

## **SIGNIFICANCE STATEMENT**

Nephronectin (NPNT) is a known component of the glomerular basement membrane (GBM) and a ligand of  $\alpha 8\beta 1$  integrin. These studies demonstrate for the first time a receptor-ligand interaction between the GBM and mesangial cells *in vivo* at specialized adhesion structures, linking nephronectin in the GBM and  $\alpha 8\beta 1$  integrin in mesangial cells. The work establishes the role of nephronectin in the glomerulus using a mouse model, in which nephronectin knockout disrupted GBM-mesangial adhesions and led to mislocalization of  $\alpha 8\beta 1$  integrin. The studies provide evidence that nephronectin is an endogenous regulator of mesangial cell number and matrix production.