The Exocyst Complex Regulates Cell Differentiation During Ureter Development

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ABSTRACT

Congenital urinary tract obstructions are the leading cause of chronic kidney disease and end-stage renal disease in children. The most common cause of these obstructions is a blockage at the ureteropelvic junction (UPJ), where the kidney transitions into the ureter. Prenatal UPJ obstructions cause severe hydronephrosis, which is swelling of the kidney due to the accumulation of urine in the kidney. There are few non-surgical mouse models of this disease and the causes are poorly understood. Sec10 is a central component of the eight-protein exocyst complex involved exocytosis and cell signaling. We have created a unique transgenic mouse model that deletes the protein Sec10 in the urinary tract epithelial cells. Sec10 conditional knockout mice have severe hydronephrosis caused by an UPJ obstruction, and the pups die at birth. Here, we analyzed the failure of epithelial differentiation in the ureters of these mice, which leads to cellular overgrowth of the ureter lumen during embryonic development. This unique mouse model will be a useful tool to study the molecular causes of human urinary tract obstructions.

Key Words: Protein Sec 10, Ureteropelvic Junction (UPJ), Exocyst

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