



Research: Molecular Mechanisms Involved in Airway Epithelial Cell Responses and Chronic Mucous Production

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Disease/Condition: Cystic Fibrosis, Asthma and COPD

Mucous hypersecretion is a hallmark of chronic airway diseases, and several factors including pro-survival mechanisms help sustain growth and proliferation of mucous producing cells, but the factors regulating the prosurvival mechanisms in airway epithelial cells remain elusive. Collectively, the studies identified this mechanism, which has been otherwise shown to regulate programmed cell death during development and injury, and repair processes and can lead to cancer development when cell proliferation is deregulated. The studies are focused on identifying inflammatory mediators that modulate expression or prosurvival proteins in airway epithelial cells (AECs) because these mediators could be useful to enhance repair processes.

Researchers at LRRRI have been working with various animal models exposed to lipopolysaccharide (LPS), or cigarette smoke (CS), to mimic acute and chronic exposure conditions that are observed in subjects with cystic fibrosis and chronic obstructive pulmonary disease (COPD), respectively. Factors that upregulate prosurvival mechanisms were identified and these factors were observed to be present at higher levels in airway epithelial cells of patients with cystic fibrosis and chronic bronchitis, as well as respective animal models compared to the controls. Therefore, targeting these factors to block mucous-producing cells could provide a new therapeutic approach to regulate airway epithelial cells in chronic airway diseases. On the other hand, studies are being followed to understand the mechanism involved in epithelial cell death and extrusion pathways, the biological processes important in resolving airway epithelial inflammation. In this regard, various in vivo, ex vivo, and in vitro models have been developed to understand the mechanism involved in resolution of inflammatory airway epithelial cells. These studies will help develop the intervention strategies to enhance the resolution of airway inflammation otherwise compromised in chronic airway diseases.