SIGNIFICANCE STATEMENT

AKI is a serious clinical complication with high morbidity and mortality. Despite substantial progress in understanding the mechanisms contributing to the pathophysiology of AKI, there is no effective therapy available to treat or prevent AKI. This article elucidates the role of Gpr97, an orphan adhesion G protein-coupled receptor, in the pathogenesis of AKI. In two independent murine AKI models, ischemia–reperfusion injury and cisplatin-induced AKI, Gpr97 exacerbates AKI by the regulation of semaphorin 3A, a potential early diagnostic biomarker of renal injury, thereby contributing to inflammatory responses and tubular epithelial cell death. This study indicates that targeting Gpr97 may be an innovative therapeutic strategy for patients with AKI.