

SIGNIFICANCE STATEMENT

The distal convoluted tubule (DCT) and cortical collecting duct (CCD) play unique and diverse roles in water and electrolyte handling, but little is known about the unique subset of regulatory proteins in these cells. This manuscript combines proteomics and bioinformatics to identify differentially expressed proteins in the DCT and CCD under various physiological stimuli. The different regulatory proteins within each cell type likely infer their unique transport properties. We show that one regulatory protein highly expressed in the CCD, the E3 ubiquitin ligase CHIP, modulates the function of the water channel aquaporin-2 and plays a role in renal water handling. Pharmaceutical modulation of CHIP function could be a novel approach to treat various water balance disorders.