KSN 2017 Abstract

Pendrin from bench to bedside

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Pendrin is a Na+−independent Cl−/HCO3− exchanger that is expressed in the apical regions of type B and non−A, non−B intercalated cells of the connecting tubule (CNT) and the cortical collecting duct (CCD). In so doing, pendrin mediates the absorption of Cl− and the secretion of HCO3− secretion. This exchanger is upregulated with aldosterone and with angiotensin II and in models of metabolic alkalosis, such as following administration of aldosterone or NaHCO3. While pendrin has some role in acid−base balance, probably of more significance is its role in blood pressure regulation and NaCl balance, which has been demonstrated not only in mice, but also in humans. Pendrin mediates not only aldosterone−sensitive Cl− absorption, but also modulates the aldosterone−sensitive Na+ absorption mediated by ENaC. Pendrin changes ENaC channel activity by changing both channel open probability (Po) and surface density (N), at least in part, by altering luminal HCO3− and ATP concentration. Thus, aldosterone and angiotensin II stimulate pendrin expression and function, which stimulates ENaC activity, thereby contributing to the pressor response of these hormones. However, pendrin may modulate blood pressure partly through its extra−renal effects, such as through it expression in the adrenal medulla. This review summarizes the signaling mechanisms that regulate pendrin abundance and function as well as the contribution of pendrin to distal nephron function and how pendrin inhibitors might represent a new class of antihypertensives.