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Role of SNARE proteins in epithelial apical lumen formation

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Epithelial-gland morphogenesis is a fundamental process characterized by the emergence of ducts and acini, in which a polarized epithelial cell layer attached to a basal lamina surrounds a luminal space. Acute injury of major epithelial organ systems is one of the most important causes of death worldwide, and understanding the polarization of epithelia will be important in analyzing the response of a tissue to acute injury and in developing regeneration-based therapies. Studies of epithelial cells in 3D cultures and in vivo models have shown that lumen formation depends on a complex series of events, including: stimulation of morphogenesis, for example by cues such as cell attachment (to either other cells or the extracellular matrix); apical-basal polarization; lumen expansion. It is also clear that intracellular vesicle transport pathways are important for epithelial-gland morphogenesis, but our understanding of how they are regulated remains unclear. Soluble N-ethylmaleimide-sensitive factor attachment receptor (SNARE) proteins contribute to intracellular cargo transport by regulating the fusion of donor vesicles to their target membranes. Our published studies using human endothelial cells have shown that syntaxin 6 (Stx6), a member of the target membrane-associated SNARE (t-SNARE) family protein plays an important role in VEGFR2/KDR and alpha5 beta1 integrin trafficking and angiogenesis [Blood 117, 1425-35 (2011); J Biol Chem. 286, 36749-61 (2011)]. In contrast, confluent 2D and 3D epithelial cell cyst culture show downregulation of Stx6 with concomitant up-regulation of Stx16, suggesting a role for Stx16 in morphogenesis. Furthermore, Stx16 knockdown in epithelial cells show defect in morphogenesis and forms multiple lumens in 3D cysts. Ongoing studies in the lab are investigating role for Stx16 in the protein and lipid trafficking patterns that are required to maintain the cell-cell adhesion and cell polarity, events that are essential to achieve epithelial lumen formation. These studies may provide a better understanding of the fundamental mechanisms that regulate cell polarization, information that will be needed to improve the response of tissues to acute injury as well as to identify ways to avoid fibrosis and EMT after chronic injury.

Biography

Dr. Choudhury completed his PhD from Punjab University in India and postdoctoral studies from University of Nebraska Medical Center and Mayo Clinic, Rochester, MN. He is currently an Assistant Professor in the Department of Anatomy and Cell Biology at the University of Iowa. Dr. Choudhury has a long-standing interest in understanding how intracellular membrane trafficking is regulated during physiological and pathological conditions. Studies in the lab are focused on understanding role of specific vesicle trafficking regulatory proteins in cell dynamics during angiogenesis, cancer metastasis, and epithelial lumen formation. Dr. Choudhury is the PI of NIH grant (HL089599), and serves as a faculty mentor in various graduate programs (Anatomy and Cell Biology, Biosciences, Molecular and Cellular Biology, and Medical Scientist Training Program), at the University of Iowa, Iowa City, IA.

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