

## **SIGNIFICANCE STATEMENT**

Podocytes play a key role in the formation of a proper glomerular filtration barrier. Their complex 3D morphology is highly dependent on an intact actin cytoskeleton. This manuscript describes the role of palladin, an essential actin-binding protein, for podocyte function *in vitro* and *in vivo*. The results demonstrate that cultured podocytes developed disorganized actin filaments and smaller focal adhesions after the knockdown of palladin. Moreover, the podocyte-specific palladin-knockout mouse showed glomeruli with a disturbed morphology and a mild effacement of podocyte foot processes. After the injection of nephrotoxic serum, a model for GN, palladin-knockout mice developed higher levels of proteinuria than controls. Taken together, our results demonstrate an important role of palladin for podocyte architecture as well as for proper filtration.