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Mucosal Layer Functions and Dysfunctions

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Description

Epithelial cells lining mucosal surface essentially define the border between the environment and ourselves. At some mucosal surfaces, the epithelial border is only one cell thick, interfacing either the environment over huge surface areas. These vast and delicate epithelial barriers, typified by the intestinal, respiratory and urogenital mucosa, have to distinguish between components of the outside world and selectively transport huge quantities of those essential for life to the lamina propria or systemic circulation. At the same time, the epithelial cell must also defend against invasion and absorption of unwanted, toxic and pathogenic molecules and microbes as well as producing and secreting some factors required to provide for such host defense. From this pivotal position, including immunocompetent cells of the lamina propria and those comprising the mucosal immune system cell types at a distance that effect systemic immunity, metabolism and orgn function and molecules and microbes, in the luminal space of the outside world. Therefore the mucosal immune system cannot be understood without first understanding the epithelial cell and its developmental and molecular biology that underlie mucosal physiology and immunology.

Barrier function

The epithelial barrier of mucosal surfaces separates a wealth of foreign antigen that consists of the commensal flora and ingested food, on the luminal side, and the mostly sterile environment harbouring the mucosal immune system on the other side. This barrier function, which is as much physiologic as it is structural, is set up to efficiently defer any single incoming pathogen. Remarkably the characterized commensal microbial communities associated with each mucosal surface and molecular components of the luminal space are required for the development of both the mucosal and systemic immune systems, the establishment of the epithelial barrier itself, and repair after the injury associated with inflammation. Non-structural components of the mucosal barrier including mucus produced by goblet cells and anti-microbial peptides produced by paneth cells, play a fundamental role in mucosal protection. The compostion of mucus includes anti-microbial peptides, such as defensin which influence the composition of the gut microbiota. Together, mucins and anti-microbial peptides form a secreted mucosal barrier that provides protection against an array of microbes. Components of both the innate and adaptive mucosal immune systems contribute to goblet cell and paneth cell regulation in response to specific environmental challenges.

Inappropriate barrier function

Regulation of the physical epithelial barrier is necessary for the maintenance of homeostasis the normal composition of the mucosa associated lymphoid tissue and the avoidance of inflammation. In animal models, disruption of junctional adhesion molecules or cadherins on epithelial cells, which may link the latter to beta catenin and potentially to adenoma formation. Such disruptions of the physical barrier which may be genetically determined are possibly predisposing factors for the development of chronic intestinal inflammation as observed in inflammatory bowel disease. Proper nuclear factor signalling is required for maintaining the integrity of the epithelium and the functional linkage of the epithelium with subjacent immune cells.

Normal physiologic epithelial barrier function is also necessary for intestinal homeostasis. Signals emanating from the microbiota and detected by cell surface and intracellular pattern recognition receptors regulate anti-microbial peptide secretion. Consequently, loss of this activity may leads to alterations in the commensal microbiota and susceptibility to pathogens and pathobionts.