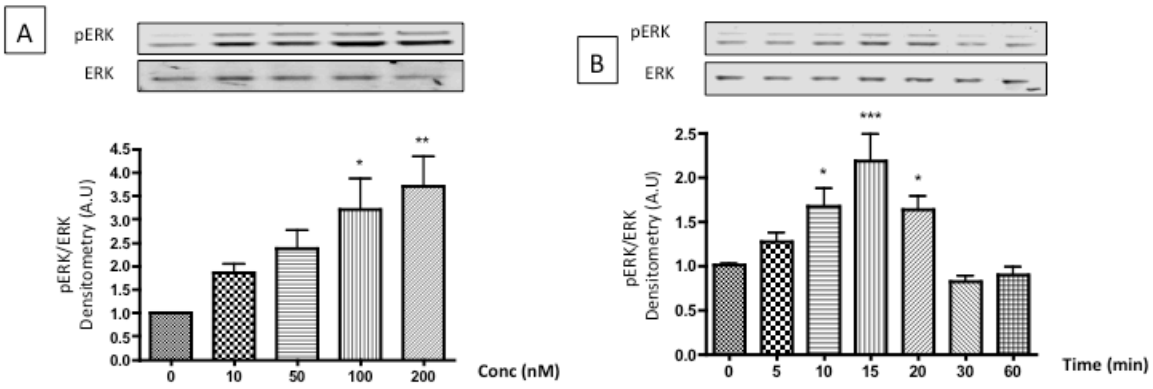
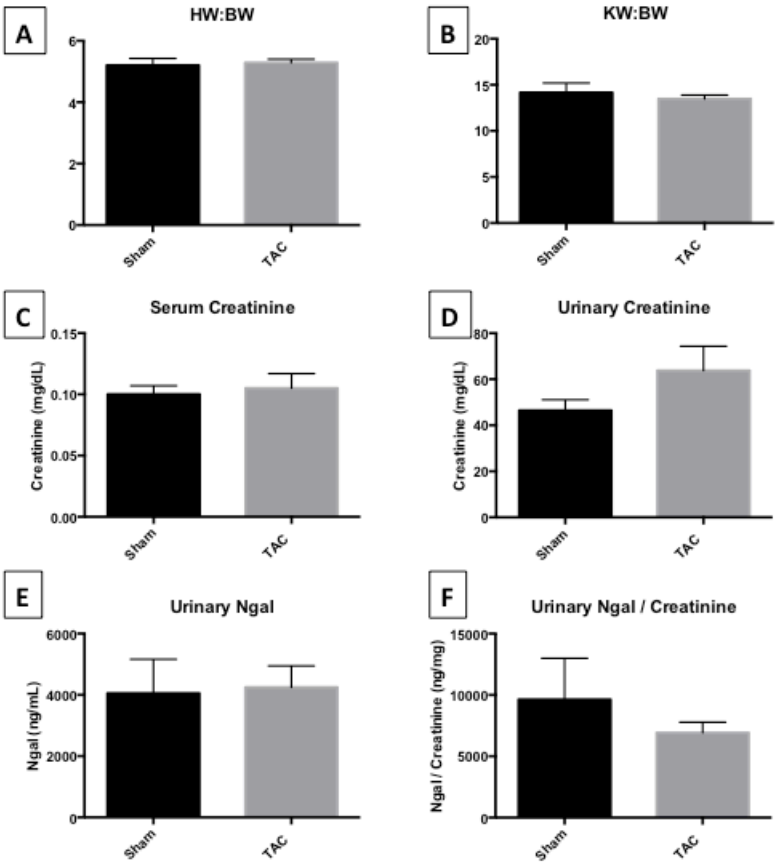
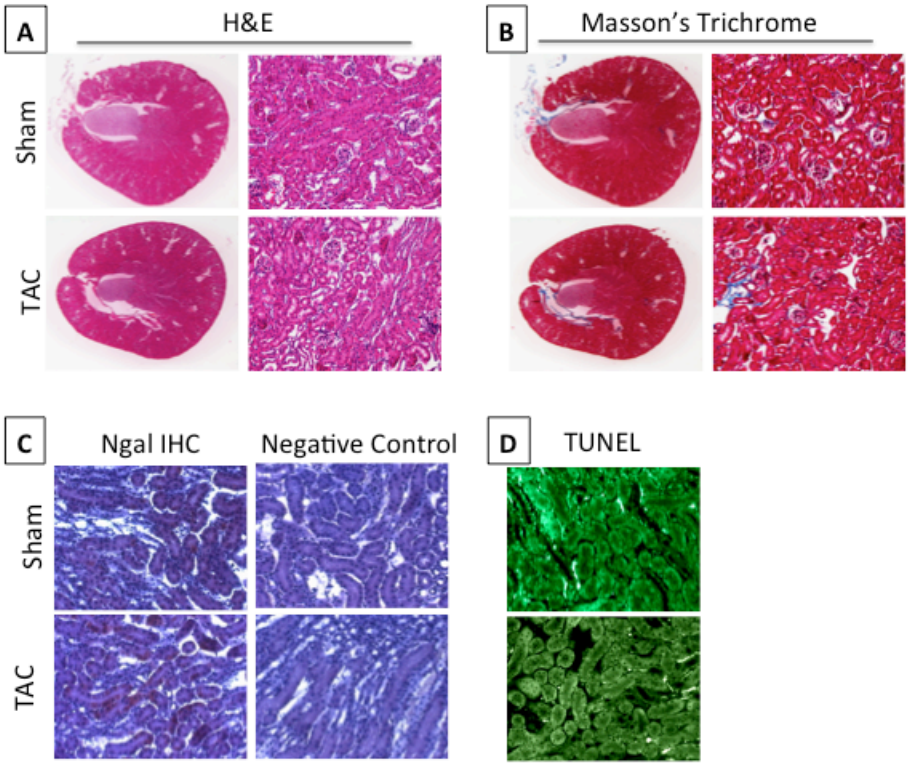


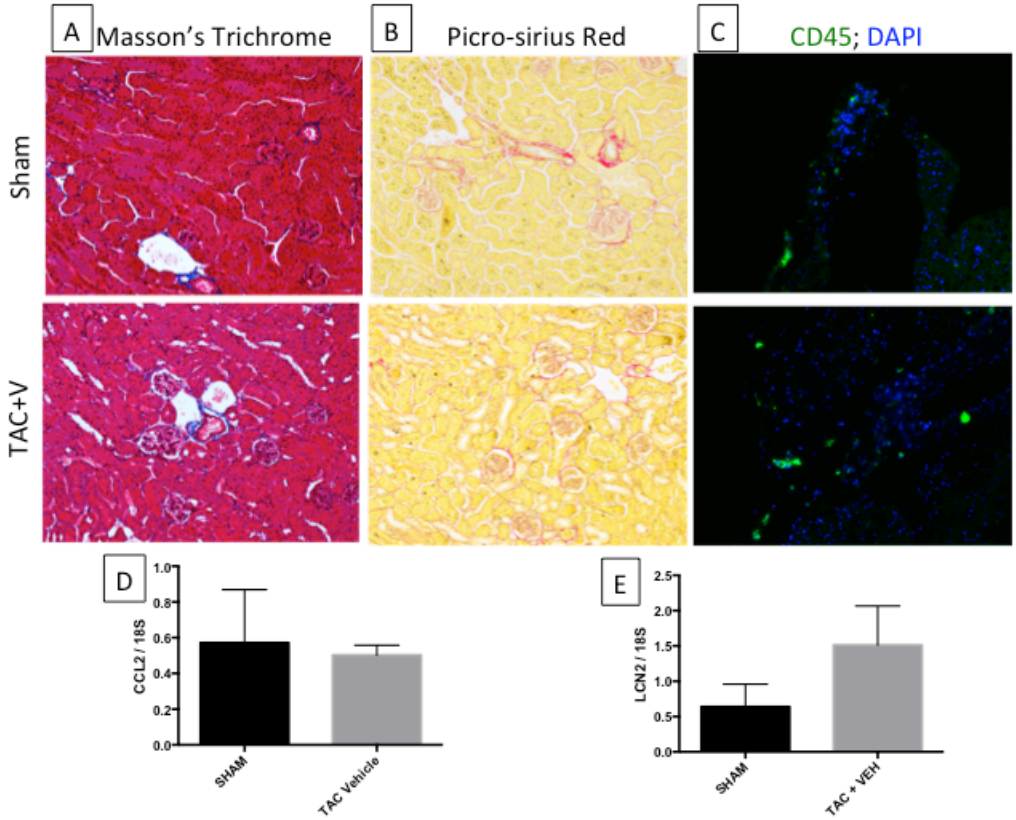
Supplementary Figure 1. (A) Dose-response study in MEFs showed that ET-1 (100 nM) induces submaximal phosphorylation of ERK1/2. (B) Time-course study in MEFs showed that ET-1 (100 nM) induces maximal ERK1/2 phosphorylation 15 minutes after stimulation. ****P<0.001*, ***P<0.01* and **P<0.05*; N=5.



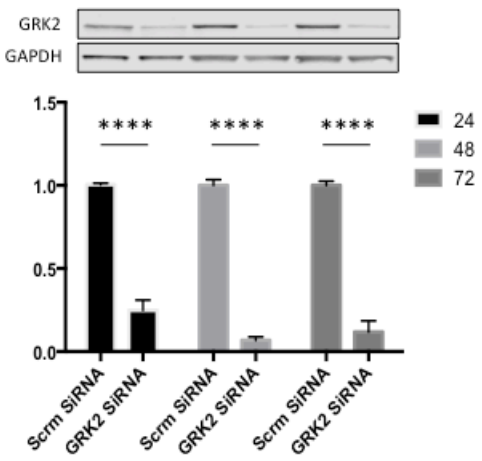
Supplementary Figure 2. No evidence of AKI 24 hours following TAC. Twenty-four hours following Sham/TAC surgeries, heart weight/body weight (HW:BW), kidney weight/body weight (KW:BW), serum and urinary creatinine, urinary Ngal, and urinary Ngal/ urinary creatinine were not different between Sham and TAC mice. N=4/group



Supplementary Figure 3. No histological evidence of AKI 24 hours following TAC. Twenty-four hours following Sham/TAC surgeries, kidneys were isolated, formalin fixed, paraffin embedded and sections were used for hematoxylin-Eosin (H&E) staining, Masson's trichrome staining, Ngal immunohistochemistry (IHC) and TUNEL staining. There was no difference between kidneys of sham and TAC mice. N=4/group



Supplementary Figure 4. Histological analysis of kidneys isolated from mice 7 days post-TAC revealed minor expansion of inter-tubular space but no evidence of fibrosis following TAC (A: Masson's trichrome and B: picrosirius red staining). (C) Mild increase in CD45 positive staining by immunofluorescence, particularly in the perivascular region, was observed in the kidneys 7 days post-TAC. (D) Kidney Ccl2 inflammatory gene expression was not changed 7 days post-TAC. (E) Gene expression of the acute kidney injury marker NGAL was non-significantly increased in TAC mice. N=3/ group



Supplementary Figure 5. Time-course study of GRK2 specific siRNA transfection shows sustained GRK2 knock-down that is maintained up to 72 hours post-transfection. Scrambled siRNA (scrm) was used as a control. *****P<0.0001*; N=4