## SIGNIFICANCE STATEMENT

Distal renal tubular acidosis (dRTA) is defined by the inability of the distal nephron to acidify the urine and can be associated with sensorineural deafness. About one third of patients with inherited dRTA have no identified causative mutations in known disease genes. Here, we report recessive mutations in the forkhead transcription factor FOXI1 as a novel cause of dRTA with deafness. Our findings enable a precise diagnosis in affected patients, inform genetic counseling as well as cascade screening, and provide insight into the transcriptional regulation of transport proteins in the distal nephron and inner ear by FOXI1.