SINGLE-CELL ANALYSIS REVEALS CHARACTERISTICS OF MYELOID CELLS IN PULMONARY PASC

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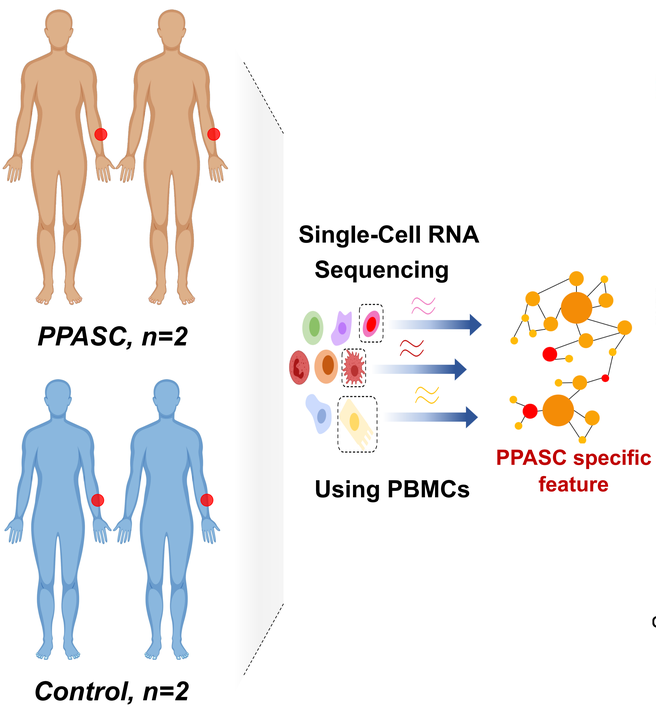
BACKGROUND

Although our understanding of immunopathology in the risk and severity of COVID-19 disease is evolving, a detail of immune response in long-term consequences of COVID-19 infection remains unclear. Recently, few studies have detailed the immune and cytokine profiles associated with PPASC. However, dysregulation of immune system driving pulmonary PPASC is still largely unknown.

METHODS

To characterize the immunological features of PPASC, we performed droplet-based scRNA-sequencing using 10X genomics to study the transcriptomic profiles of peripheral blood mononuclear cells (PBMCs) from participants naïve to SARS-CoV-2 (Control, n=2) and infected with SARS-CoV-2 with chronic pulmonary symptoms (PPASC, n=2).



RESULTS

Analysis of more than 37,000 PBMCs by integrating our dataset with previously reported control datasets generated cell distribution and identified 11 immune cell types based on canonical gene expression. The proportion of myeloid-lineage cells (CD14⁺ monocyte, CD16⁺ monocyte, and dendritic cells) were increased in PPASC compared with those of controls. Specifically, PPASC displayed up-regulated of *VEGFA* and transcription factors, such as *ATF2, ELK,* and *SMAD* in myeloid-lineage cells. Also, *TGF-β* and *WNT* signaling pathways were up-regulated in these cell population. Cell-cell interaction analysis identified that myeloid-lineage cells in PPASC participated in the regulation of fibrosis and immune response. Such as *VEGFA* (increased) and *MIF* (decreased) interactions.

Fig 1A

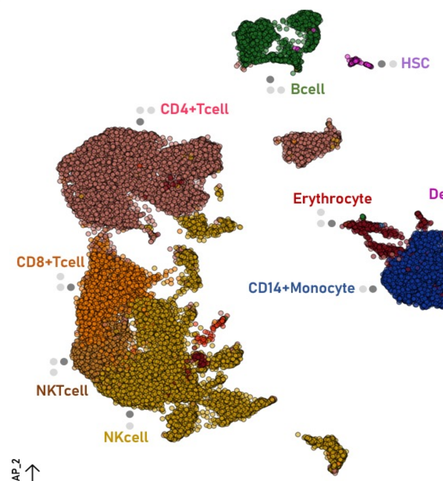


Fig 1B

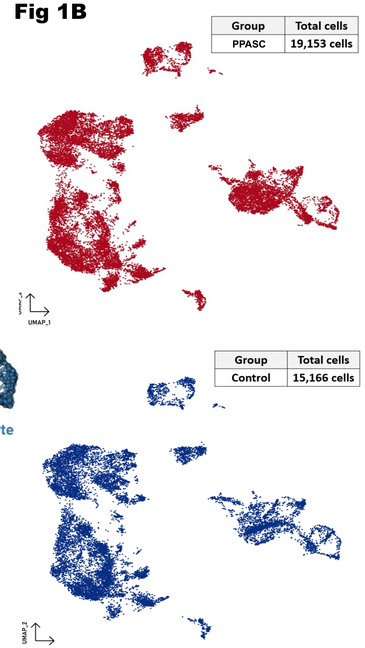


Fig 1C

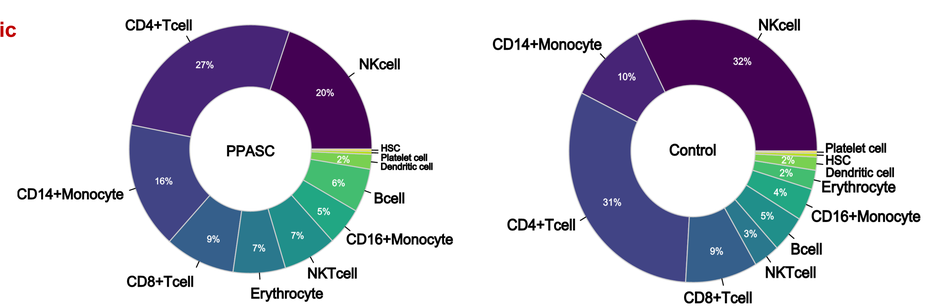


Fig 1A. Single-cell data was integrated with both the PPASC and control groups. **Fig 1B.** The total number of cells in the PPASC (red) and control (blue) groups. **Fig 1C.** The proportion of cell types in the PPASC and control groups.

Fig 2A

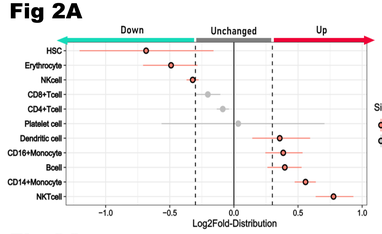


Fig 2B

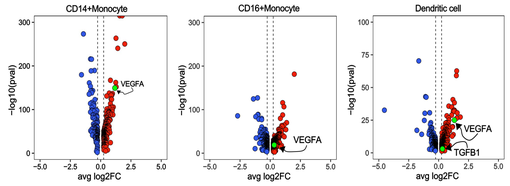


Fig 2C

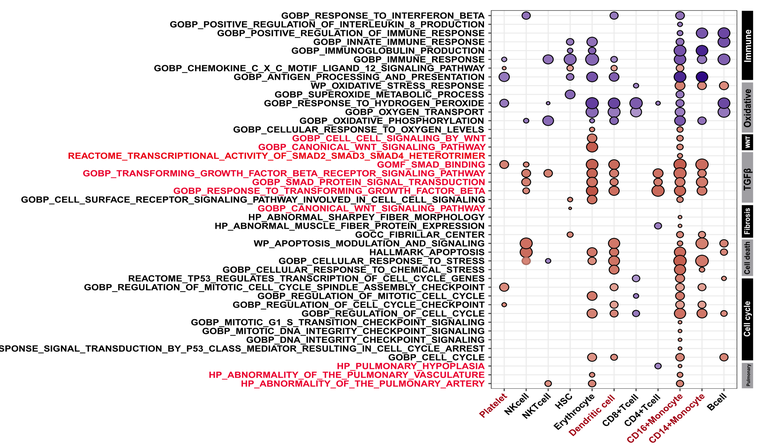


Fig 2D

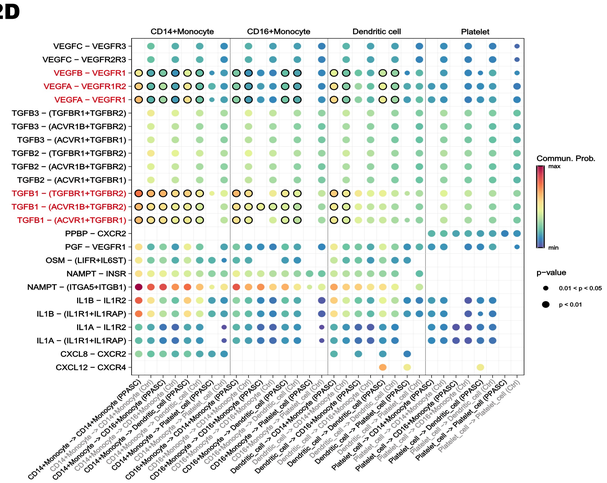


Fig 2E

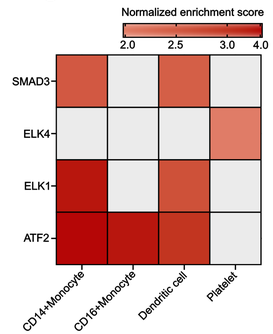


Fig 2A. The differential proportion of cell types between the PPASC and control groups. **Fig 2B.** Differential gene expression among myeloid cell types. **Fig 2C.** Differential pathway enrichment across all cell types. **Fig 2D.** Differential cell to cell interactions among myeloid cell types. **Fig 2E.** Differential transcription factor enrichment among myeloid cell types.

CONCLUSIONS

Together, this study provides high-resolution insights into immune landscape in PPASC.
Our results emphasize differences in myeloid lineage-mediated fibrosis and immunity between PPASC and Control, suggesting they could act as potential pathological drivers of PPASC.