SIGNIFICANCE STATEMENT

AKI, a devastating condition with high morbidity and mortality, is characterized by tubular injury, inflammation, and vascular impairment. Whether fibroblasts in renal interstitium play a role in the pathogenesis of AKI is unknown. This paper demonstrates a crucial role of fibroblast-specific signaling in dictating the outcome of AKI. Ablation of β-catenin in a fibroblast-specific fashion protects kidneys from tubular injury and apoptosis and inhibits renal inflammation. This is largely mediated by an enhanced expression of hepatocyte growth factor. The present study identifies hepatocyte growth factor as a novel target of Wnt/β-catenin signaling. It also unravels a previously unrecognized role for interstitial fibroblasts in the pathogenesis of AKI.