STRONG CHILDREN'S RESEARCH CENTER

Summer 2012 Research Scholar

Name: **Ryan Larochelle**

School: **Bowdoin College**

Mentor: **George Schwartz, MD**

ABSTRACT

Title: **Regulation of Anion Exchanger Expression and Distribution in the Renal Cortical Collecting Duct during Acidosis**

The α- and β- intercalated cells (ICs) of the renal cortical collecting duct (CCD) are largely responsible for maintenance of pH homeostasis via the activity of an H+ ATPase pump and anion exchangers. These two cell subtypes exhibit opposite polarity with respect to ion secretion and reabsorption, allowing for adaptation to pH changes via alterations in the bicarbonate and proton fluxes in the CCD. This may be achieved at least in part by regulating surface expression via alterations in transporter synthesis, degradation, or endosomal trafficking within the cell. In both in vivo and in vitro models, we have previously observed a decrease in bicarbonate secretion into the tubular lumen for excretion in response to acidosis (JCB 1989). Rabbit kidneys contain a preponderance of β-ICs due to their alkaline ash diet, so the apical β-IC chloride-bicarbonate exchanger pendrin was examined in this study. The goal of this study was to characterize the morphological changes in pendrin cap shape and size as a possible indication of altered trafficking and expression within the cell. In the in vivo model, CCDs were micro-dissected from normal (urine pH: 8.19, HCO_3^-: 25.9), 3-day acidotic (urine pH: 4.69, HCO_3^-: 16.4), and recovery rabbits which were transitioned from 3-day acidotic to 16-18 h of alkali loading (recovery; urine pH: 8.08, HCO_3: 28.1). For the in vitro model, CCDs from normal rabbits were incubated at either pH 7.4 or pH 6.8 to observe the acute response to acidosis. In vivo response to acidosis was characterized by a significant decrease in pendrin cap area (28.0%) and depth (13.1%), while recovery CCDs exhibited a large up-regulation in response to alkali loading (57.6% increase in area, 46.4% increase in depth) compared to acidotic CCDs. This most likely reflects alterations in pendrin synthesis and degradation in response to acid/base status. CCDs incubated in vitro exhibited significant reorientation of the cytoskeletal architecture within β-ICs, as evidenced by condensation of the ZO-1 tight junction protein and recession of the pendrin cap relative to the ZO-1. This probably indicates the importance of luminal flow in maintaining the structural integrity of the cell. Such changes presumably overwhelmed the acid-induced alterations in transporter localization. Future studies will be aimed at quantitating surface expression as a measure of the fraction of transporter participating in chloride-bicarbonate exchange.