

## **SIGNIFICANCE STATEMENT**

Nephrin is a key structural component of the podocyte slit diaphragm. Regulation of its expression is critical for the integrity of the glomerular filtration barrier. The studies reported here identify the signaling molecule ShcA as a novel regulator of nephrin endocytosis, and demonstrate that ShcA is upregulated in several human proteinuric kidney diseases. Further studies will reveal whether ShcA can serve as a biomarker of podocyte injury.