

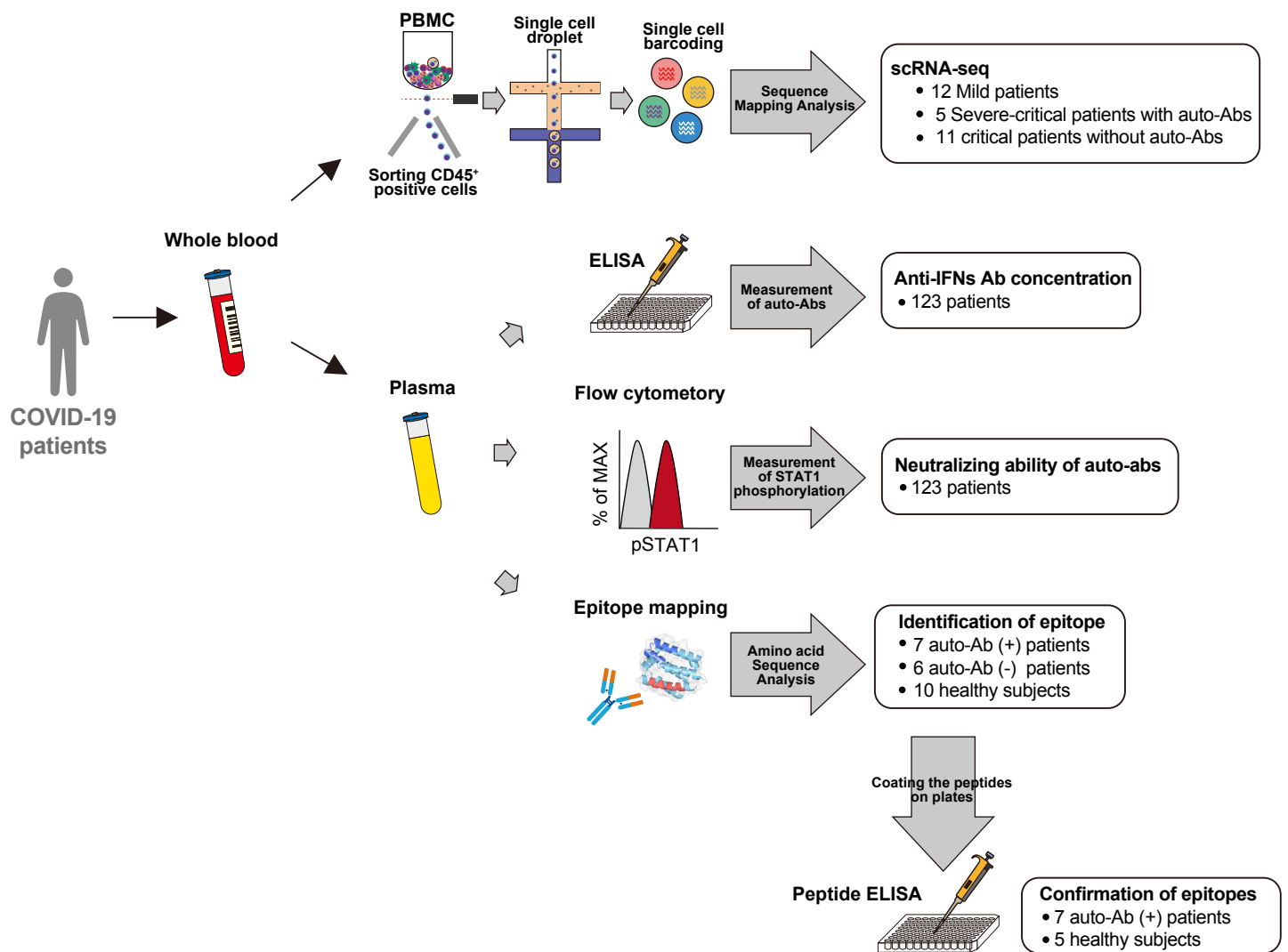


Fig. S1 Overview of the analyses in this study

Whole blood samples were collected from 123 people including healthy controls. CD45⁺ cells were analyzed by single-cell RNA-seq. Plasma samples were used to determine the presence of neutralizing auto-abs to type I IFNs and the epitopes.

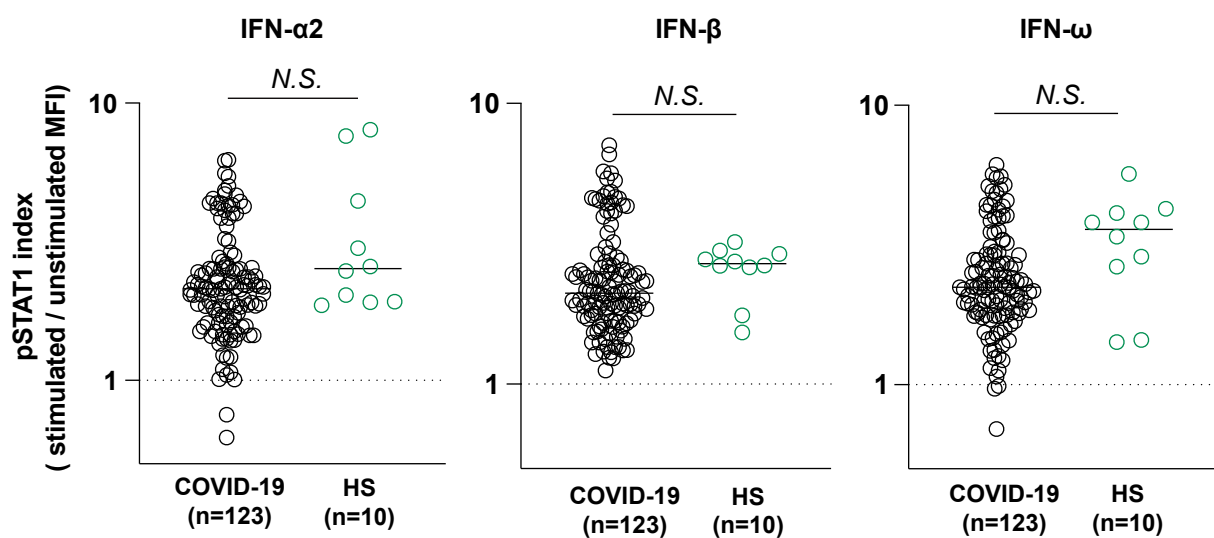


Fig. S2. Neutralizing activity to type I IFNs in plasma from COVID-19 patients

The phosphorylation of STAT1 in U937 cells stimulated with recombinant human IFN- α 2, IFN- β or IFN- ω was evaluated in the presence of 10% plasma from patients (n=123) or healthy control subjects (HS, n=10). Mann-Whitney *U* test was used for the statistical analyses. The bar indicates Median.

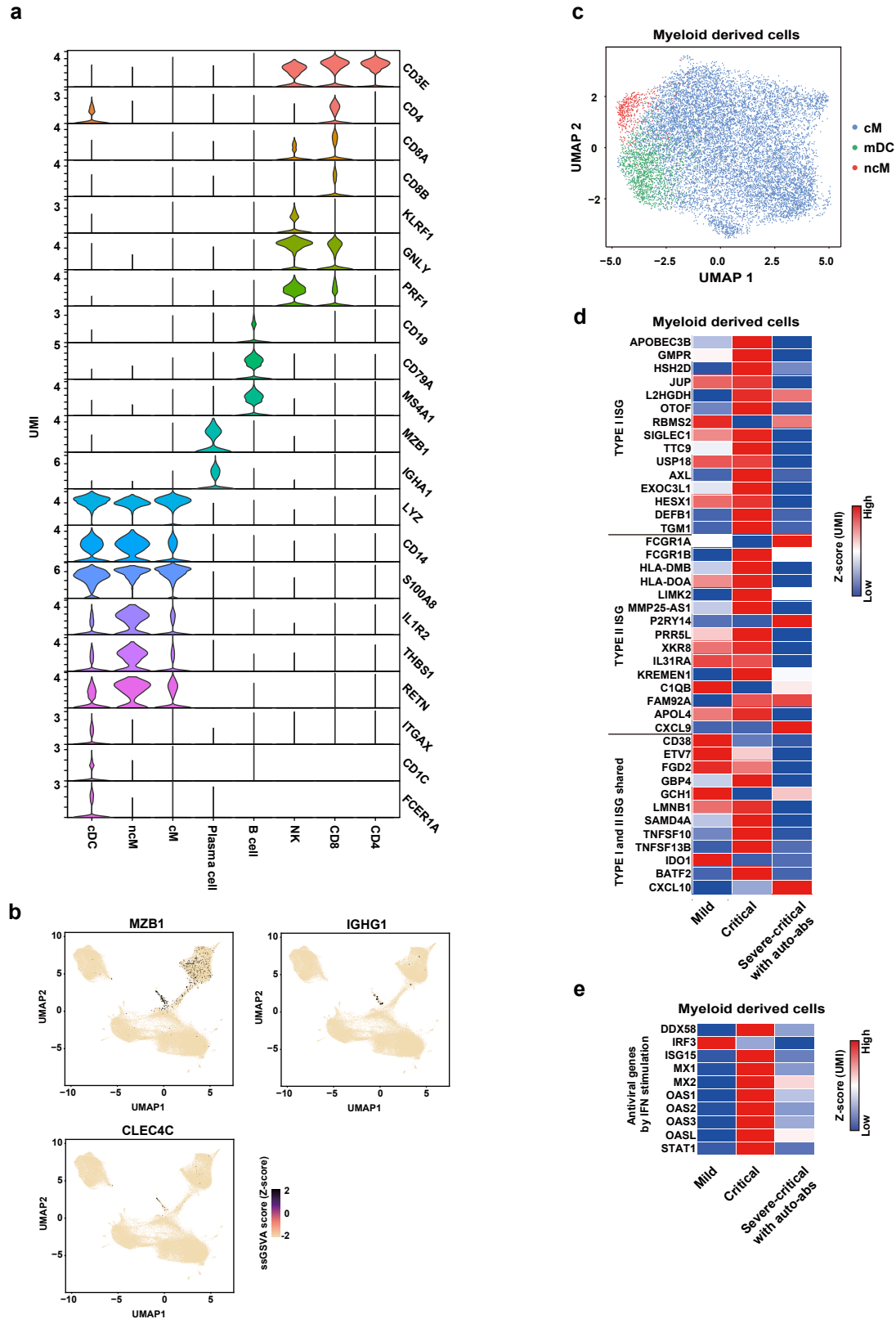


Fig. S3. Gene expression characterizing immune cells and type I IFN-related gene expression in myeloid derived cell from COVID-19 patients.

a. Violin plots depicting the expression of signature genes to identify each immune cell. **b.** The UMAP shows the expression of genes to determine plasmacytoid DCs with color intensity. **c.** The UMAP projection of CD14⁺ cells from mild, severe, and critical COVID-19 cases is depicted and colored according to the cellular populations. **d and e.** Heat map depicting the expression of ISGs (**d**) or antiviral genes induced by IFN stimulation (**e**). The color represents the Z-score for each gene.

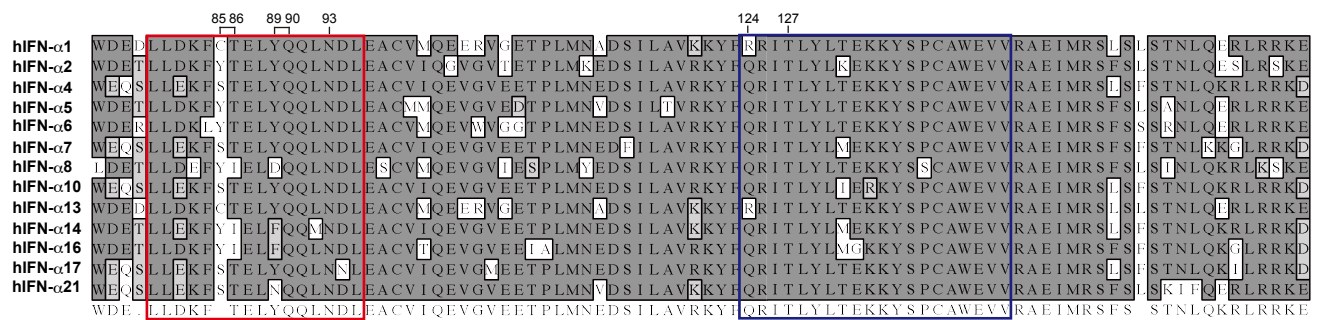


Fig. S4. A comparison of amino acid sequences between the subtypes of IFN- α
 IFN- α 2 80-95 is indicated by a red rectangle, while IFN- α 2 124-143 is indicated by a blue rectangle. Each number on top is the binding site to IFNR1.