

SIGNIFICANCE STATEMENT

Although plasticity of mature cells has potential advantages, appropriate maintenance of functionally diverse cell types in organized structures, such as the kidney, is essential. Notch signaling is required for normal kidney development, including principal cell fate selection, but inappropriate activation of Notch in adult kidneys promotes CKD progression. In this study, the authors describe a novel physiologic requirement for endogenous Notch signaling in adult kidneys: preventing mature aquaporin-2-expressing epithelial cell types in the connecting segment and collecting ducts from directly converting into ionocytes, or intercalated cells. The authors' findings indicate that maintenance of mature epithelial cell types is an active process, and identify inappropriate transdifferentiation between epithelial cell types as a possible underlying cause of disease, such as acquired nephrogenic diabetes insipidus.