Exploring IL13 effects on the remodeling of airway epithelial cell populations by single-cell RNA sequencing

Asthma - mechanism, Epithelial cell, Genomics

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The airway epithelium is mainly composed of basal cells, mucus-secreting goblet cells and multiciliated cells. The beating of the cilia at the surface of the multiciliated cells allows the clearing of the pathogen-trapping mucus. In asthma, the airway epithelium is subjected to chronic inflammation and impaired regeneration leading to remodeling, decrease in multiciliated cells and goblet cell hyperplasia. Interleukin-13 (IL13) secreted by Th2 cells is an important cytokine in the pathogenesis of the disease. The implication of the immune system in this inflammation is well characterized, however, the epithelium-specific mechanisms of asthma are unclear and whether multiciliated cells can transdifferentiate into goblet cells is still up for debate. To identify cell trajectories giving rise to the asthma-related population imbalance, differentiated human airway epithelial cells were treated with IL13. Epithelial remodeling was observed after eight days of treatment. In order to mimic recovery, we then subjected the cells to a wash-out period of two weeks which resulted in a restoration of the initial cell composition. To identify recovery trajectories and elusive cell type intermediates, we performed single-cell RNA sequencing after IL13 and after the wash-out period. Single-cell RNA-seq confirmed that IL13 treatment leads to epithelial remodeling and identified cell type-specific IL13 target genes with for instance SERPINB10 expressed in multiciliated cells, or PIGR expressed in secretory cells including goblet cells. Further analyses are ongoing, such as trajectory inference, in order to identify cellular and molecular events leading to epithelial remodeling and recovery.