Supplemental Figure 1. Temperature (**A**), weight (**B**), and saturation of peripheral oxygen (SpO2) (**C**) levels were measured prior to and for 6 weeks following SARS-CoV-2 inoculation of SIV+ pigtail macaques. Day 0 indicates time of SARS-CoV-2 infection, 48 weeks post SIVmac239 exposure.

NV18

A. Pre-SARS-CoV-2 Infection   B.   1-wpi   C.   2-wpi   D.   5-wpi

NV19

E. Pre-SARS-CoV-2 Infection   F.   1-wpi   G.   2-wpi   H.   5-wpi
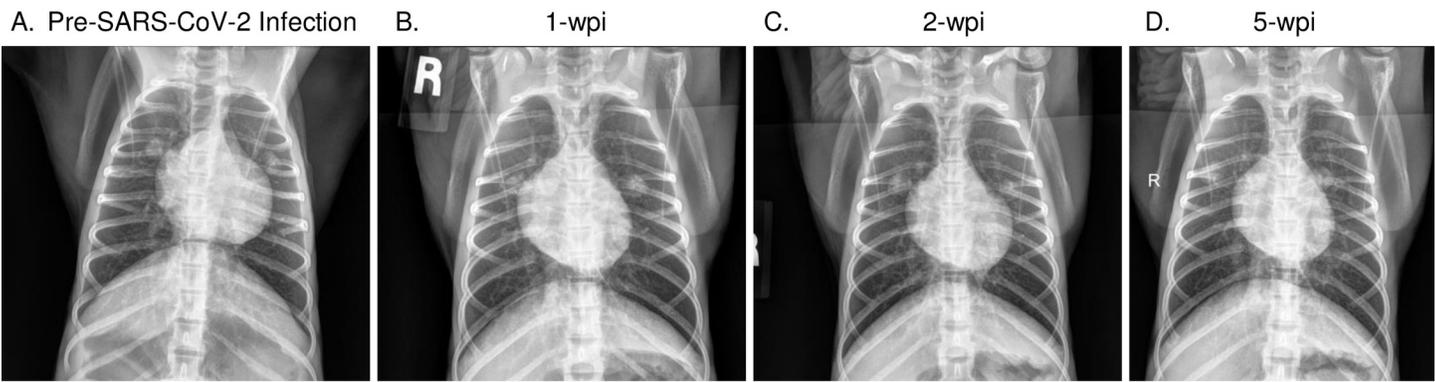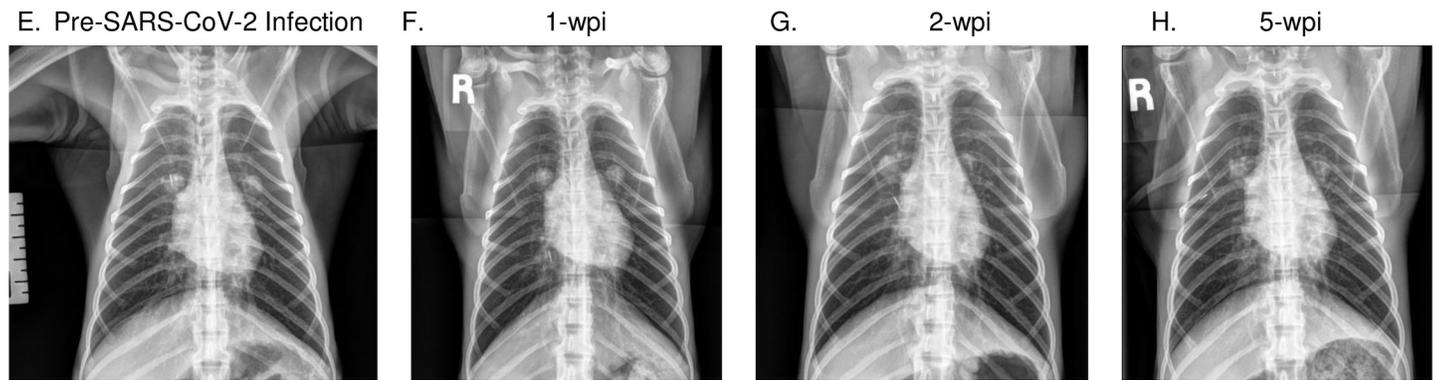
Supplemental Figure 2. Radiographs of SIV-infected pigtail macaques (PTM) challenged with SARS-CoV-2.
Radiographs were obtained prior to SARS-CoV-2 infection and at weeks 1-, 2-, and 5-weeks post infection (wpi).
Baseline was established at 2 weeks prior to SARS-CoV-2 inoculation.

Cytokines

A.
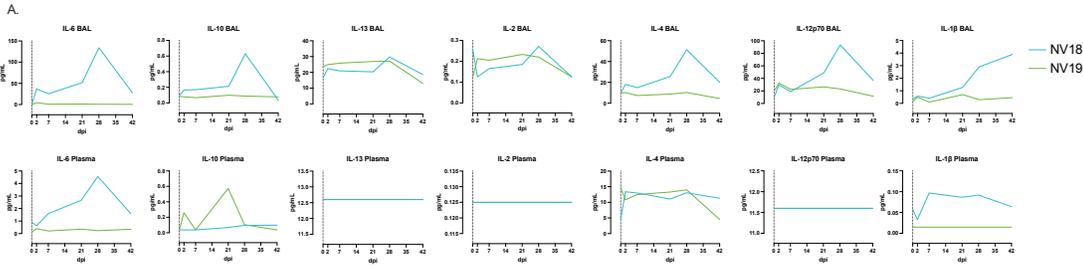
Proinflammatory Cytokines

B.

Chemokines

C.
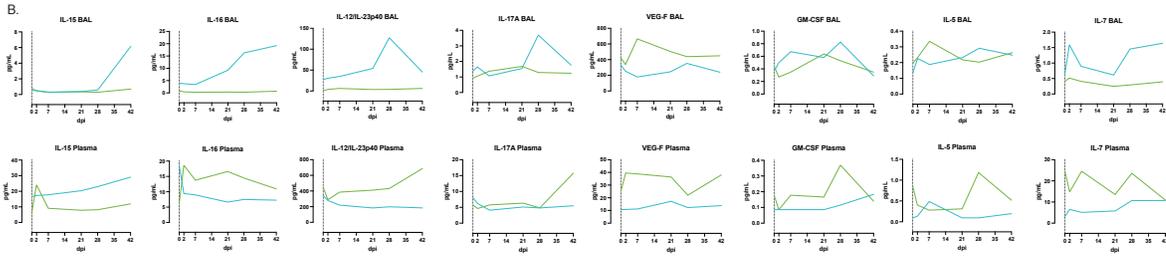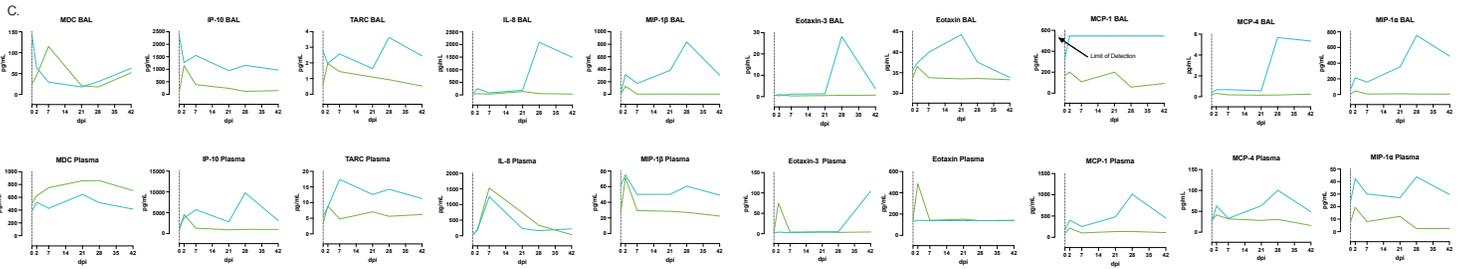
Supplemental Figure 3. Meso Scale analysis of cytokine and chemokine fluctuations in blood and BAL in PTM coinfected with SIV and SARS-CoV-2. **A-C.** Line graphs illustrating cytokine, proinflammatory cytokine, and chemokine dynamics in BAL supernatant and plasma before and 2-, 7-, 21-, 28-, and 42-days post SARS-CoV-2 infection.
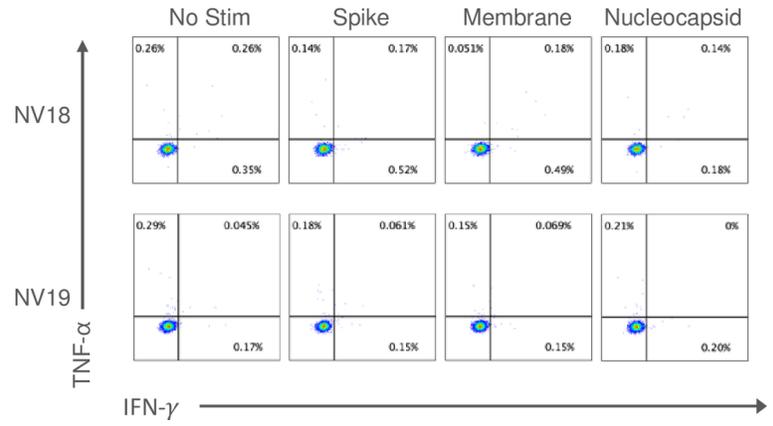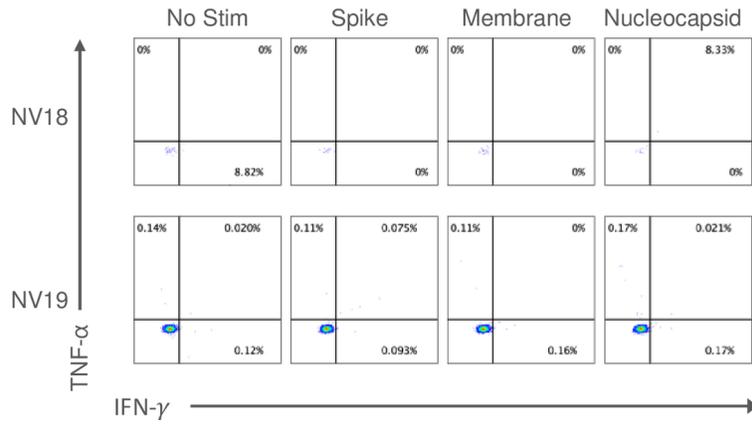
Supplementary Figure 4. Peripheral SARS-CoV-2 specific T cell responses were undetectable 21-days-post-infection. Two female pigtail macaques (PTM, NV18 & NV19) co-infected with SIVmac239 and SARS-CoV-2 shown. **A&B.** Flow cytometry dot plots demonstrating the IFN-γ and TNF-α response of CD4+ (**A**) and CD8+ (**B**) T cells to overnight SARS-CoV-2 peptide (spike, membrane, and nucleocapsid) stimulation. No Stim = cells incubated overnight without peptide stimulation.
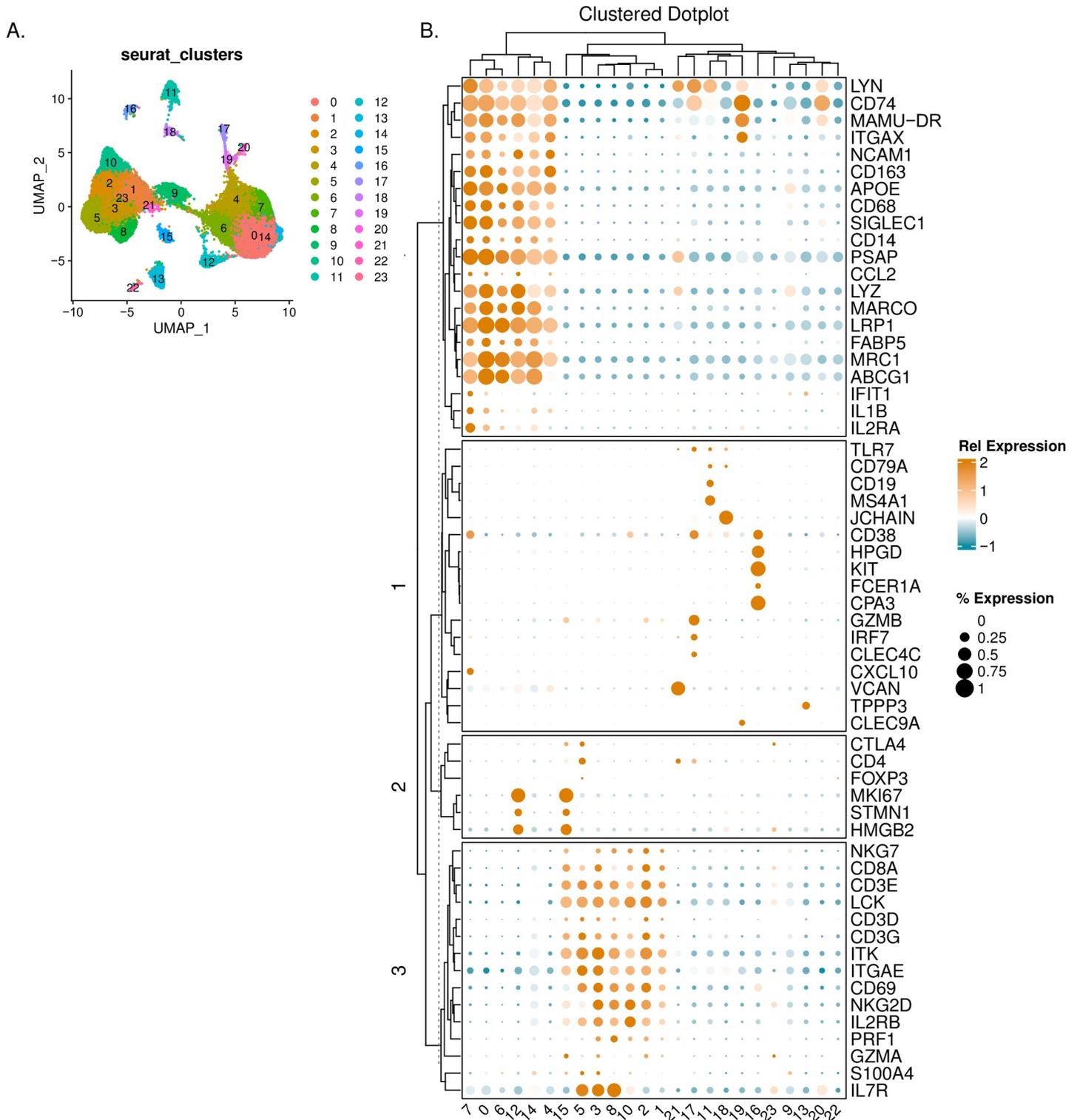
Supplementary Figure 5. Defining Seurat clusters. A. UMAP displaying Seurat-derived clusters obtained from FindAllMarkers function in Seurat. **B.** Dot plot depicting markers used to identify cell types. Hierarchical clustering method (hclust) was used to cluster columns and rows. The color of the dots indicates the relative gene (Rel. Expression). Dot size represents the percentage of cells expressing the gene (% Expression).
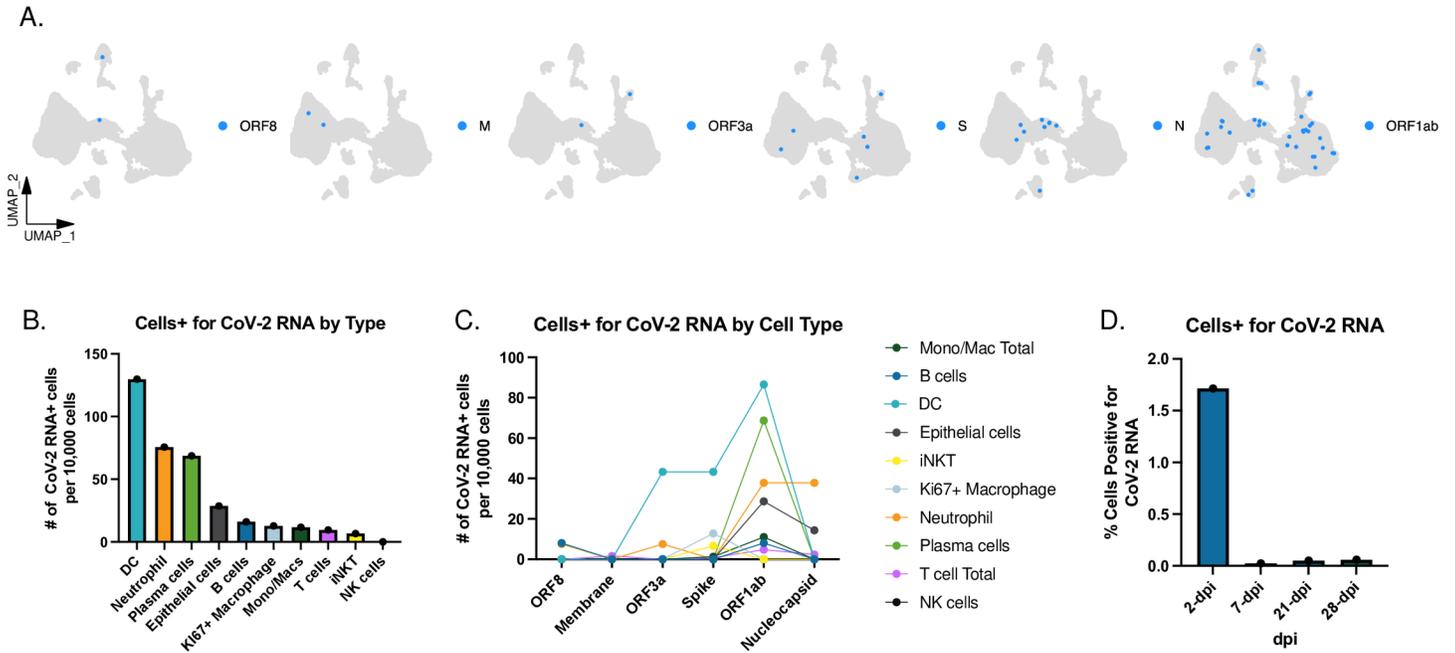
Supplemental Figure 6. Single-cell analysis of SARS-CoV-2 positive cells in BAL of SIV+ PTM. A. UMAP plots highlighting cells with detectable SARS-CoV-2 transcripts. **B.** Distribution of cells by cell type positive for any SARS-CoV-2 transcript. **C.** Number of cells positive for specific SARS-CoV-2 transcripts grouped by cell type. **D.** Percentage of cells positive for SARS-CoV-2 transcripts by days post-infection (dpi).
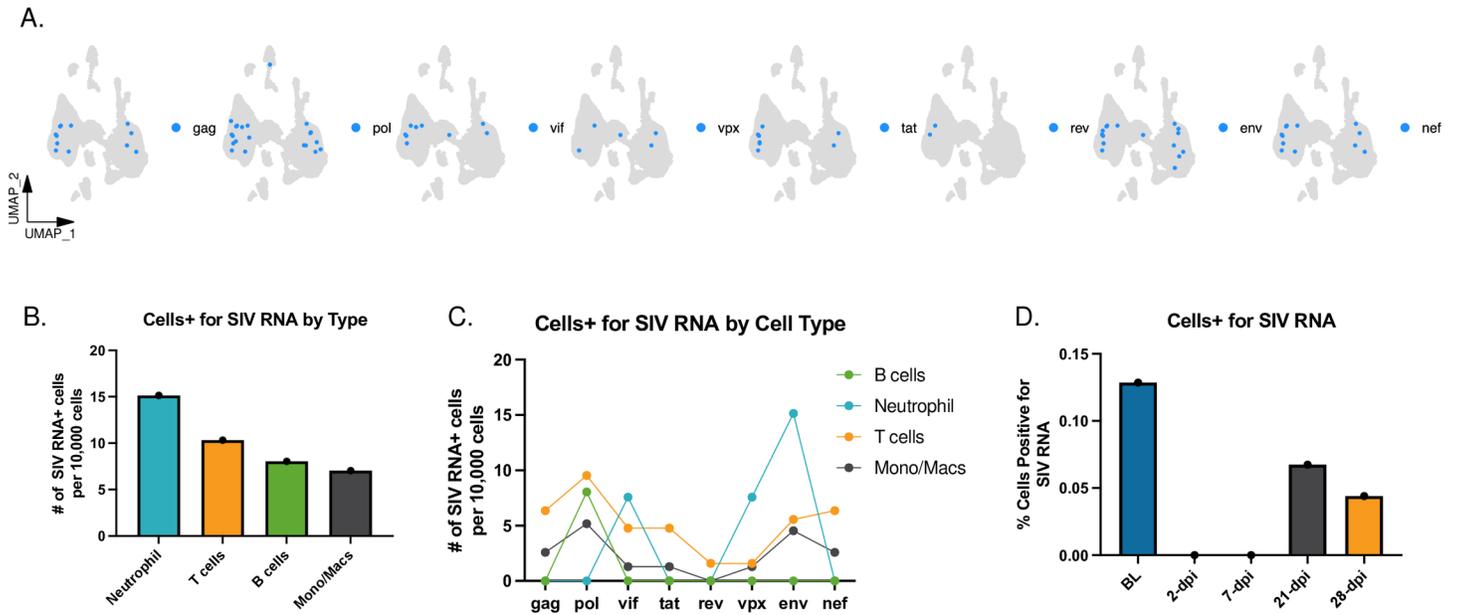
Supplemental Figure 7. Single-cell analysis of SIV positive cells in BAL of coinfected PTM. A. UMAP plots highlighting cells with detectable SIV transcripts. **B.** Distribution of cells grouped by type exhibiting any SIV transcripts. **C.** Number of cells positive for specific SIV transcripts grouped by cell type. **D**. Percentage of cells positive for SIV transcripts by days exposure.
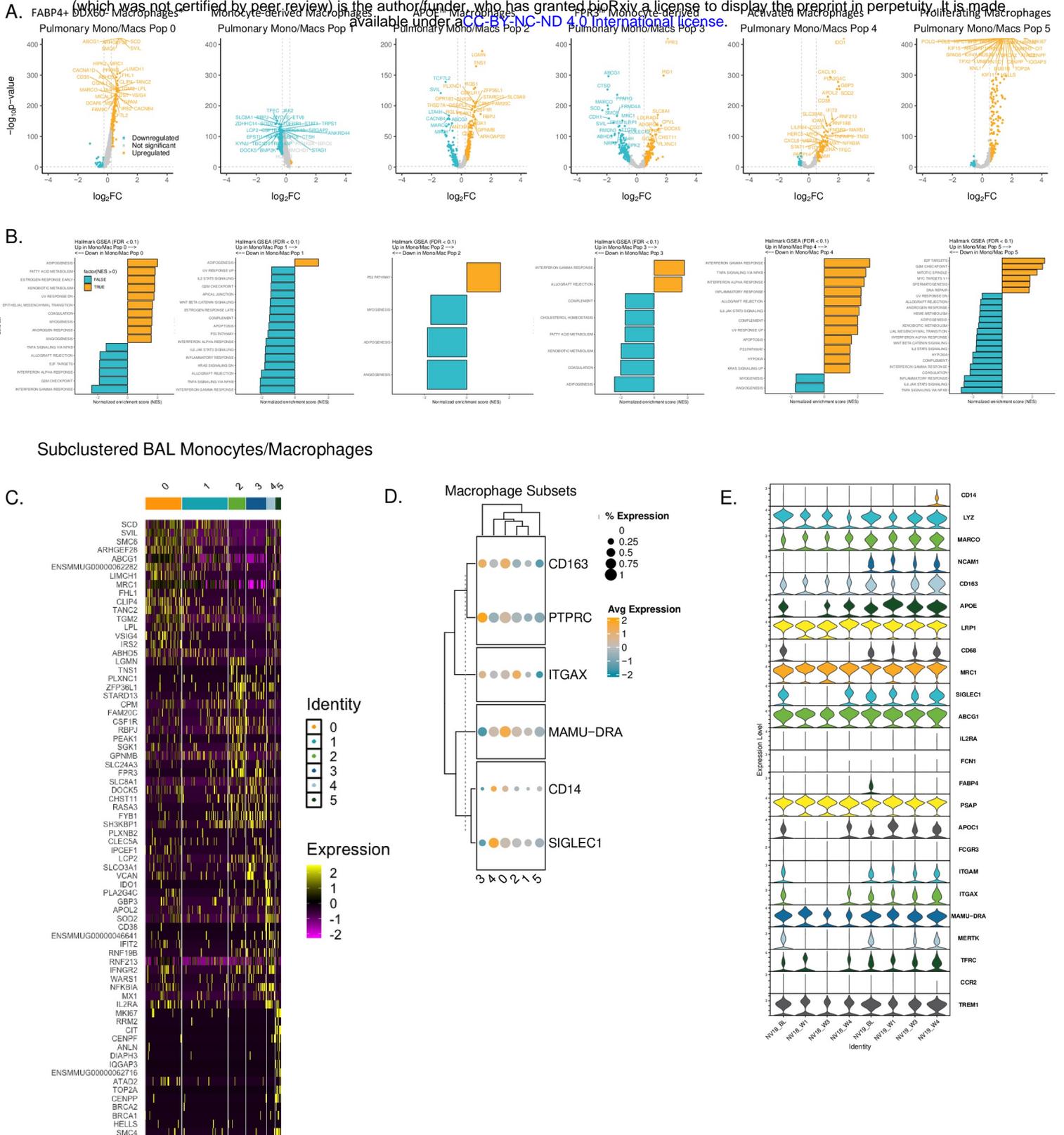
Supplementary Figure 8. Single-cell monocyte/macrophage characterization. A. Volcano plots displaying significantly upregulated and downregulated differentially expressed genes (DEGs) in the Monocyte/macrophage populations. **B.** Bar plots depicting normalized net enrichment score (NES) from gene set enrichment analysis (GSEA) of Hallmark biological pathways. A false discovery rate (FDR) cutoff of 0.1 was used to determine significance. **C.** Heatmap of top 10 differentially expressed genes for each monocyte/macrophage cluster. **D.** Dot plot illustrating gene expression differences among the Seurat-derived clusters, corresponding to markers used in flow cytometry analysis (Figure 4 panel K). Hierarchical clustering (hclust) was used for column and row clustering. Dot color represents relative gene expression (Rel Expression), while dot size indicates the percentage of cells expressing the gene (% Expression). **E.** Stacked violin plot illustrating gene expression patterns of monocytes/macrophages at baseline (BL) and weeks 1, 3, and 4 post-SARS-CoV-2 infection.
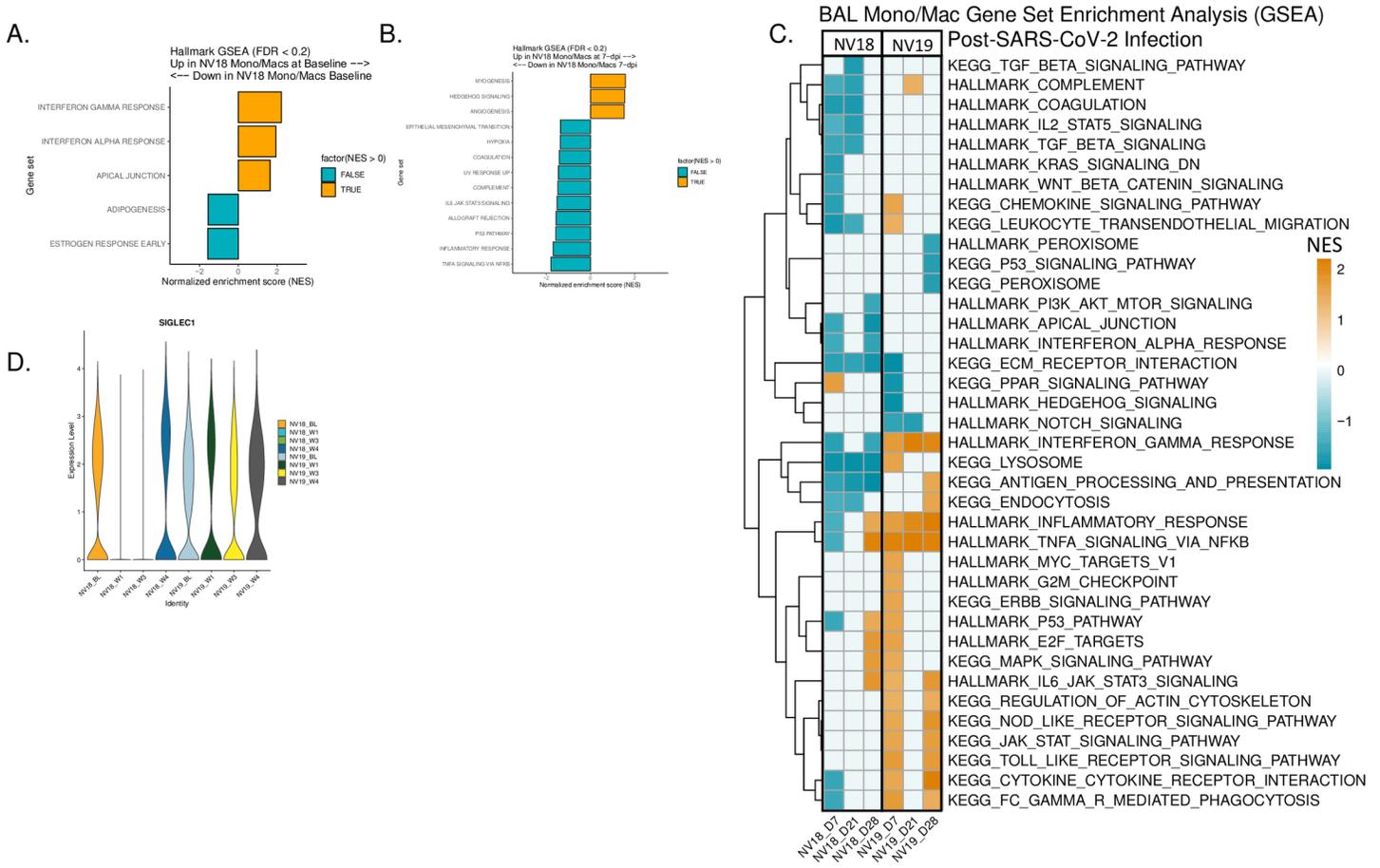
Supplemental Figure 9. Differential gene expression (DEG) and enrichment analysis of Monocyte/Macrophage Subsets in NV18 and NV19. A&B. Gene set enrichment analysis (GSEA) of DEGs comparing NV18 and NV19 at baseline (**A**) and 7-dpi (**B**). **C.** GSEA results comparing DEGs at days 7, 21, and 28 post-exposure to baseline. A false discovery rate (FDR) cutoff of 0.2 was used to determine significance. **D.** CD169 (*SIGLEC1*) expression kinetics.