SIGNIFICANCE STATEMENT

For proteinuric diseases that are characterized by podocyte injury, such as FSGS and minimal change disease, therapeutic agents are limited and have systemic toxicities that hinder chronic use. Previous studies showed that the loss of the kidney-enriched zinc finger transcription factor Krüppel-like factor 15 (KLF15) increases susceptibility to proteinuric kidney disease and attenuates salutary effects of retinoic acid and glucocorticoids on the podocyte. The authors show that podocyte-specific induction of *KLF15* ameliorates kidney injury and improves overall survival in proteinuric mice by directly and indirectly upregulating the expression of genes critical for podocyte differentiation. The study's findings provide evidence for a potential role of KLF15 as a therapeutic target in proteinuric kidney disease.