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Characterization of a novel epithelial cell type in sinonasal cavity and its potential disarray in patients having both upper and lower respiratory tract diseases

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Therapeutic approaches for numerous conditions involving respiratory tract have been artificially categorized into upper and lower airways and treated independently. Recently, an increasing number of studies have reported similar pathobiological mechanisms between upper and lower airways, thereby providing a scientific rationale for the development of therapeutic agents effectively working on united airways. Chronic rhinosinusitis with nasal polyps (CRSwNP) is an upper airway disease characterized by persistence of sinusitis, inflammation of the nasal mucosa and nasal polyp formation, which commonly manifests concurrently with lower respiratory tract inflammatory conditions such as bronchiolitis. However, the mechanism behind this interrelationship remains largely unknown. Herein, we attempt to elucidate this mechanism using single-cell transcriptome analysis of sinonasal tissues from CRSwNP patients. We observed a consistent downward trend in the composition of a particular subset of epithelial cells in NP tissues, compared to that in normal sinonasal tissues. This cell type was revealed as glandular cells in upper airways based on the established public datasets. Further, when this subset of epithelial cells was simultaneously annotated based on the established set of cell types from lower respiratory tract public datasets, gene expression profiles were consistent with submucosal glandular cells in larger airways such as trachea and bronchus. Moreover, those cells were shown to have the characteristics of progenitors such as distal airway-specific secretory cells, concurrently. Each endotype of CRS (eosinophilic versus non-eosinophilic) displayed different patterns not only in cell-cell communication but also lineage of differentiation involving this cell type. Our results suggest that the dysfunction a novel epithelial subset harboring lower respiratory gene signatures in upper airways may be critically implicated in the pathogenesis of CRSwNP, and imply that its potential disarray may play a role in the pathogenesis of united airway disease.