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Expression of H-ATPase in Inner Medullary Collecting Duct (IMCD) of Aquaporin-1 (AQP1) Null Mice

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Phenotype analysis has demonstrated that AQP1 null mice are polyuric and manifest a urinary concentrating defect because of an inability to create a hypertonic medullary interstitium. Deletion of AQP1 was also associated with a decrease in urine pH from 7.0 to 6.0. To explore the mechanism of the decrease in urine pH we examined the expression of H-ATPase in kidneys of AQP1 null. There was a slight decrease in H-ATPase immunoreactivity in both intercalated cells and proximal tubule cells of AQP1 null mice. However, strong labeling for H-ATPase was observed in the apical membrane of IMCD cells in AQP1 null mice, whereas no H-ATPase labeling of IMCD cells was seen in wild type mice. In addition, there was an increase in the number of type A intercalated cells, identified by labeling for band 3 protein, in the IMCD of AQP1 null mice. Western blot analysis confirmed the increased expression of H-ATPase in the inner medulla of AQP1 null mice. These results represent the first demonstration of apical H-ATPase immunoreactivity in IMCD cells in vivo and suggest that the urine acidity observed in AQP1 null mice is due to upregulation of H-ATPase in the IMCD. The induction of H-ATPase expression in IMCD cells of AQP1 null mice may be related to their chronically low interstitial osmolality or high levels of antidiuretic hormone. The challenge will be to identify the molecular signal responsible for the de novo H-ATPase expression. Our results suggest a possible new therapy for distal renal tubular acidosis involving induction of IMCD H-ATPase expression.