High-Throughput Single-Cell Analysis Revealed Transcriptional Response of Dendritic Cell Subsets During SARS-CoV-2 Infection

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Keywords: COVID-19, conventional dendritic cells, single-cell RNA-sequencing

Abstract:
Growing evidence suggests that conventional dendritic cells (cDCs) undergo aberrant maturation during SARS-CoV-2 infection and this negatively affects T cell activation. cDCs are a heterogeneous population originally classified in cDC1s and cDC2s. Recently, single-cell RNA sequencing revealed the complexity of cDC2s, which were stratified into two subpopulations, DC2s and DC3s. Given the pivotal role of these cells in the orchestration of adaptive immune responses, a deep characterization of their transcriptional signatures during COVID-19 may provide novel insights to understand the immune system's reaction to infection.

Here, we analysed two available and a newly generated single-cell transcriptomic datasets of peripheral blood mononuclear cells from COVID-19 patients and healthy donors (HD). We observed that, during infection, DC3s showed increased frequencies in patients, which positively correlated with disease severity. When comparing cDCs in severe versus mild patients, we identified an important number of differentially expressed genes. Specifically, inflammatory genes not related to the activation of adaptive immunity, like complement and coagulation factors, were upregulated in cDC2s from severe patients. Conversely, genes encoding MHCII molecules, the costimulatory molecule CD86 and cytokines, showed a progressive downregulation from HD to mild and finally severe patients. Therefore, as disease severity increases, cDC2s progressively skew toward inflammatory activities and lose the antigen presenting function.

In conclusion, we unravelled the transcriptional signatures, reflecting the functional state, of cDC subsets during COVID-19. Importantly, by inducing the downregulation of crucial molecules required for T cell activation, the virus implements an efficient immune escape mechanism that correlates with disease severity.