**Abstract** for 10/31/14 CHE-399 Chemistry Seminar Presentation

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Staying hydrated requires Notch signaling mediated binary cell fate decisions during kidney collecting duct development

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The mammalian kidneys are responsible for water, electrolyte and acid-base homeostasis. The basic structural and functional unit of the kidney, a nephron, is a tubular structure organized into segments each consisting of a distinct epithelial cell type. The nephrons connect to the collecting ducts which consist of intermingled epithelial cell types. The majority of the collecting ducts consist of vasopressin responsive principal cells that uniquely express aquaporin-2 apically and arginine-vasopressin receptor-2, aquaporin-3 and aquaporin-4 on the basolateral membranes to regulate water homeostasis. Intermingled among the principal cells are the intercalated cell types that are responsible pH homeostasis, rich in mitochondria and express carbonic anhydrases along with the vacuolar H+ ATPase pumps and anion exchangers. Although the collecting ducts consist of critical cell types, which when defective result in diseases such as Nephrogenic Diabetes Insipidus and Distal Renal Tubular Acidosis, the molecular regulators of collecting duct cell type differentiation are only beginning to be identified. We have determined that Notch signaling is required to ensure that a sufficient number of immature collecting duct progenitors select the principal cell fate, without which mice have a reduced number of principal cells, a concomitant increase in intercalated cells and excessive production of dilute urine. Based on our studies of the molecular details of this evolutionarily conserved role for Notch signaling in binary cell fate decisions, we conclude that collecting duct cell type differentiation does not simply involve lateral inhibition mediated by Notch signaling to suppress intercalated cell fate selection and instead also involves Notch signaling mediated transcriptional activation of principal cell specific genes.