

## **SIGNIFICANCE STATEMENT**

Type 4 renal tubular acidosis (RTA) is the most common form of RTA observed in clinical practice, but the mechanism of the metabolic acidosis is not well understood. This study examines a novel mouse model of hyperkalemia in which type 4 RTA develops despite normal  $K^+$  intake, intact mineralocorticoid hormone production, and without medications that alter acid-base transport. Urine acidification is intact, but net acid excretion is decreased due to decreased ammonia excretion. There is decreased expression of ammonia-generating proteins and the collecting duct ammonia transporting protein, Rhcg, decreased apical polarization of H-ATPase, and increased ammonia-recycling protein expression. Correcting the hyperkalemia corrects the acidosis and reverses the abnormal protein expression. Thus, hyperkalemia suppresses ammonia generation and transport, and is causal for the metabolic acidosis in type 4 RTA.