Symposium 1: Immunity and pathogenesis of AR and CRS

Epithelial barrier dysfunction in CRS

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The important functions of nose and sinuses are frequently neglected in human which is reflected by the fact that nasal obstruction and mouth breathing are very common symptoms encountered. As a rhinologist, the most important mission is to draw attention of the general population on the physiological roles of nose and sinuses. Clinically, chronic rhinosinusitis (CRS) is one of the most prevalent chronic diseases in modern society. It is a heterogeneous, multifactorial disease with multiple distinct factors, including genetic, environmental, infectious, immune, anatomic, allergic, and inflammatory components. Recently, epithelial barrier dysfunction has been linked to chronic inflammatory disease of multiple organ systems including atopic dermatitis, inflammatory bowel disease, asthma, and CRS.

The sinonasal airway is at the gateway between the external airborne environment and the human body. Thus, the sinonasal epithelial cell is constantly engaged in immunomodulation between the host and the environment. The first line of defense is the mucociliary clearance of a blanket of mucus containing a variety of antimicrobial agents. Subsequently, disruption of airway epithelial barrier functions may occur by various factors including pathogens, oxidative stress, PM, allergen etc. Disruption of barrier function plays as a two-edge sword which in one way facilitates healing process by releasing submucosa mediator, cellular component or epithelial-mesenchymal transition (EMT) of epithelial cells; which in another way render more susceptible to have inflammation triggered by external stimuli. In general, epithelium may be considered as a battle field between external stimuli and internal homeostatic force.

Mechanism of epithelial barrier destabilization include proteolytic activity of the HDM Der p 1, IL-33 interplay with ILC2s to increase IL-13 expression, and exacerbation with PM or DEP. Cigarette smoke induced sinonasal epithelial cells barrier dysfunction is reversible by Nrf2 activation. Therefore, the Nrf2 antioxidant pathway may represent a potential therapeutic target for cigarette smoke-associated sinonasal inflammation.

In addition to barrier function, sinonasal epithelial cells have an important role as both mediators and

regulators of innate immune responses and adaptive immune responses in the pathogenesis of chronic nasal inflammatory diseases. Sinonasal epithelial cells monitor the external environment by using pattern recognition receptors (PRRs) to sense potentially dangerous inhaled materials. They express various PRRs, including Toll-like receptors (TLRs), RIG-I-like receptors (RLRs) and NOD-like receptors (NLRs). TLRs are now increasingly relevant, and recognition by TLRs can directly activate immune cell responses. “Epimmunome” is all the compounds used by sinonasal epithelial cells to instruct immune cells. Future studies to identify the molecules of epimmunome will help to understand the importance of epithelial barrier dysfunction in CRS and whether barrier stabilization may improve CRS pathophysiology.