Crucial Pathogenic Role of Elevated Mast Cells in Pulmonary Fibrosis Revealed by Single-Cell RNA-Sequencing Analysis

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Pulmonary fibrosis occurs when lung tissue becomes damaged or scarred and can be progressive in nature, impacting an individual's ability to breathe. Idiopathic pulmonary fibrosis (IPF) and systemic sclerosis-associated interstitial lung disease (ssILD) are two high-mortality pulmonary fibrosis diseases with limited treatment options. Previous studies have found increased connective tissue mast cell populations in the lung parenchyma area of IPF and ssILD patients. However, the exact role of these cells in the progression of pulmonary fibrosis is unknown. Addressing this research gap, this study utilized in-depth single-cell RNA-sequencing (scRNA-seq) analysis of lung tissue samples to elucidate the role of mast cells in the pathogenesis of IPF and ssILD. 32 samples were analyzed in total: 14 healthy control, 5 IPF, and 13 ssILD. 91,656 lung cells were divided into 17 clusters, including one mast cell cluster, and analyses were performed to identify up and downregulated genes within the different cell clusters. The results indicated an increased population of mast cells in the lungs of IPF and ssILD patients. The findings suggest that mast cells not only directly contribute to pulmonary fibrosis through mast cell mediators, but also promote the differentiation and proliferation of other cell types through ligand-receptor interactions, thus cascading inflammation and fibrosis in lungs affected by IPF and ssILD. By shedding new light on the crucial role of mast cells in the progression of IPF and ssILD, this study paves the path for future therapeutic developments to treat these life-threatening diseases.

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