Apical Targeting of Pendrin in Collecting Duct of Furosemide-treated Rat Kidney

Department of Anatomy and MRC for Cell Death Disease Research Center
College of Medicine, The Catholic University of Korea,
The Water and Salt Research Center University of Aarhus Denmark,*
Department of Medicine, University of Florida Gainesville Florida USA †

Hyun-Kuk Song · Ki-Hwan Han · Wan-Young Kim · Hyun-Wook Lee
Soren Nielsen* · Kirsten M. Madsen† · Jin Kim

Pendrin, a novel anion exchanger responsible for Cl- reabsorption and HCO3- secretion, is expressed in the apical plasma membrane and intracellular vesicles of type B and non-A-non-B intercalated cells in mouse and rat kidney collecting duct, and may be regulated by trafficking between the two membrane compartments. The purpose of this study was to investigate the influence of the loop diuretic, furosemide, which causes metabolic alkalosis and increases Cl- delivery to the distal nephron, on the expression and distribution of pendrin in the rat kidney. Male Sprague Dawley rats received furosemide (12 mg/kg/day) for 1, 2, 3, 5, and 7 days. Kidneys were preserved by in vivo perfusion with 2% paraformaldehyde-lysine-periodate and processed for light and electron microscopic immunocytochemistry using a rabbit polyclonal antibody against pendrin. Pendrin was localized in type B and non-A-non-B intercalated cells of the connecting tubule and cortical collecting duct in control animals. In type B intercalated cells, pendrin immunoreactivity was observed mainly in intracellular vesicles with little labeling along the apical plasma membrane. In non-A-non-B intercalated cells, intense pendrin immunoreactivity was detected along the apical plasma membrane. From 2- to 7 days following furosemide infusion, pendrin immunoreactivity as well as the number of pendrin-positive cells was slightly increased both in the cortex and outer medulla. Immunoelectron microscopy demonstrated that both type B and non-A-non-B intercalated cells were remarkably hypertrophied in furosemide-treated animals. Moreover, in type B intercalated cells, pendrin immunoreactivity in the intracellular vesicles was markedly decreased and labeling was predominantly located in the apical plasma membrane. We conclude that furosemide treatment may activate type B and non-A-non-B intercalated cells and stimulate bicarbonate secretion/chloride absorption, at least in part, by trafficking of pendrin to the apical plasma membrane