A109 · Investigating the Transcriptional Program of ACKR1+ Venous Endothelial Cells in Pulmonary Fibrosis Using Single-Cell RNA-sequencing

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Idiopathic pulmonary fibrosis (IPF) is a progressive, age-associated lung disease characterized by irreversible scarring and loss of lung function. Vascular remodeling is a hallmark of IPF, driven in part by endothelial dysfunction and altered immune-vascular interactions. Venous endothelial cells (VECs), marked by the expression of Atypical Chemokine Receptor 1 (ACKR1), have emerged as an important endothelial population associated with disease progression. Analysis of a publicly available single-cell RNA-sequencing (scRNA-seq) data demonstrates that ACKR1+ VECs expansion in IPF lungs is associated with increasing fibrosis. Gene ontology analysis exhibits enrichment of genes encoding factors involved in leukocyte recruitment, hypoxia (e.g. HIF1a), inflammation (e.g. CXCL1), and cytoskeletal reorganization (e.g., TAGLN2). These findings suggest that ACKR1+ VECs acquire an activated phenotype that promotes processes contributing to lung fibrosis. Receptor-ligand analysis via CellChat identified numerous signaling interactions among VECs, myeloid immune cells and mesenchymal cells, driven via inflammatory chemokines, including those mediated by CCL18, CXCL8, and CCL2. Similar findings were made from the analysis of scRNA-seq data of fibrotic mouse lungs, which identified an ACKR1+ VEC population with a comparable inflammatory and immune-recruiting transcriptional signature. This conserved transcriptional program identifies ACKR1+VECs as a disease-associated endothelial state and supports the relevance of endothelial signals to fibrotic progression. Thus, ACKR1+ VECs represent an important population for investigating the development of the profibrotic niche in IPF and may offer a promising target for therapeutic intervention.

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Abstract

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