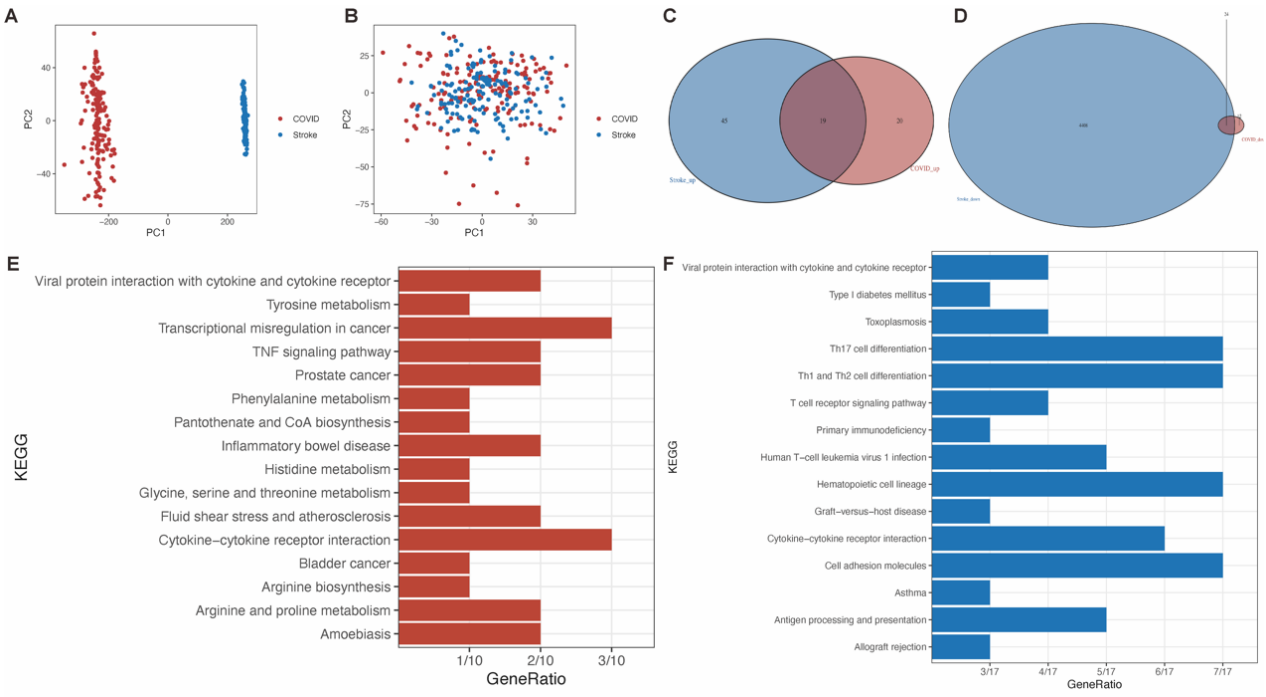
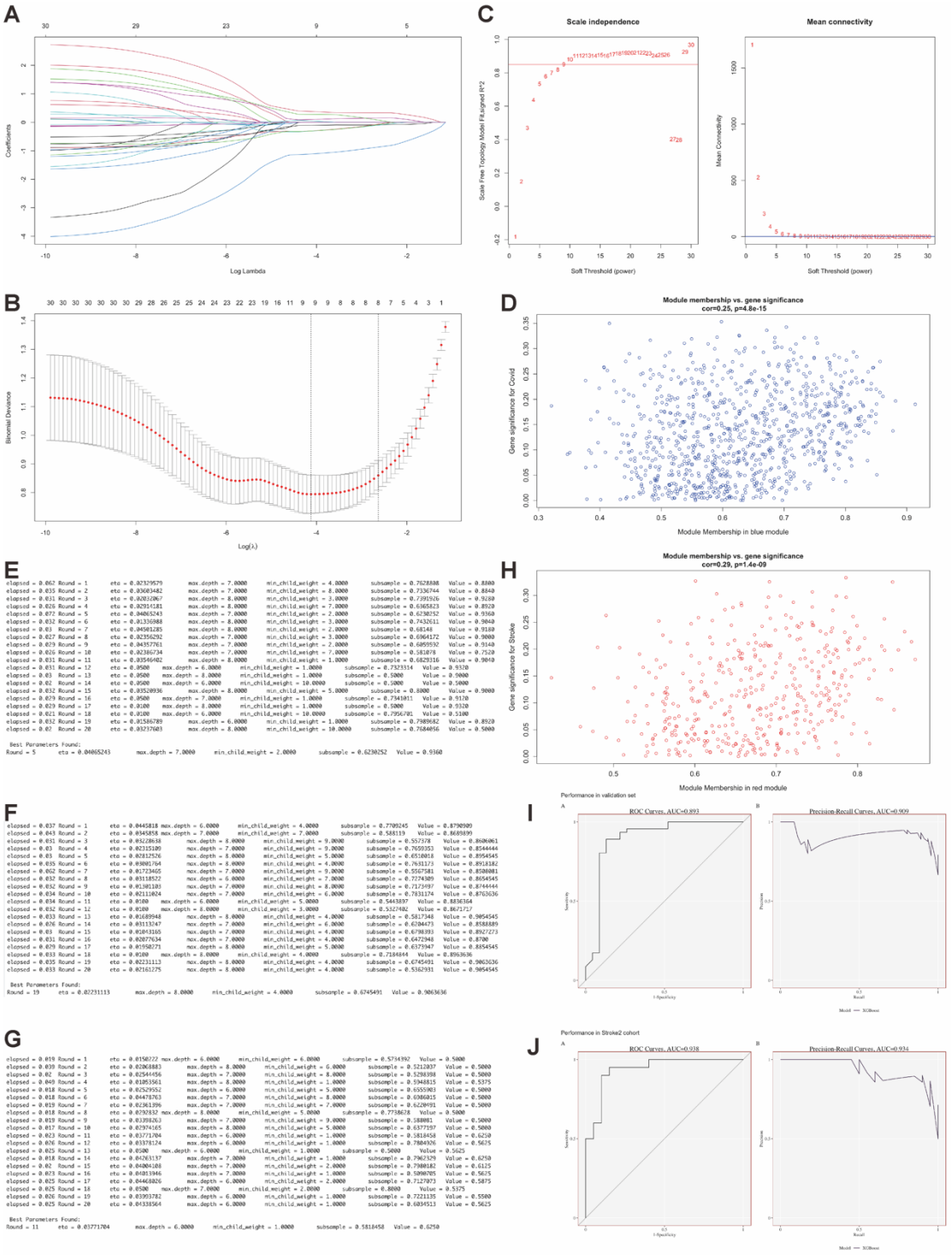
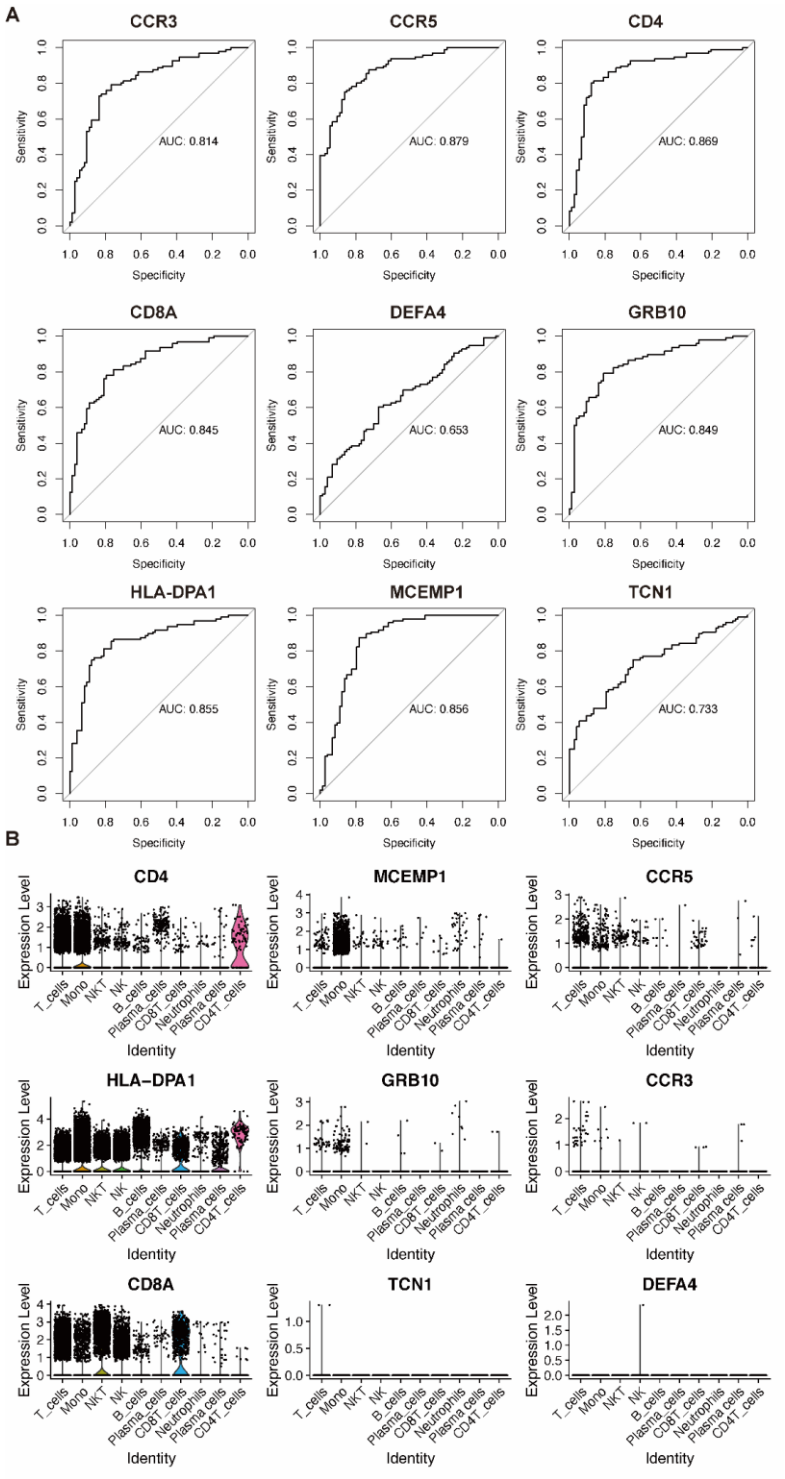


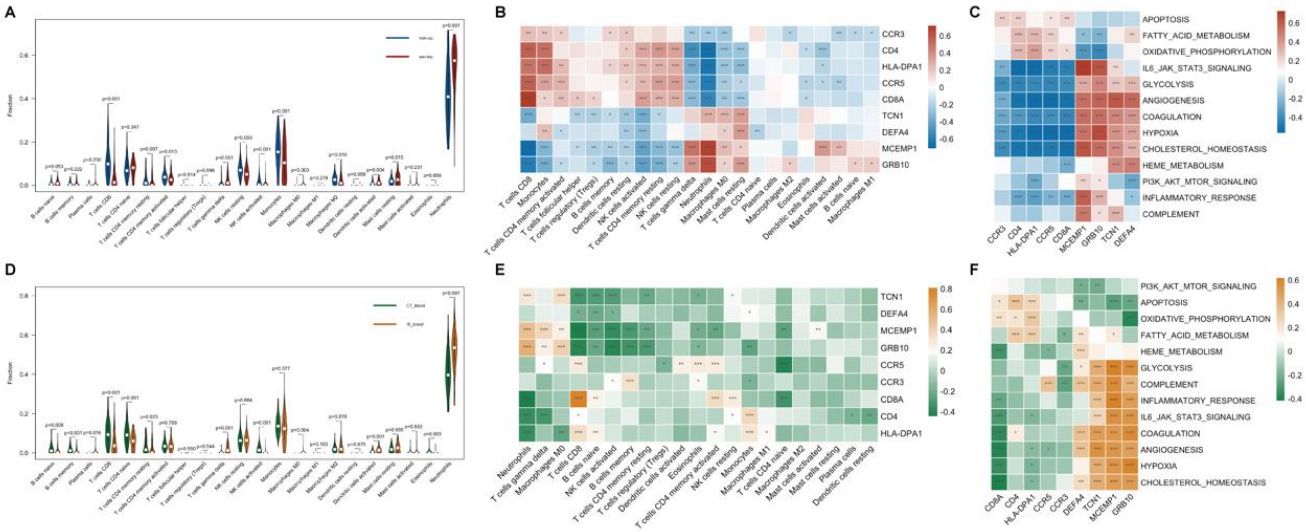
Supplementary Figure S1. A, B – PCA map shows the distribution of two datasets before and after batch effect elimination. **C** – The Venn figure of 19 up-regulated DEGs in both stroke and COVID. **D** – The Venn figure of 24 down-regulated DEGs in both stroke and COVID. **E, F** – KEGG pathway enrichment of 19 up-regulated DEGs and 24 down-regulated DEGs in both stroke and COVID



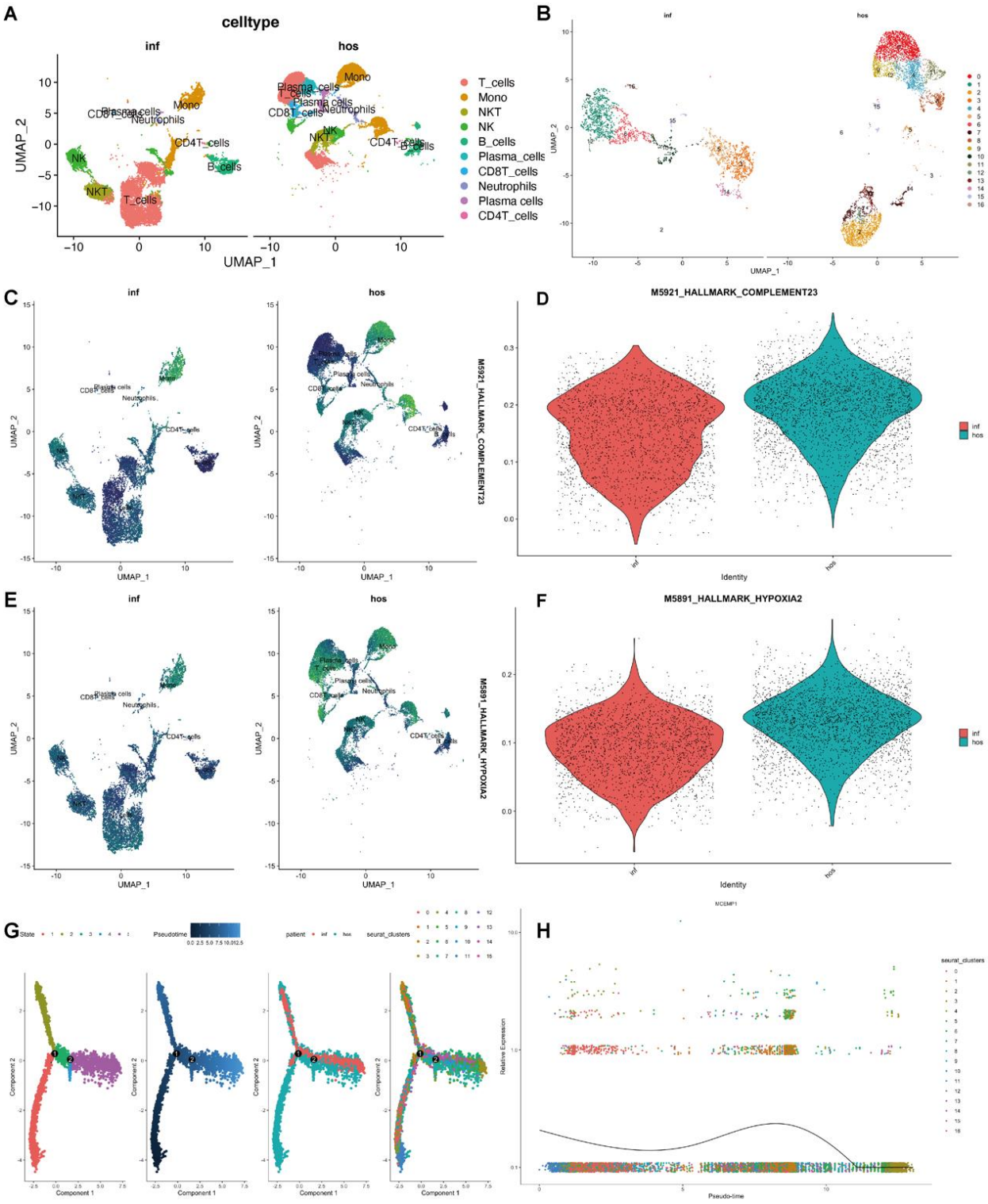
Supplementary Figure S2. A, B – Lasso regression to select 9 hub genes for the regression model. **C** – Scale independence and mean connectivity in WGCNA analysis. **D** – The correlation between Gene significance and module membership in COVID dataset. **E–G** – The 20 rounds of XGboost super-parameter optimization for COVID training set, and two stroke validation sets. **H** – The correlation between Gene significance and module membership in stroke dataset. **I** – The ROC and PRC validation of the diagnostic model in sCOVID testing dataset. **J** – The ROC and PRC validation of the diagnostic model in external stroke dataset



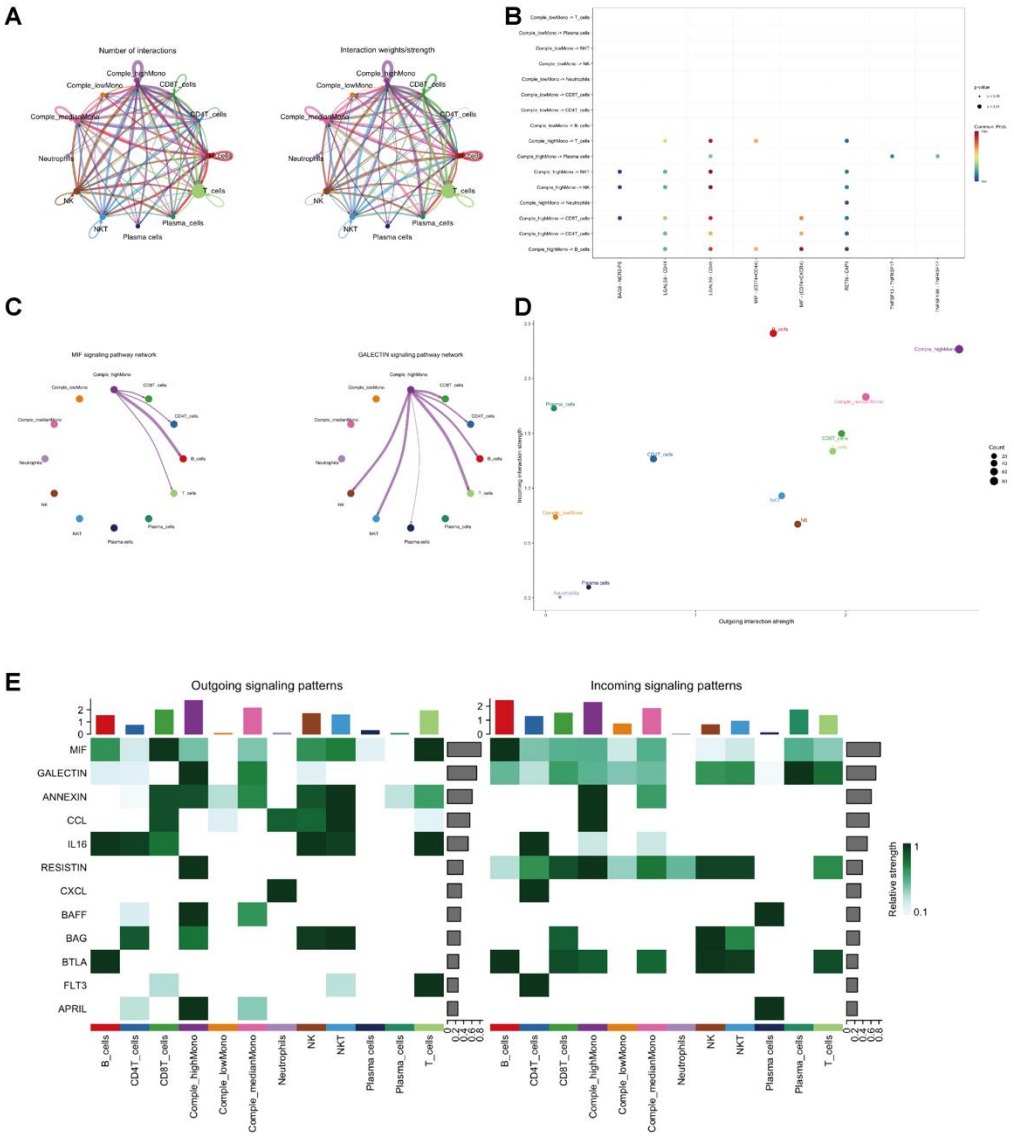
Supplementary Figure S3. A – The ROC of each hub gene in the COVID model. **B** – The violin plot of each hub gene in the sc-RNA seq COVID dataset



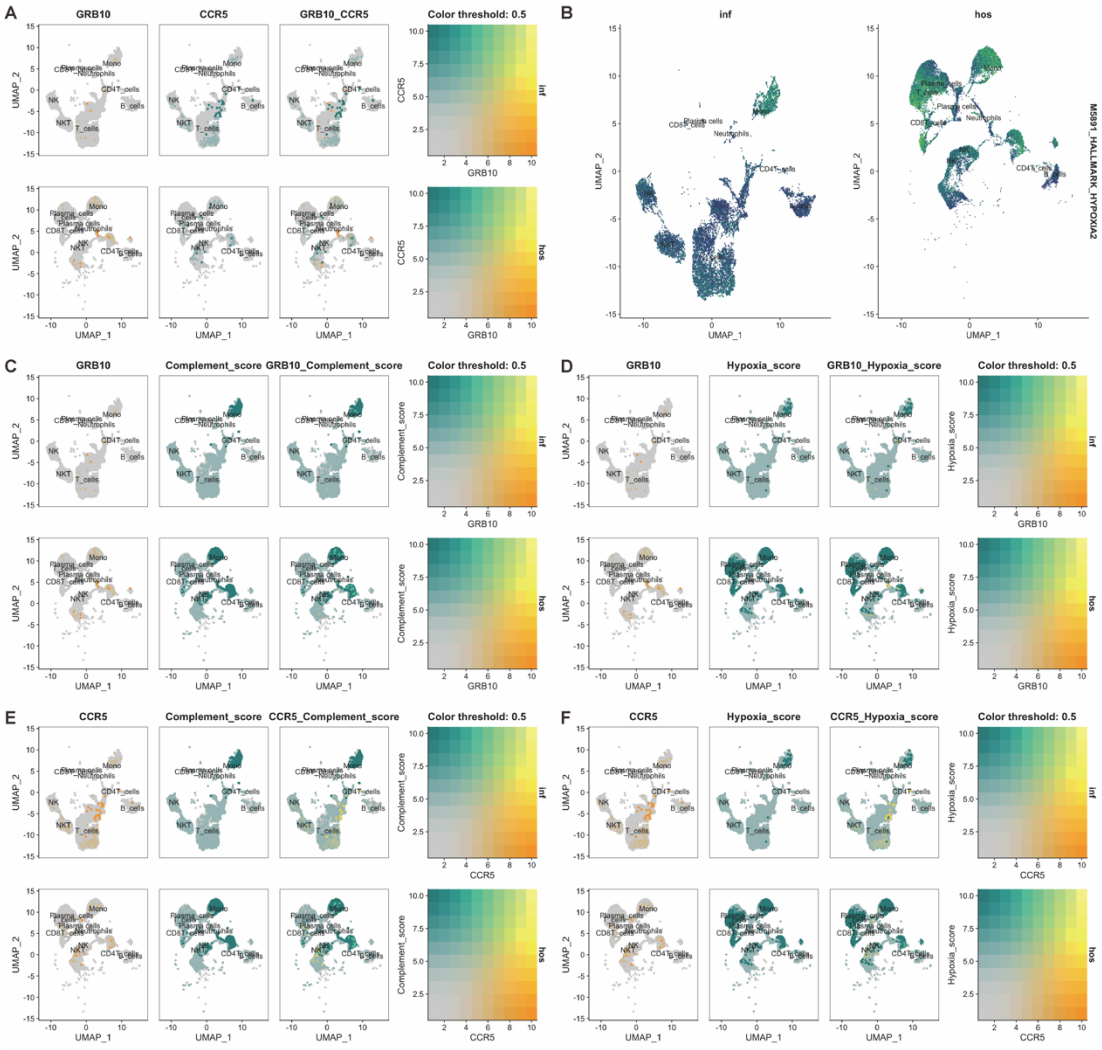
Supplementary Figure S4. The comparison of immune infiltration and metabolic pathways in sCOVID and stroke. **A, D** – Box plot shows the immune infiltration between the two groups. **B, E** – The heatmap shows the correlation between hub genes and infiltrated immune, inflammatory cells between the two groups. **C, F** – The heatmap shows the correlation between hub genes and metabolic pathways between the two groups



Supplementary Figure S5. The pathway score comparison between severe COVID and normal COVID patients. **A**, **B** – The UMAP shows the cell annotations between the two groups; **C** – The UMAP shows the complement score between the two groups. **D** – Violin plot shows the quantitative comparison of complement score in different cell clusters between severe COVID (hos) and normal COVID (inf). **E** – The UMAP shows the hypoxia score between the two groups. **F** – Violin plot shows the quantitative comparison of hypoxia score in between severe COVID (hos) and normal COVID (inf). **G** – Pseudo-time analysis of different cluster between the two grops. **H** – The pseudo-time analysis of MCEMP1 in different sub-clusters shows the stage transition from normal COVID to severe COVID.



Supplementary Figure S6. Cell-cell interaction at single-cell level in COVID. **A** – The number of interactions and interaction weights between several cell types. **B** – The bubble plot shows the relationship between cell types and ligand-receptor. **C** – MIF and GALECTIN signaling pathway network between several cell types. **D** – The correlation map of different cell clusters. The size of the circle indicates the counts of related genes involved. The x-axis is outgoing interaction strength and the y-axis is incoming interaction strength. **E** – The outgoing and incoming signaling patterns in different cell clusters with related signaling pathways. The relative strength is shown from shallow to deep color



Supplementary Figure S7. A – The co-expression of GRB10 and CCR5 on the uMAP. **B** – The hypoxia score distribution in different cell clusters between two COVID groups. **C** – The co-expression of GRB10 and complement score on the uMAP. **D** – The co-expression of GRB10 and hypoxia score on the uMAP. **E** – The co-expression of CCR5 and complement score on the uMAP. **F** – The co-expression of CCR5 and hypoxia score on the uMAP