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Sealing the ducts
Tight junctions of ductal epithelium

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The transitional epithelium lining the ducts of various glands such as salivary and mammary glands, and organs such as liver, pancreas, kidney and lung must bear a permeability barrier as they are in direct contact with the hostile environment in the lumen. The barrier function of pancreatic ductal epithelium is essential for preventing the back flux of proteases, lipases and DNAases from the pancreatic secretion into the interstitial tissue. Disruption of ductal epithelial barrier is associated with the pathogenesis of pancreatitis and development of pancreatic cancers.[1] Bile acids constitute more than 60 percent of organic composition of bile. Bile ducts play crucial role in the formation and secretion of bile and excretion of circulating xenobiotic substances. Bile acids are toxic if they are regurgitated into the liver parenchyma. Bile duct epithelial barrier plays an important role in preventing such bile regurgitation, and bile acid-induced tissue injury is known to be associated with the pathogenesis of many biliary diseases, such as primary biliary cholangitis and primary sclerosing cholangitis.[2] Similarly, airway epithelial barrier is required to prevent the entry of toxins, allergens and pathogens from the inhaled air. Luminal surface of the entire airway is lined with the transitional epithelium with a well-developed barrier function. Airway epithelial barrier is disrupted in pathophysiologic conditions such as asthma and chronic obstructive pulmonary disease.[3] Epithelial barrier function in all transitional epithelia is ascribed to well-developed tight junctions. Therefore, understanding the molecular structure and regulation of ductal epithelial tight junctions are crucial to understand the pathogenesis of a variety of diseases associated with the ducts of different organs and glands.

The classic work of Farquhar and Palade (1963)[4] first attributed the barrier function to tight junctions not only in the mucosal and glandular epithelia, but also in the epithelia of pancreatic, hepatic and salivary ducts. Although the importance of ductal epithelial barrier function was recognized early, the progress in understanding the structure and regulation of tight junctions of these ductal epithelia has been very slow. Encouragingly, there has been some momentum in this field of investigations during the past decade. The main goal of this special issue is to shed light into this area of research by presenting selected review and research articles that discuss the current understanding of the structure and regulation of tight junctions and barrier function in some of the ductal epithelia.

Kojima etal[5] address the current understanding of the regulation of tight junctions in pancreatic duct epithelium by intracellular signaling elements. They describe the role of protein kinase C isoforms and c-Jun-N-terminal kinase in regulation of pancreatic duct epithelial tight junctions. Rao and Samak[6] summarize the physiology and pathophysiology of bile duct epithelium. This article describes the structure and regulation of bile duct epithelial tight junctions and mechanisms involved in tight junction disruption by injurious factors such as lipopolysaccharide and hydrogen peroxide and protection of mucosal barrier by epidermal growth factor. Review article by Sajjan and coworkers[7] presents the current knowledge in regulation of different components of airway epithelial barrier function and implication of its dysfunction in chronic airway-associated diseases. This article describes the cellular diversity in airway epithelium, structure and composition of airway epithelial tight junctions, and addresses different cellular models currently used in investigating airway epithelial tight junctions. Hopkins and colleagues[8] discuss the biology of mammary duct epithelial tight junctions and barrier function, models used in studies on mammary epithelial tight junctions and pathology of mammary duct barrier in relation to breast cancer. This article discusses how dysfunctional tight junctions contribute to hyper proliferation and uncontrolled cell migration. They also discuss the potential of adhesion proteins as targets in breast cancer treatment.

Hou and colleagues[9] discuss a novel imaging technique named Potentiometric Scanning Ion Conductance Microscopy (P-SICM). The unique combination of voltage scanning and topographic imaging enables P-SCIM to capture paracellular conductance within a nominal radius of several hundred nanometers. The article also includes the summary of recent advances in paracellular conductance recordings.

Following the review articles are four research articles that complement the review articles. Naydenov et al.[10] report a novel mechanism of cytokine-induced disruption of tight junctions in the pancreatic duct epithelium. This article describes a signaling pathway involving janus kinase and protein kinase D in interferon-γ-induced tight junction disruption in pancreatic duct epithelium. Aggarwal etal[11] report the role of aquaporin 5 in regulation of airway duct epithelial barrier function. Loss of aquaporin 5 reduces tracheal epithelial permeability and protects against cigarette smoke-induced increase in epithelial permeability. This barrier protection was associated with an increased expression of E-cadherin. Furthermore, Casio and colleagues[12] analyzed tight

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junctions of four different cell lines that form bile canaliculi and express typical hepatocyte polarity. Some of the significant findings include lack of claudin-1 in these hepatocyte cell lines and differences in expression of claudin isoforms among cell lines. This study also reports that tight junction proteins are settled in sequence in a specific order during the de novo assembly of tight junctions. Finally, Twiss etal[13] discovered that hepatocyte growth factor modulates mobility of claudin-3 at the junctions of renal tubular epithelial cells. This effect of hepatocyte growth factor is regulated by tyrosine phosphorylation at the C-terminal domain of claudin-3.

In essence, articles in this issue address the ductal epithelial barrier function and project the diversity in structure and properties of tight junctions in different ductal epithelia. It is likely that the structure and composition of tight junctions are different in ductal epithelia in different organs and glands and within individual organs and glands. Further unraveling the specific signaling mechanisms associated with the assembly and disruption of these ductal epithelial tight junctions will be invaluable to our understanding of the pathogenesis of various diseases and design of treatment strategies. Therefore, further investigations in this area of research are encouraged.

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