Determining How Sec10 and the Exocyst Complex Regulate Ureter Development

Olivia Yoshida

Mentor: Ben Fogelgren, Ph.D, University of Hawaii

Other Mentor: Amanda J. Lee, Ph.D, University of Hawaii

Coordinating Center: University of Hawaii at Manoa

ABSTRACT:

The exocyst trafficking complex is used to direct polarized exocytosis of certain intracellular vesicles to the plasma membrane and the establishment of epithelial cell polarity. The *Sec10* protein is a central component of the exocyst complex and loss of *Sec10* results in degradation of the entire exocyst complex. Our lab has shown that *Sec10* knockout in mouse ureter epithelial cells during embryonic development causes an obstruction in the ureteropelvic junction (UPJ), where the kidney transitions into the ureter. This obstructions prevents the outflow of urine from the kidney and is neonatal lethal in these mice. We have also shown that the first microscopic sign of these UPJ obstructions in *Sec10* knockout mice occur when the ureter epithelium shows widespread cell death at embryonic stage 17.5 (E16.5), although we hypothesize that molecular changes occur earlier. The purpose of this study is to follow up genomic analysis by performing qPCR gene expression measurement in *Sec10* knockout and control ureters at E16.5 to identify abnormal cell signaling which may underlie the observed cell death. We have measured abnormal expression of several genes associated with epithelial cell stress in mutant ureters, which could represent candidate genes in the analogous human disease. This work has clinical significance because UPJ obstructions occur in approximately 1 in 2,000 births and are the leading causes of hydronephrosis (kidney swelling due to urine accumulation) and congenital obstructive nephropathy (CON) in infants.

Keywords: Sec10, exocyst complex, ureteropelvic junction obstructions, epithelial cells

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