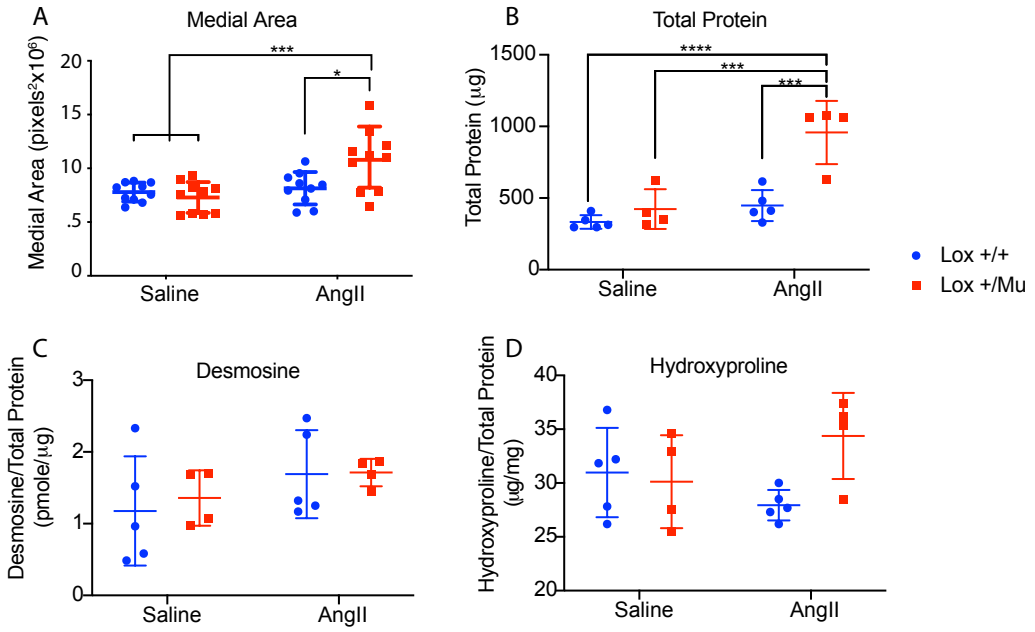
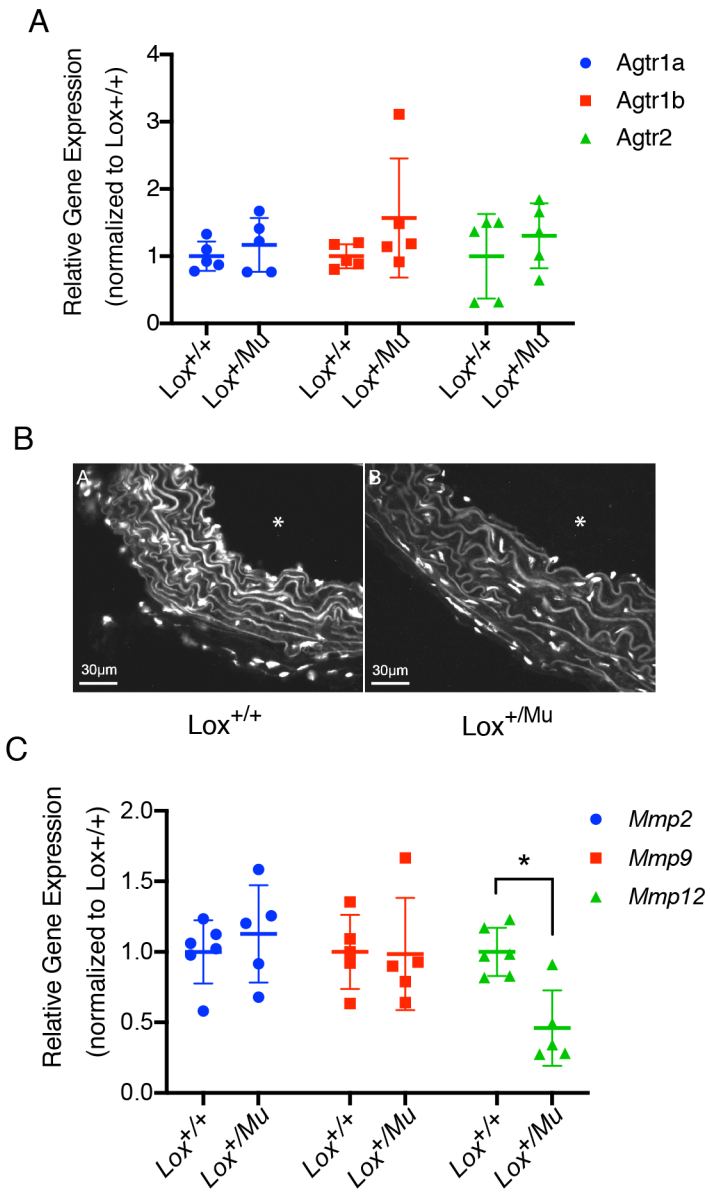
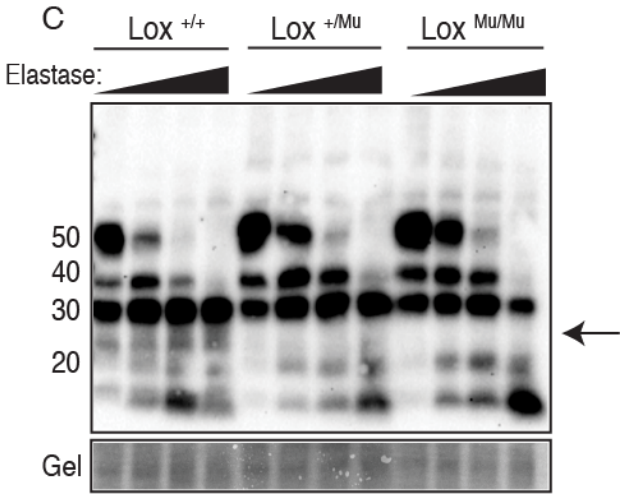
## Supplemental Figures and Tables



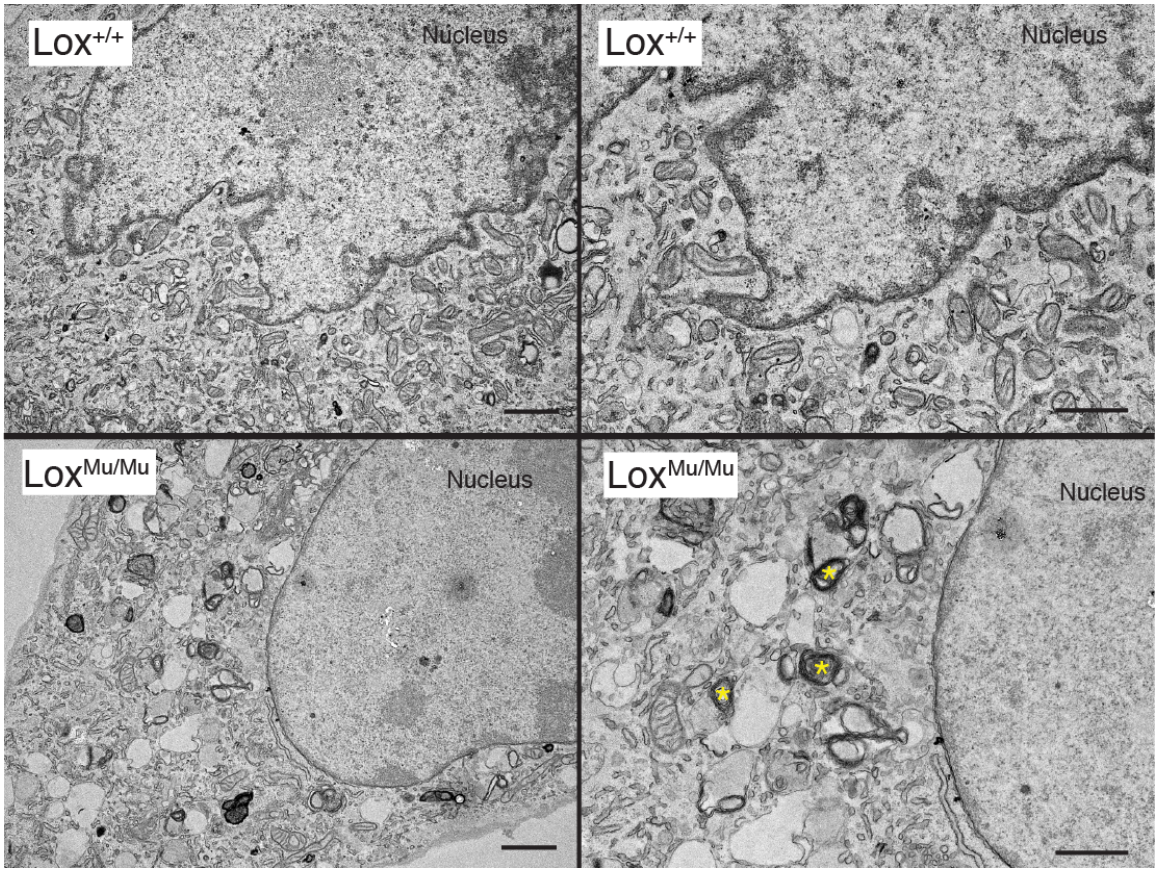

*Supplemental Figure 1. Changes in medial area, desmosine, hydroxyproline, and total protein in response to AngII treatment.* (A) Area measured between the internal and external elastic lamina from aorta cryosection images showed a significant increase in the medial area of *Lox*$^{+/Mu}$ animals after AngII treatment compared to both genotypes treated with saline and wild-type animals treated with AngII. (B) Total protein measured from ascending aorta tissue showed markedly higher protein levels in *Lox*$^{+/Mu}$ animals after AngII treatment compared to both genotypes treated with saline and wild-type animals treated with AngII. (C) Desmosine levels measured by ELISA showed no significant difference between genotypes with or without AngII treatment when normalized to total protein levels. (D) There was no difference in hydroxyproline levels in wild-type and *Lox*$^{+/Mu}$ animals treated with saline. *Lox*$^{+/Mu}$ mice treated with AngII trended toward higher hydroxyproline levels compared to wild-type animals with AngII, but the difference was not statistically significant when normalized to total protein levels. Two-way ANOVA with Tukey's multiple comparisons test with the 2 variables being genotype and treatment was used to assess differences. Data are presented as mean ± SD. *P<0.05, ***P<0.001, ****P<0.0001.



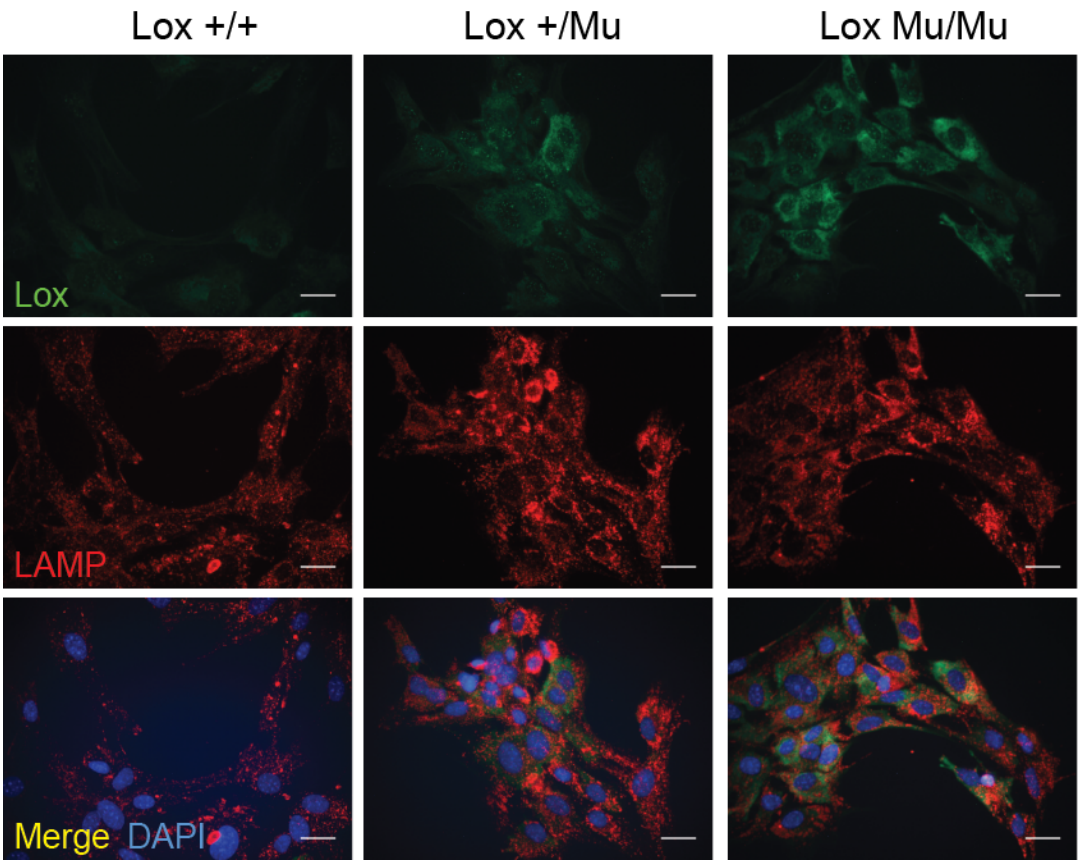

*Supplemental Figure 2. Angiotensin II receptor expression, reactive oxygen species, and matrix metalloproteinase expression in Lox$^{+/+}$ and Lox$^{+/Mu}$ mice.* (A) mRNA levels for angiotensin II receptors 1a (Agtr1a), 1b (Agtr1b) and 2 (Agtr2) in aortic tissue were determined by quantitative PCR. No difference was found between genotypes. (B) Reactive oxygen species (superoxide), detected by dihydroethidium staining, also showed no difference between genotypes. (C) Quantification of mRNA levels for MMP2, MMP9, and MMP12 showed similar levels of MMP2 and MMP9 in mutant and wild-type aorta, with reduced levels of MMP12 expression in mutant tissue. Two-way ANOVA with Tukey's multiple comparisons test with the 2 variables being genotype and gene was used to assess differences in receptor and MMP expression. Data are presented as mean ± SD. *P<0.05.



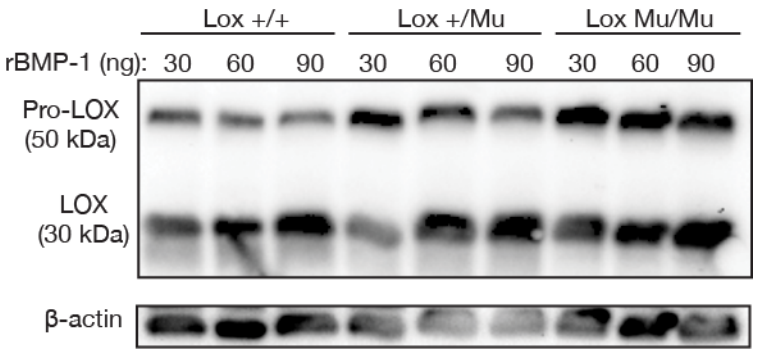

*Supplemental Figure 3. Differential elastase susceptibility of wild-type and mutant LOX.* Cell lysates from mouse embryo fibroblasts were treated with increasing concentrations of pancreatic elastase. Samples were run on SDS-PAGE and LOX fragments were detected by western blot. PonceauS-stained gel (Gel) serves as a loading control. See text for details of fragmentation differences.




*Supplemental Figure 4. Electron micrographs of wild-type and LOX mutant cells.* Transmission electron microscopy of cultured *Lox*$^{+/+}$ (top panels) and *Lox*$^{Mu/Mu}$ (bottom panels) mouse embryo fibroblasts. The mutant cells showed numerous cytoplasmic electron lucent and multimembrane organelles typical of autophagosomes, some of which are labeled with yellow stars. In wild-type cells, autophagic vesicles are seldom observed. Scale bar = 500 nm.




*Supplemental Figure 5. Intracellular mutant LOX is not found in lysosomes:* Immunofluorescence staining of $Lox^{+/+}$, $Lox^{+/Mu}$, and $Lox^{Mu/Mu}$ mouse embryo fibroblasts with anti-LOX and an antibody to the lysosomal marker LAMP2. Merged images show no co-localization between intracellular LOX and LAMP2 compartments, suggesting that mutant LOX is not cleared through lysosomes. Scale bar= 15 μm.




*Supplemental Figure 6. M292R pro-LOX is processed to the mature form of LOX by BMP1.* Cell lysates from *Lox*$^{+/+}$, *Lox*$^{+/Mu}$, and *Lox*$^{Mu/Mu}$ mouse embryo fibroblasts were incubated at 37˚C with 30, 60, or 90 ng of recombinant BMP1 (rBMP1) and then analyzed by immunoblotting using an anti-LOX antibody. Mutant LOX was proteolytically processed from pro-LOX (50 kDa) to mature LOX (30 kDa) in a dose-dependent manner.

*Supplemental Table 1.* Antibodies description and sources.

**Primary antibodies**

| **Antibody Name** | **Vendor** | **Product number** |
|---|---|---|
| Mouse Anti-β-Actin | Sigma (St. Louis, MO) | A2228 |
| Rat Anti-CD68 | Biorad (Hercules, CA) | MCA1957 |
| Rabbit Anti-Calnexin | Abcam (Cambridge, MA) | Ab22595 |
| LC3B Antiserum | Novus Biological (Littleton, CO) | NB-100-2200 |
| Mouse Anti-Lamp2 | Developmental Studies Hybridoma Bank (Iowa City, IA) | Ab1-93 |
| Rabbit Anti-Lox | Abcam (Cambridge, MA) | Ab174316 |
| Mouse Anti-p62 | Abcam (Cambridge, MA) | Ab56416 |
| Smooth muscle alpha-actin | Sigma (St. Louis, MO) | SMA-Cy |