture with containment of extravasated blood by the adventitia). (**L**) Arrows indicate outermost elastin layers and normal medial thickness in aorta with expanded external diameter. Scale bars are 200 μm.



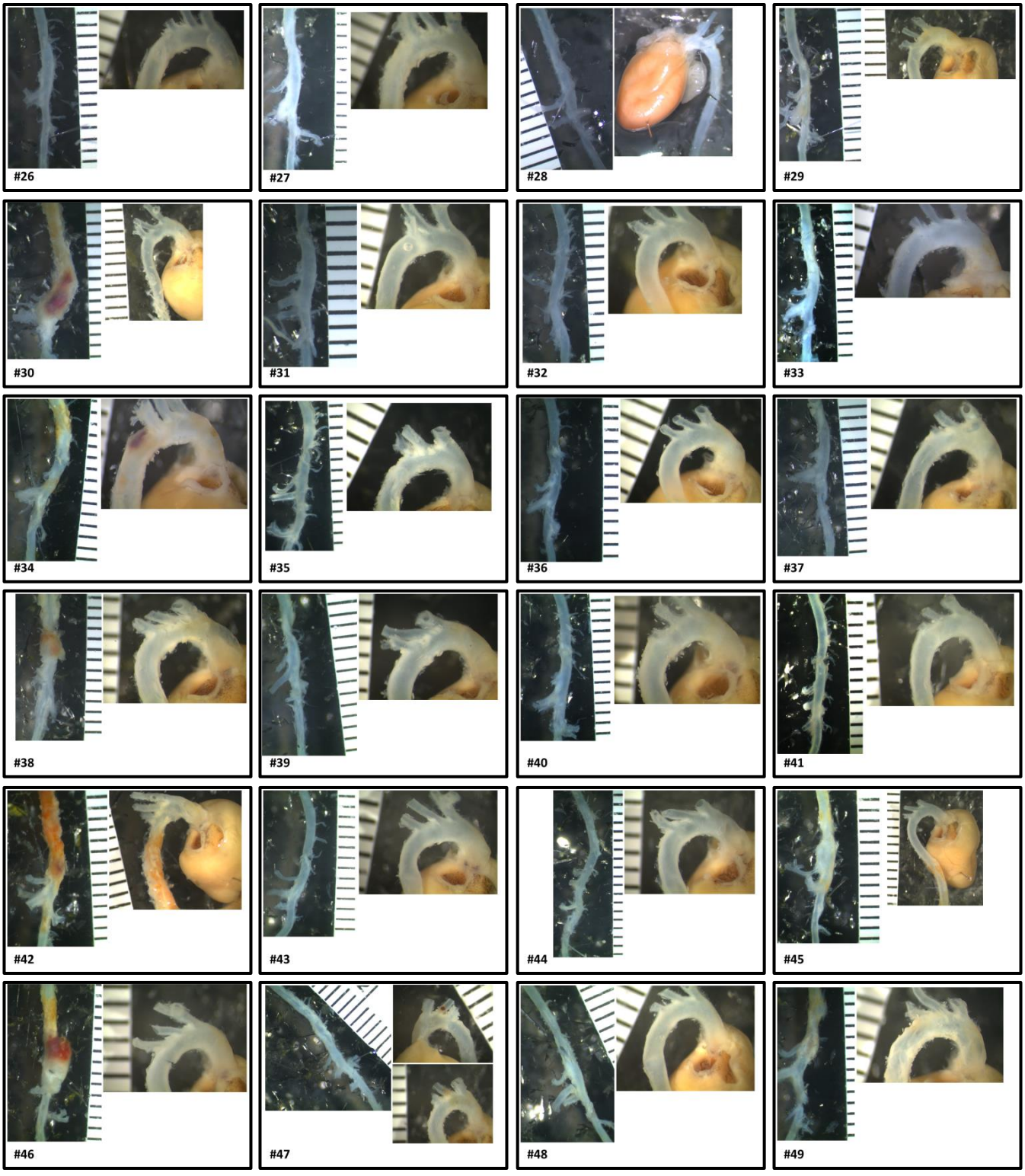
Supplemental Figure V. Macrophage accumulation in the abdominal aortic wall. Figure is for illustrative purposes. Formal comparison of macrophage accumulation among the 3 groups is in Figure 5. Images are of transverse sections of abdominal aortas of: (**A**–**C**) control mice (no TGF-β inhibition); (**D**–**F**) mice with systemic inhibition of TGF-β activity; and (**G**–**I**) mice with SMC-specific loss of TGF-β signaling. All mice also had 28 days of angiotensin II infusion. All sections were stained with the Mac-2 antibody except for (**C**), which was stained with an isotype-matched control antibody. (**A**, **D**, **G**) Areas within black and red boxes are shown in adjacent panels (**B**, **E**, **F**, **H**, **I**) at higher magnification. (**A**–**I**) hematoxylin counterstain. Scale bars are 200 μm.



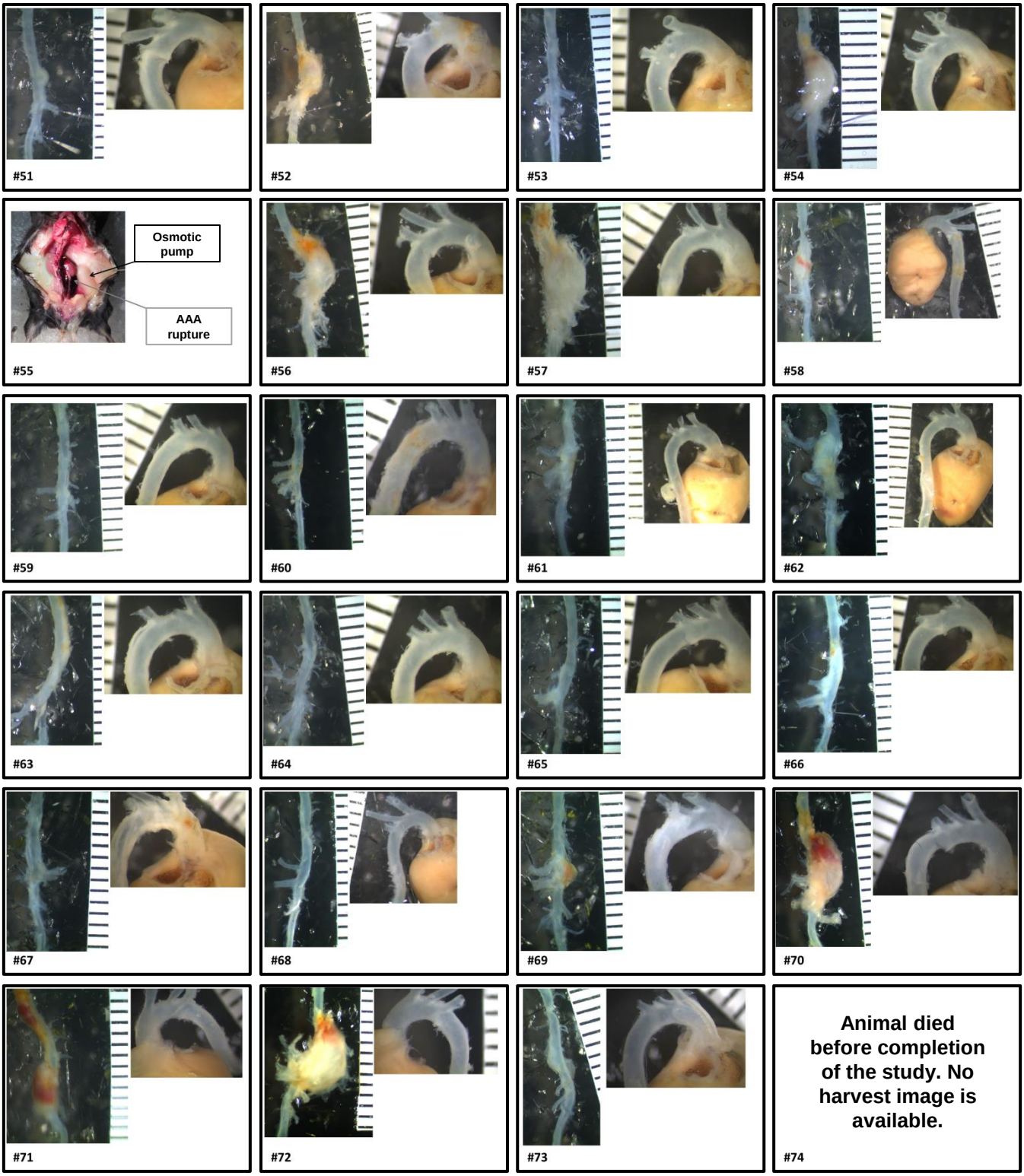
Supplemental Figure VI. Neither systemic TGF-β inhibition nor SMC-specific loss of TGF-β signaling affects macrophage accumulation in the thoracic aorta. Transverse sections of aortas of control mice (no TGF-β inhibition); mice with systemic inhibition of TGF-β activity; and mice with SMC-specific loss of TGF-β signaling were stained with an antibody to the Mac-2 antigen and the stained area was quantified by planimetry. All mice also had 28 days of angiotensin II infusion. Sections were from: (**A**) ascending aorta (AscA); (**B**) aortic arch (AR); and (**C**) cranial descending thoracic aorta (cDTA). The numbers of mice per group are indicated. Bar heights are means; variance is SEM. P values are from one-way ANOVA (**A** and **B**) or Kruskal-Wallis one-way ANOVA (**C**).



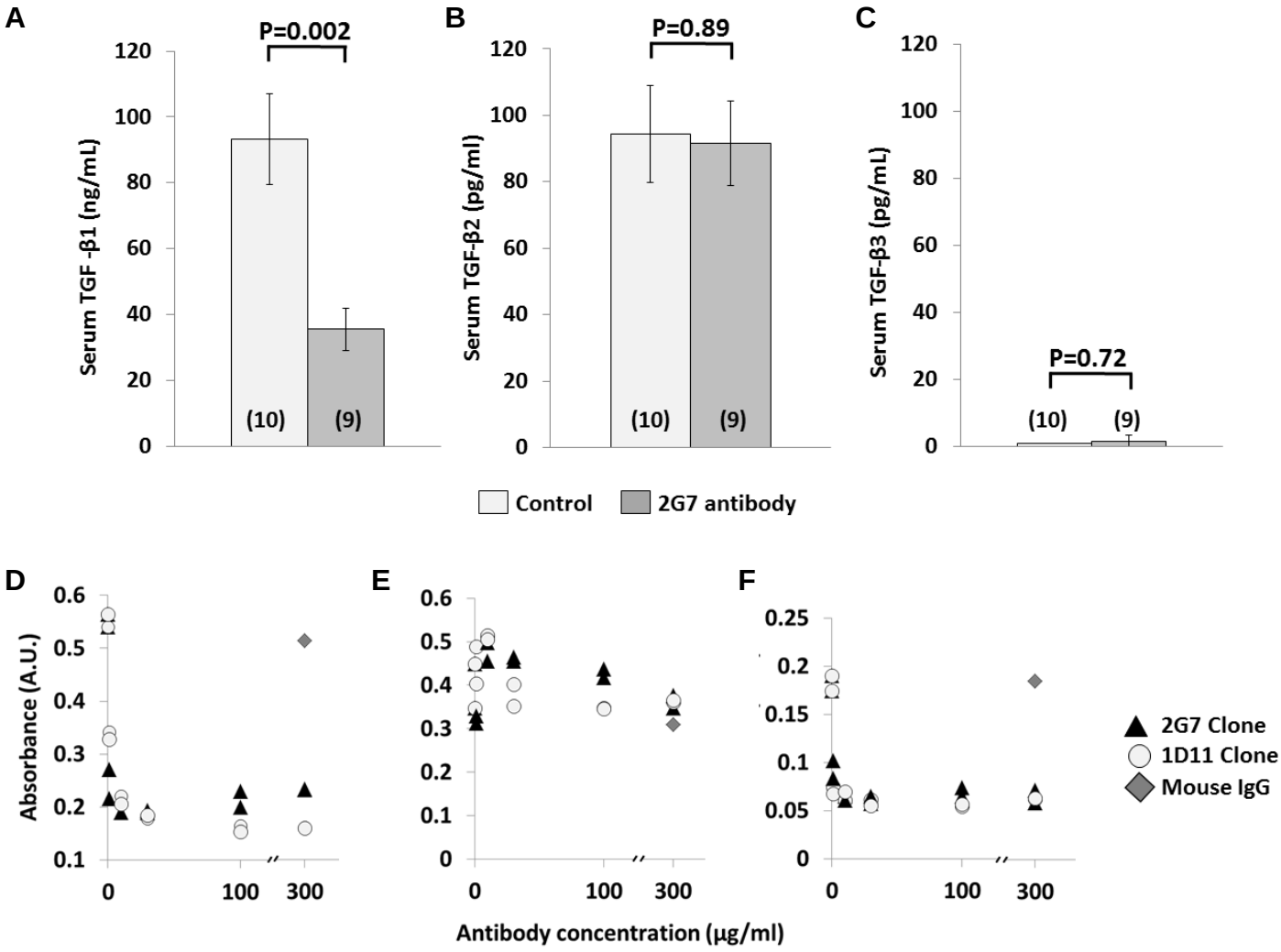
Supplemental Figure VII. Images of formalin-fixed thoracic and abdominal aortas of angiotensin II-infused C57BL/6 mice with SMC-specific loss of TBRII. Images were obtained with dissection microscope at 6-16X magnification. The ruler in each image is in mm. Panels are shown with the specimen identification number in the bottom left of each panel. Images are for illustrative purposes. Some pathological features may be difficult to discern due to small image size and specimen position. Analysis of the mouse depicted in #23 was limited due to technical issues related to specimen harvest.



Supplemental Figure VIII. Images of formalin-fixed thoracic and abdominal aortas of angiotensin II-infused C57BL/6 mice. Images were obtained with dissection microscope at 6-16X magnification. The ruler in each image is in mm. Panels are shown with the specimen identification number in the bottom left of each panel. Some pathological features may be difficult to discern due to small image size and specimen position.



Supplemental Figure IX. Images of formalin-fixed thoracic and abdominal aortas of angiotensin II-infused C57BL/6 mice with systemic, antibody-mediated, neutralization of TGF-β. Images were obtained with dissection microscope at 6-16X magnification. The ruler in each image is in mm. Panels are shown with the specimen identification number in the bottom left of each panel. Some pathological features may be difficult to discern due to small image size and specimen position. Mouse depicted in #55 died suddenly of ruptured AAA.



Supplemental Figure X. Neutralizing activity of mouse anti-TGF-β antibody clones 2G7 and 1D11. **(A-C)** 2G7 neutralizes TGF-β1 and TGF-β3, but not TGF-β2 in vivo. Angiotensin II-infused mice (n=9-10 per group) were injected three times (3 days apart) with mouse IgG (control) or with 10 mg/kg 2G7. One day after the last injection, serum was collected, TGF-β was activated by acidification of the serum and measured with an ELISA for active TGF-β1 (**A**),TGF-β2 (**B**), and TGF-β3 (**C**). (**A–C**) Bar heights are means; variance is SEM. P values in (**A**) and (**B**) are from two-tailed t-test and from rank-sum test in (**C**). Groups include mice of both sexes (control: 5M, 5F; 2G7 group: 6M, 3F). Values were similar between both sexes within each group (data not shown). **(D–F)** 2G7 and 1D11 both neutralize TGF-β1 and TGF-β3, but not TGF-β2 in vitro. Increasing concentrations (0, 1, 10, 30, 100 and 300 µg/mL) of 2G7 (black triangles) or 1D11 (grey circles) were incubated with 250 pg/mL of TGF-β1(**D**), TGF-β2 (**E**), or TGF-β3 (**F**) then assayed for TGF-β activity by ELISA. Mouse IgG (dark grey diamonds) was assayed only at the 300 µg/mL concentration. Each incubation was performed in duplicate and both points are shown.

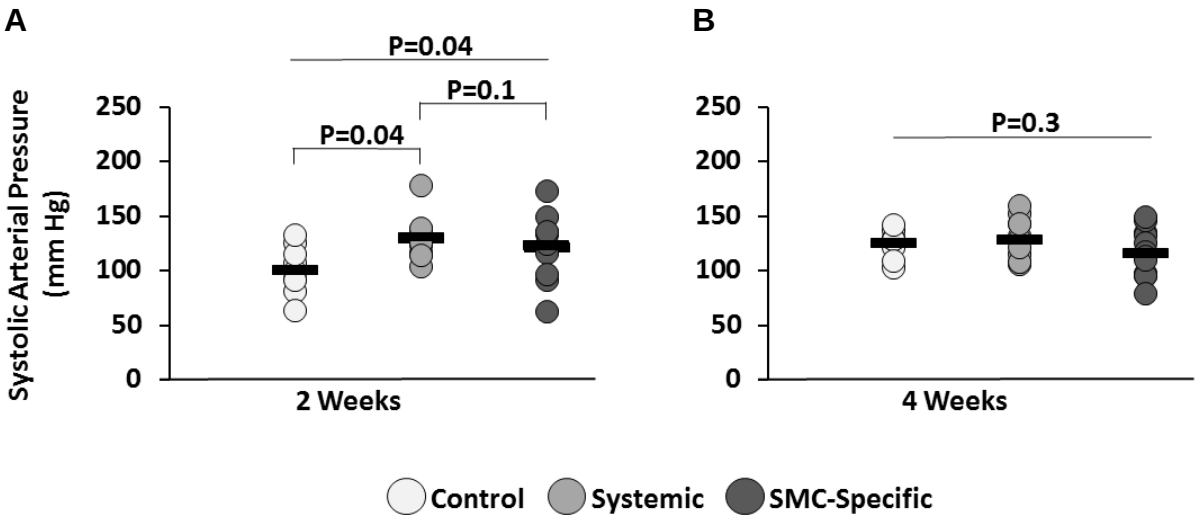


Figure XI. Differences in blood pressure do not correlate with aortic pathology. Systolic blood pressure was measured by tail volume-pressure recording both at 2 weeks (**A**) and 4 weeks (**B**) after beginning angiotensin II infusion in control mice (no TGF-β inhibition), mice with systemic inhibition of TGF-β activity, and mice with SMC-specific loss of TGF-β signaling. Each point represents data from an individual mouse (n= 9-12 per group). The mean for each group is indicated with a black horizontal bar. P values are from one-way ANOVA (overall P value is above), with Dunnett's correction for the pair-wise comparisons (**A**).