

SUPPLEMENTARY FIGURES

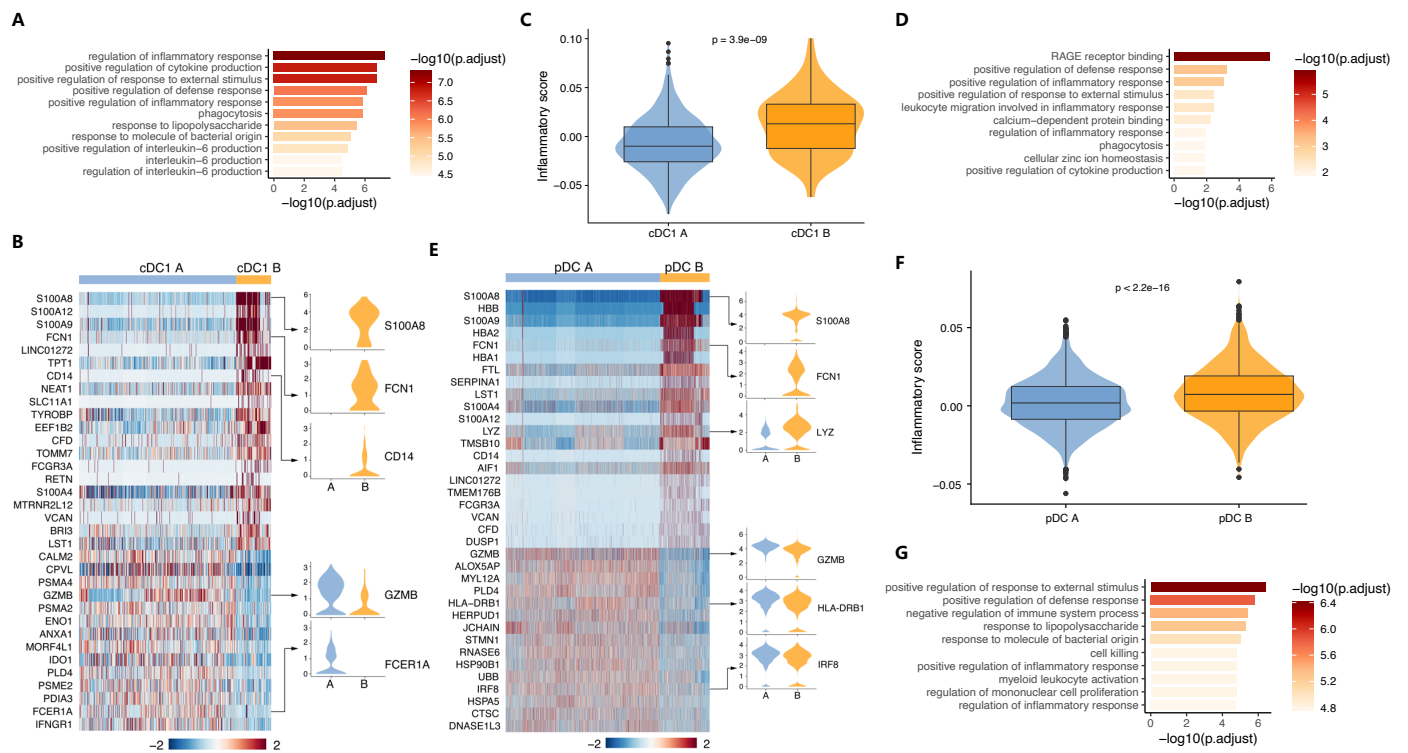


Figure S1. Transcriptome characteristics of three anergic DC subtypes. **(A)** Upregulated GO terms of cDC2 B versus cDC2 A and cDC2 C. **(B)** Top marker genes of the two cDC1 subtypes. Heatmap of the expression level of all marker genes across each cell (left). Violin plots showed the expression of selected marker genes across each cDC1 subtype (right). **(C)** Inflammatory score between two cDC1 subtypes. Significance was determined using Wilcoxon signed-rank test. **(D)** Upregulated GO terms of cDC1 B versus cDC1 A. **(E)** Top marker genes of the two pDC subtypes. Heatmap for the expression level of all marker genes across each cell (left). Violin plots for the expression of selected marker genes across each pDC subtype (right). **(F)** Inflammatory score between two pDC subtypes. Significance was determined using Wilcoxon signed-rank test. **(G)** Upregulated GO terms of pDC B versus pDC A.

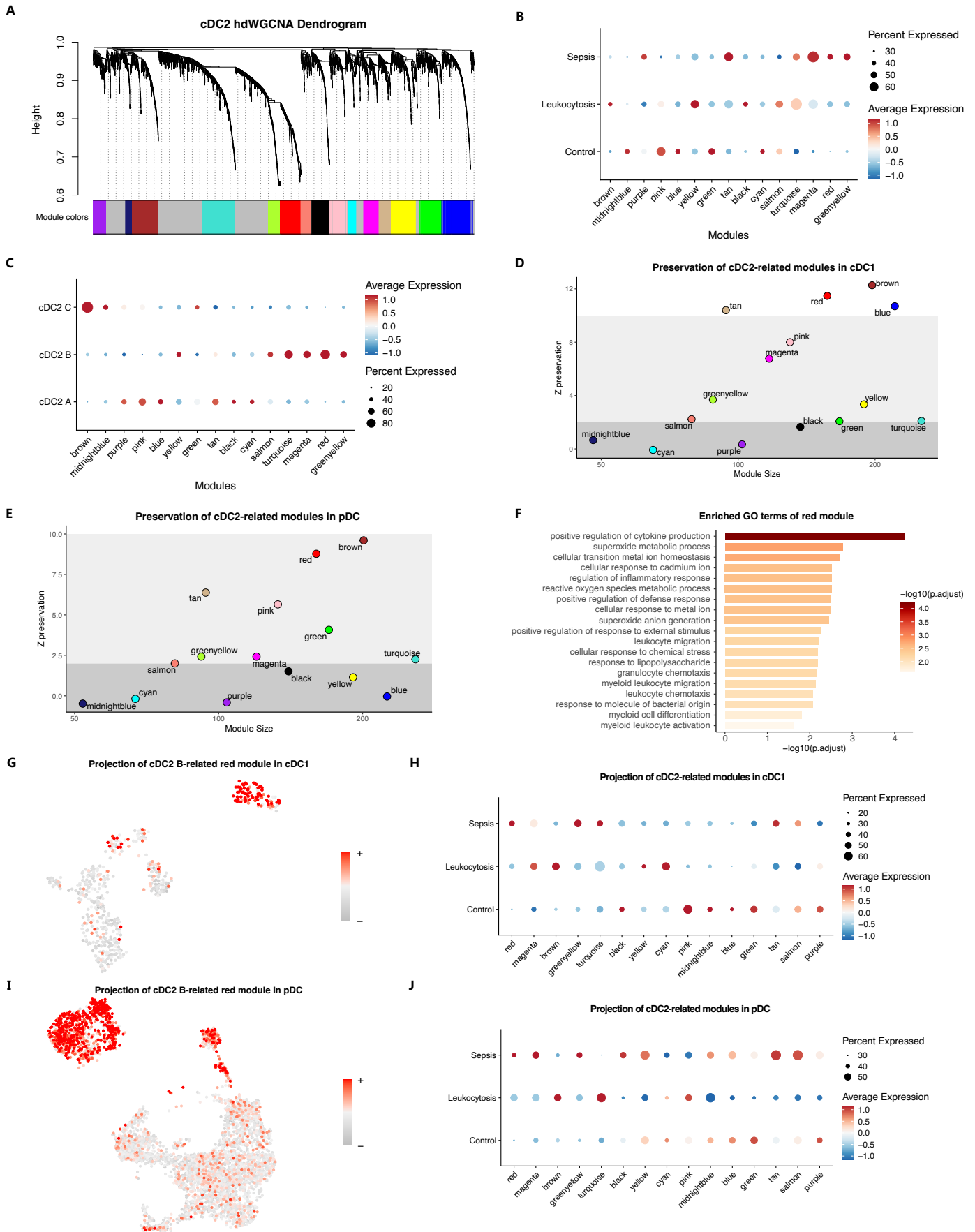


Figure S2. hdWGCNA on DC subtypes revealed anergic DC specific gene module. **(A)** The cluster dendrogram of co-expression genes of cDC2. **(B)** The expression level of each cDC2 gene module across different groups. **(C)** The expression level of each cDC2 gene module across three different subtypes. **(D)**

Module preservation analysis of the cDC2 modules in cDC1. The module's size versus the preservation statistic (Z preservation) is shown for each module. $Z < 5$: not preserved; $10 > Z \geq 5$: moderately preserved; $Z \geq 10$: highly preserved **(E)** Module preservation analysis of the cDC2 modules in pDC. **(F)** Enriched GO terms of genes in red module. **(G)** Projection of cDC2 B-related red module in cDC1 subtypes. **(H)** The expression level of projected cDC2 gene modules in cDC1 across different groups. **(I)** Projection of cDC2 B-related red module in pDC subtypes. **(J)** The expression level of projected cDC2 gene modules in pDC across different groups.

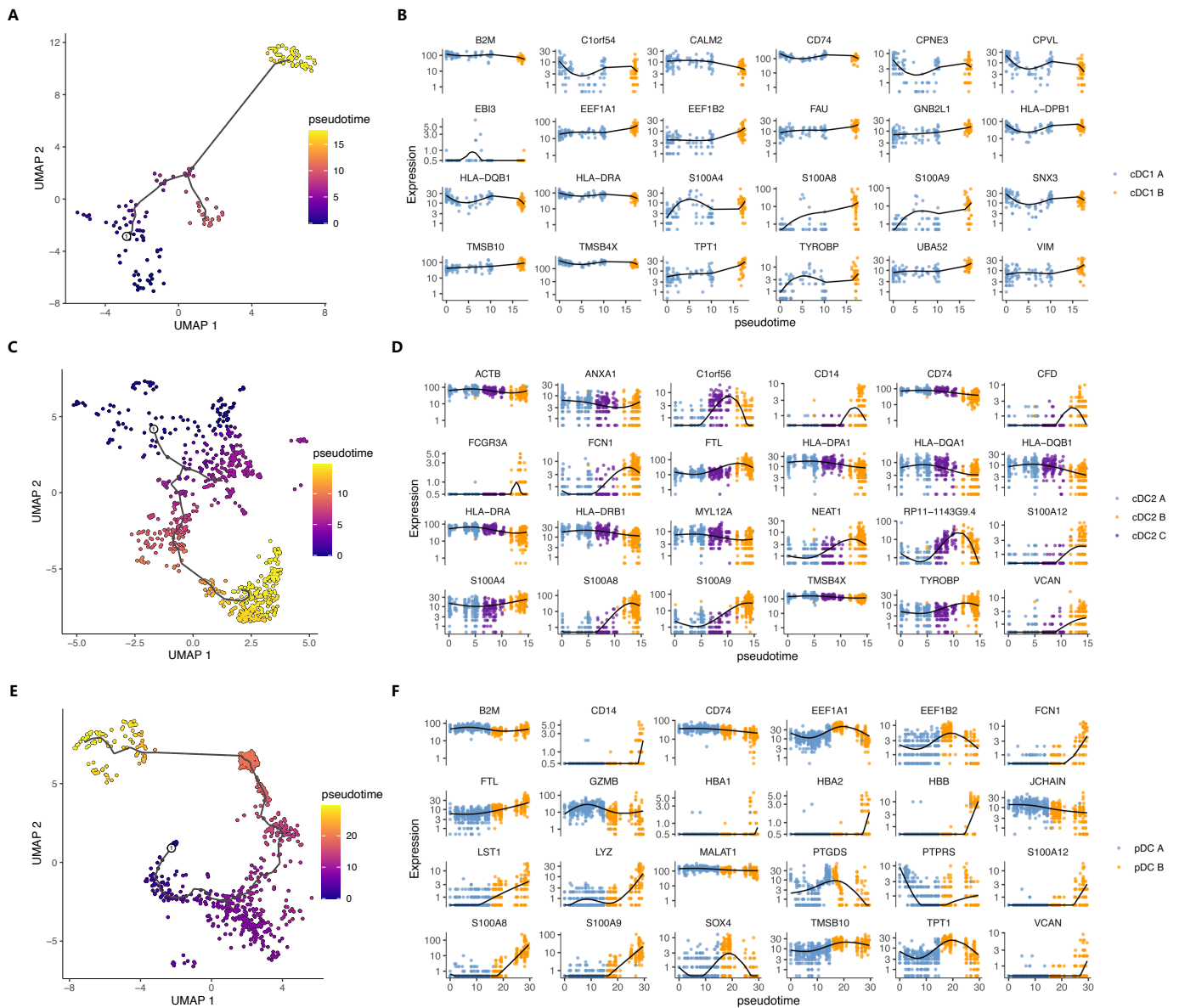


Figure S3. Trajectory and pseudotime analysis of cDC1, cDC2 and pDC in sepsis. **(A)** UMAP embedding of cDC1 colored by inferred pseudotime. **(B)** Scatter plots for the expression patterns of the top differentially expressed genes along the pseudotime of cDC1 subtypes. **(C)** UMAP embedding of cDC2 colored by inferred pseudotime. **(D)** Scatter plots for the expression patterns of the top differentially expressed genes along the pseudotime of cDC2 subtypes. **(E)** UMAP embedding of pDC colored by inferred pseudotime. **(F)** Scatter plots for the expression patterns of the top differentially expressed genes along the pseudotime of pDC subtypes.

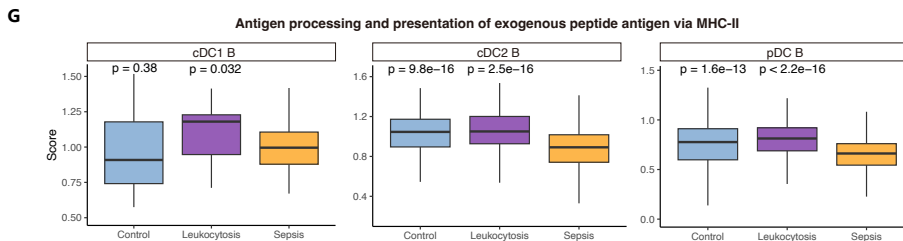
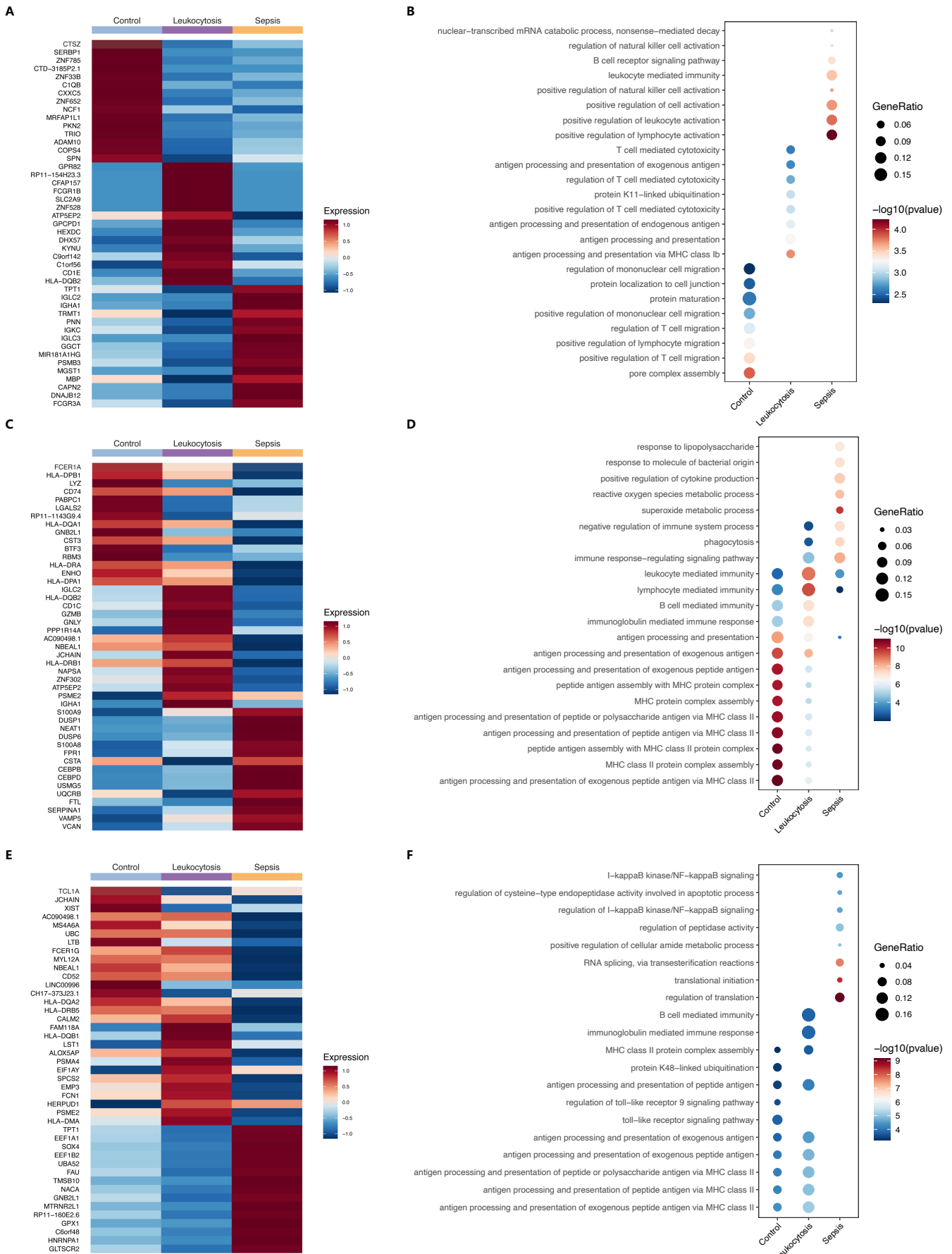


Figure S4. Phenotypic differences of anergic DCs in septic patients and controls. **(A)** Top upregulated marker genes of cDC1 B in three groups. **(B)** Dot plot showing top enriched pathways of cDC1 B in three groups. Pathways in Gene Ontology biological process database were used. **(C)** Top upregulated marker genes of cDC2 B in three groups. **(D)** Dot plot showing top enriched pathways of cDC2 B in three groups. **(E)** Top upregulated marker genes of pDC B in three groups. **(F)** Dot plot showing top enriched pathways of pDC B in three groups. **(G)** Boxplot showing the antigen-presenting capacity via MHC-II pathway in anergic DCs across septic patients and controls. Significance was determined using Wilcoxon signed-rank test.

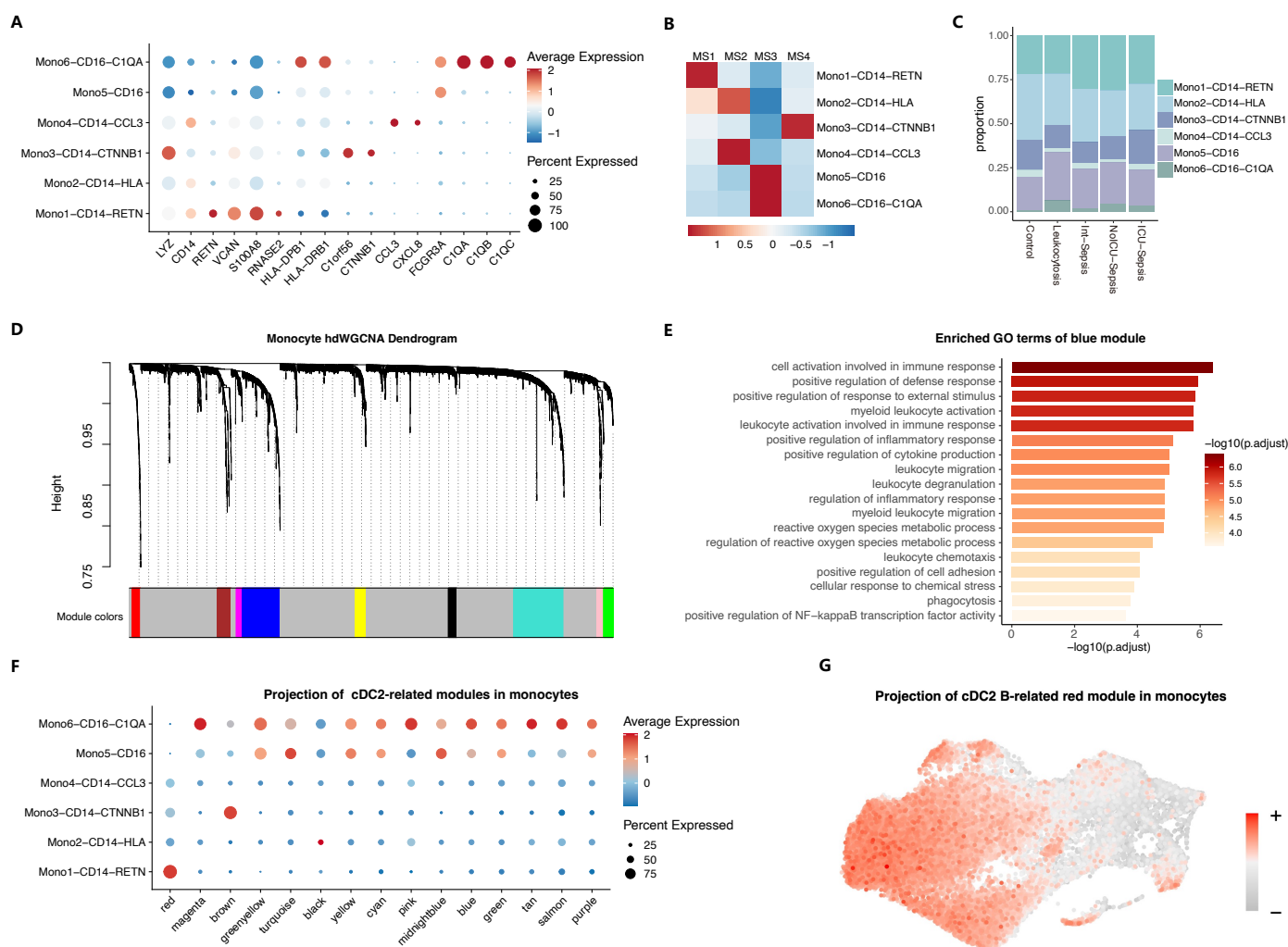


Figure S5. Characteristics of different monocyte subtypes. **(A)** Dot plot for marker genes of six monocyte subtypes. **(B)** Heatmap illustrating the normalized frequency of overlapping cell-type annotations between Reyes et al's findings and those from this study. The data were scaled by row. **(C)** Bar plot showed six monocyte subtypes' proportion in different groups. **(D)** The cluster dendrogram of co-expression genes of monocyte. **(E)** Enriched GO terms of genes in Mono1-related blue module. **(F)** The expression level of projected cDC2 gene modules in Mono1 across different groups. **(G)** Projection of cDC2-B specific red module in monocyte subtypes.

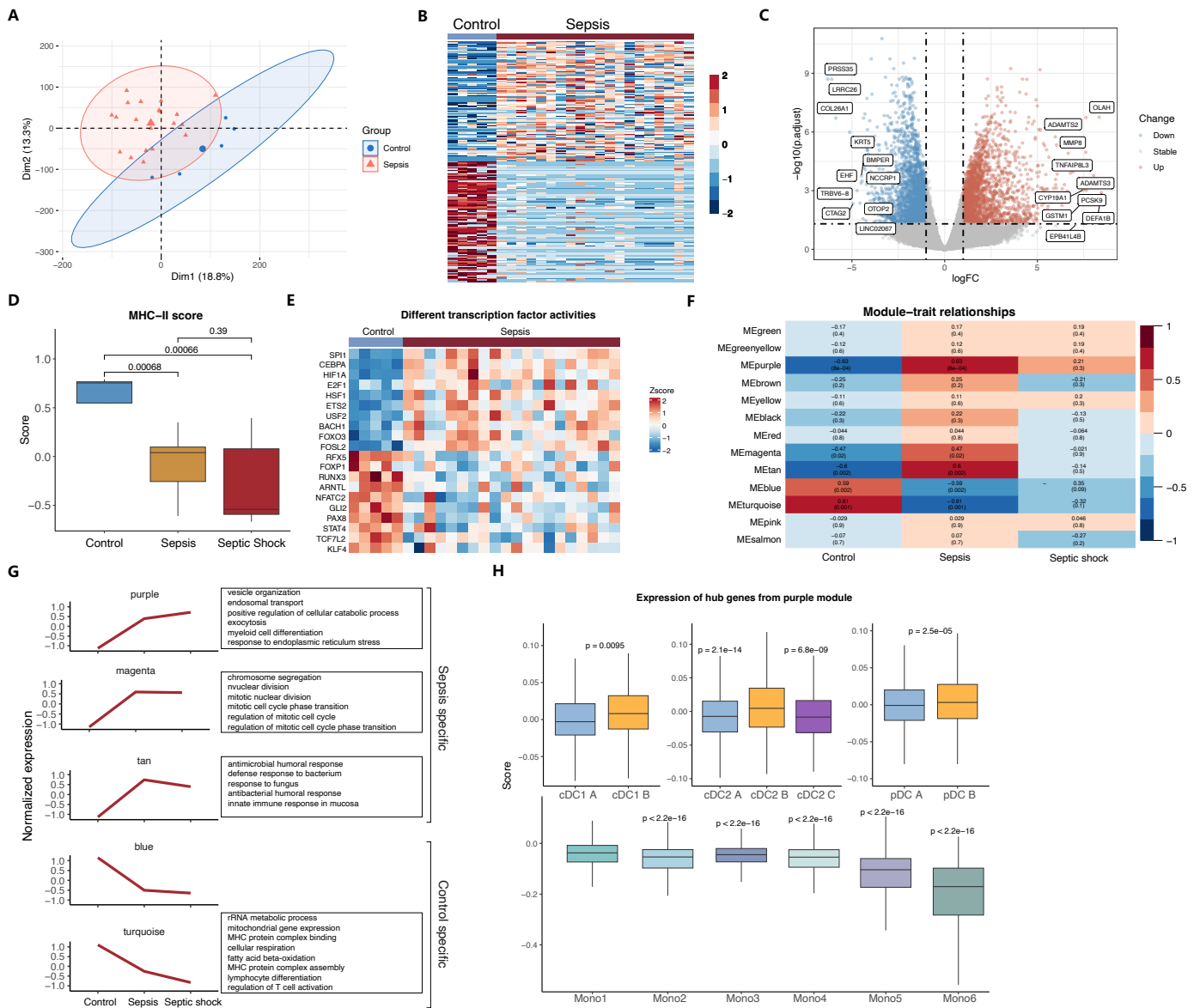


Figure S6. Different characteristics between septic patients and healthy controls. **(A)** Principal component analysis of healthy controls and septic patients. **(B)** Heatmap of top DEGs in sepsis versus control. **(C)** Volcano plot of differentially expressed genes between septic patients and healthy controls. **(D)** Gene-set score of MHC-II related genes between control, sepsis and septic shock groups. Significance was determined using Student's t test. **(E)** Heatmap showed top different expressed TFs. **(F)** Heatmap representation of module-trait relationships. Each cell contains the related correlation and P-value. **(G)** Line chart showing the different expression levels of 5 co-expression modules in control, sepsis and septic shock groups (left). Enriched GO terms of each module (right). **(H)** Expression of hub genes from purple module identified in bulk RNA-seq data across DC subtypes (top) and monocyte subtypes (bottom). Hub genes with

$|GS| > 0.7$ and $|MM| > 0.8$ were included in the analysis. Significance was determined using Wilcoxon signed-rank test.