

Supplemental Materials

**Cross-tissues single-cell atlas reveals Id2 promotes sepsis-induced tissue damage
by mediating macrophage metabolic reprogramming via Pkm2**

Supplementary figures: S1-S8

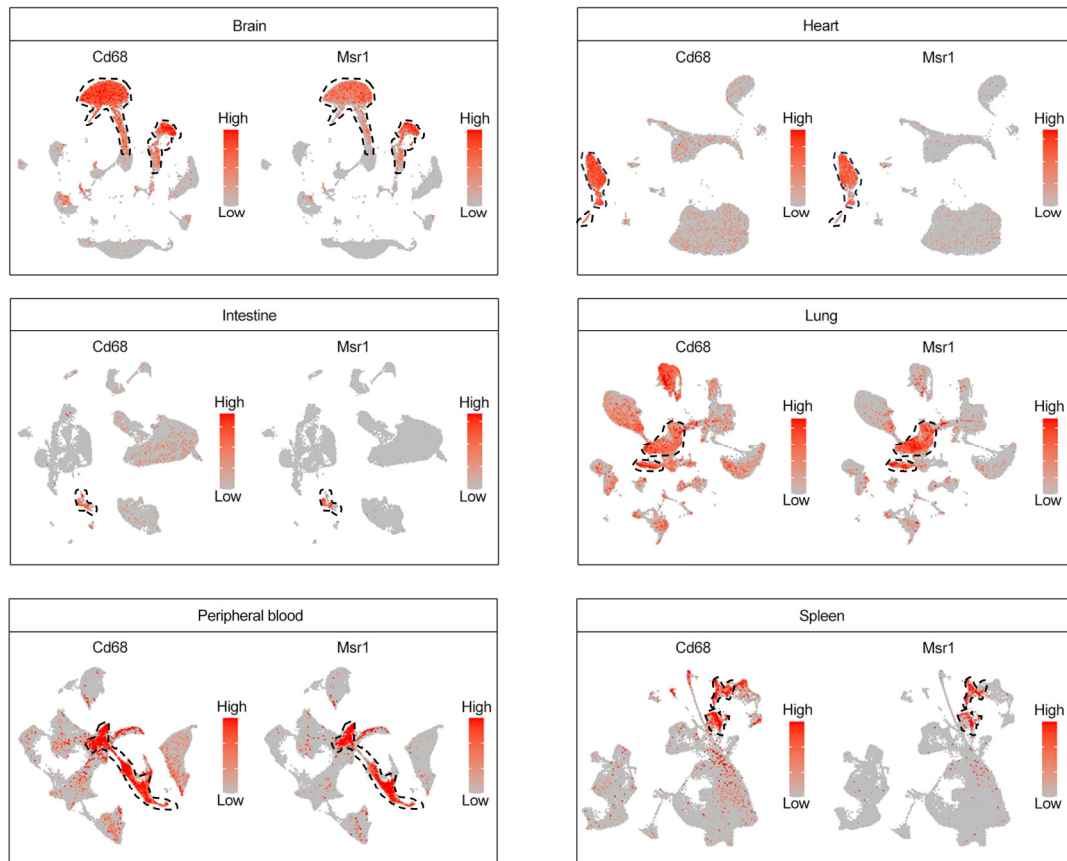


Figure S1. The expression of *Cd68* and *Msr1* in different tissues. Isolate macrophages from each tissue single-cell library based on the expression of *Cd68* and *Msr1*.

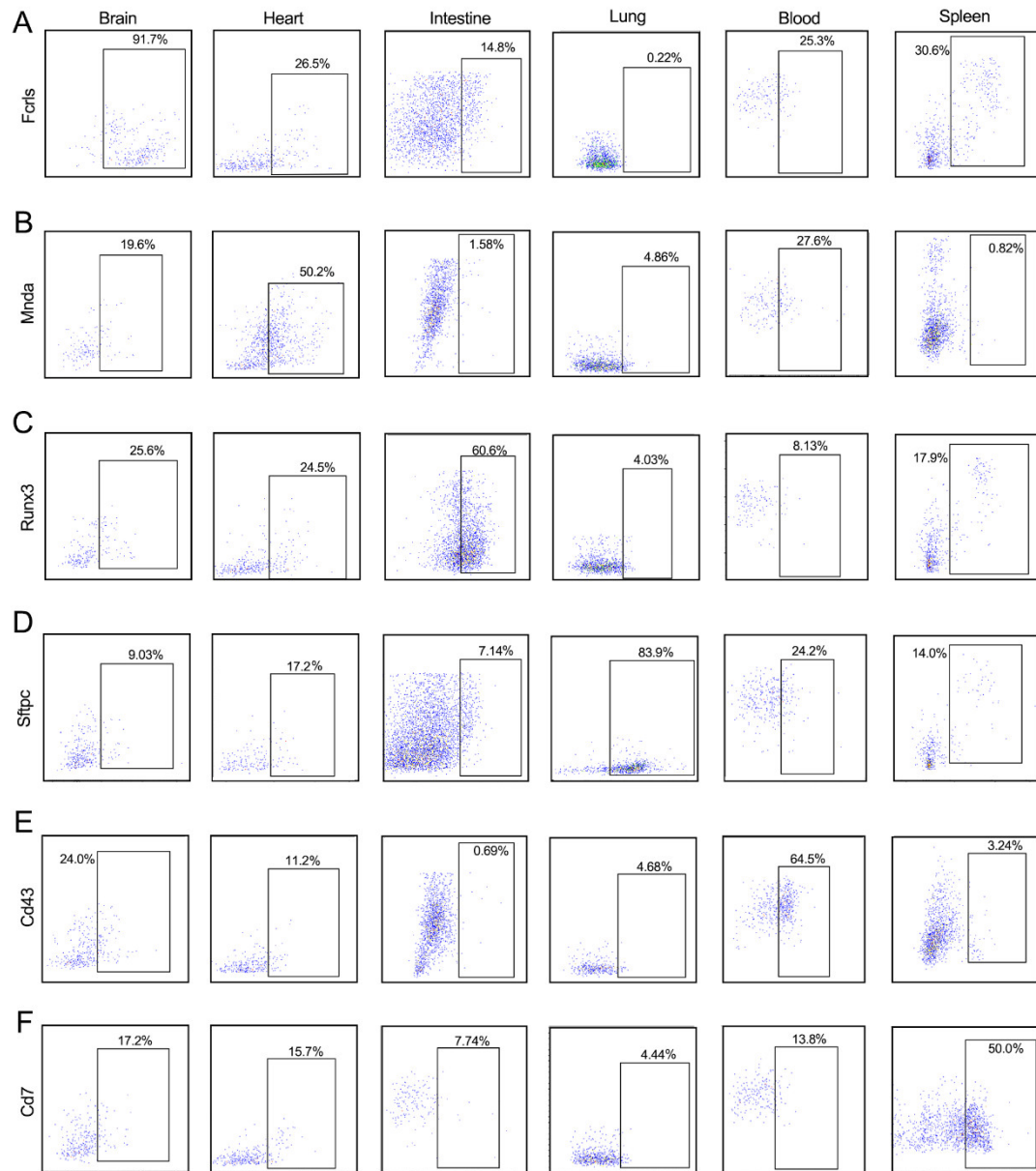


Figure S3. The marker genes of PBMCs and different tissue-resident macrophages. The proportion of Fcrls⁺ (A), Mnda⁺ (B), Runx3⁺ (C), Sftpc⁺ (D), Cd43⁺ (E) and Cd7⁺ (F) cells in pbmc or resident macrophages of brain, heart, intestine, lung and spleen

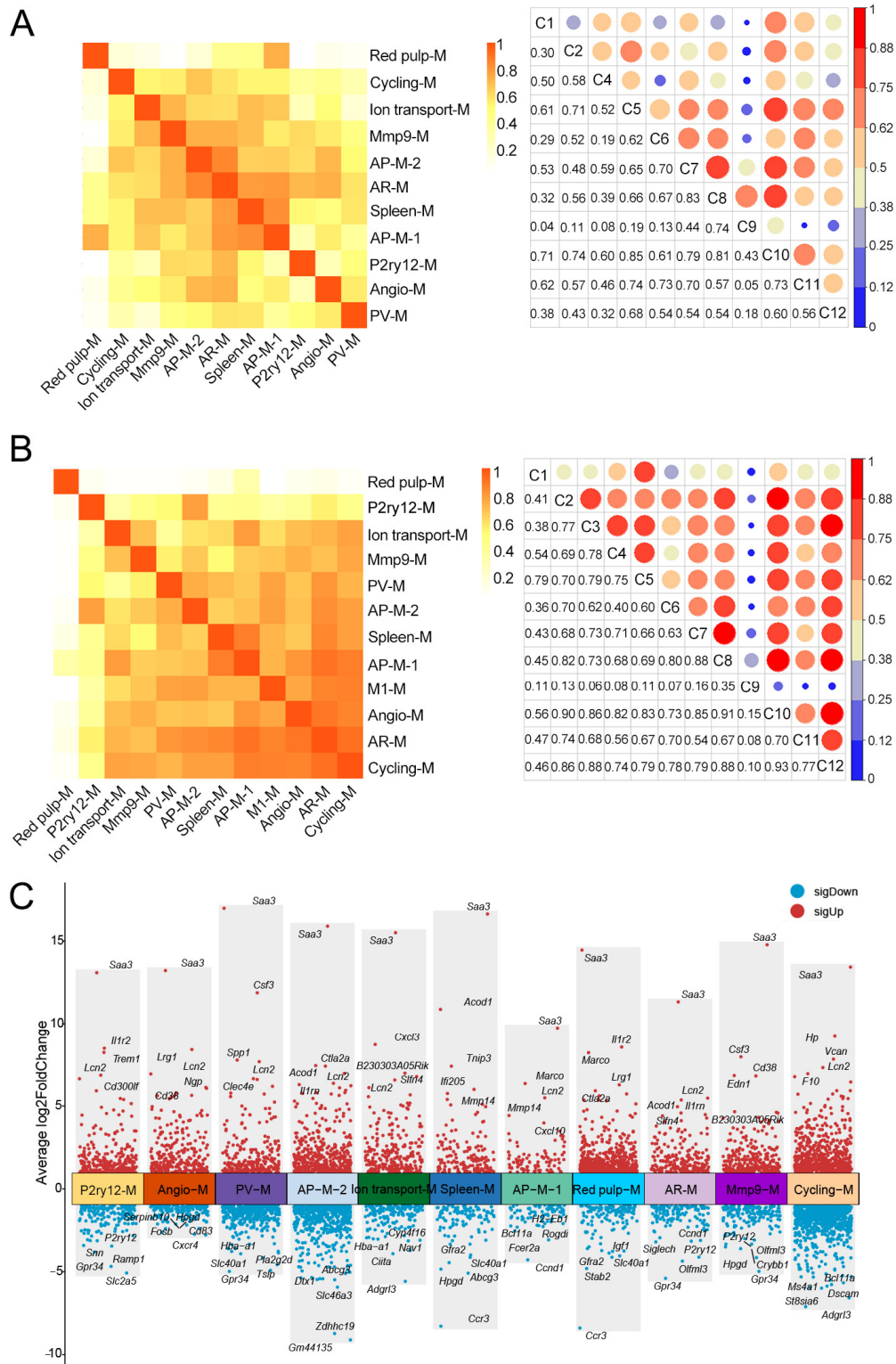


Figure S5. The changes of functional subtypes of resident macrophages after sepsis. (A) Pearson correlation between functional subtypes under steady state. (B) Pearson correlation between functional subtypes after sepsis. (C) The differentially expressed genes of functional subtypes after sepsis.

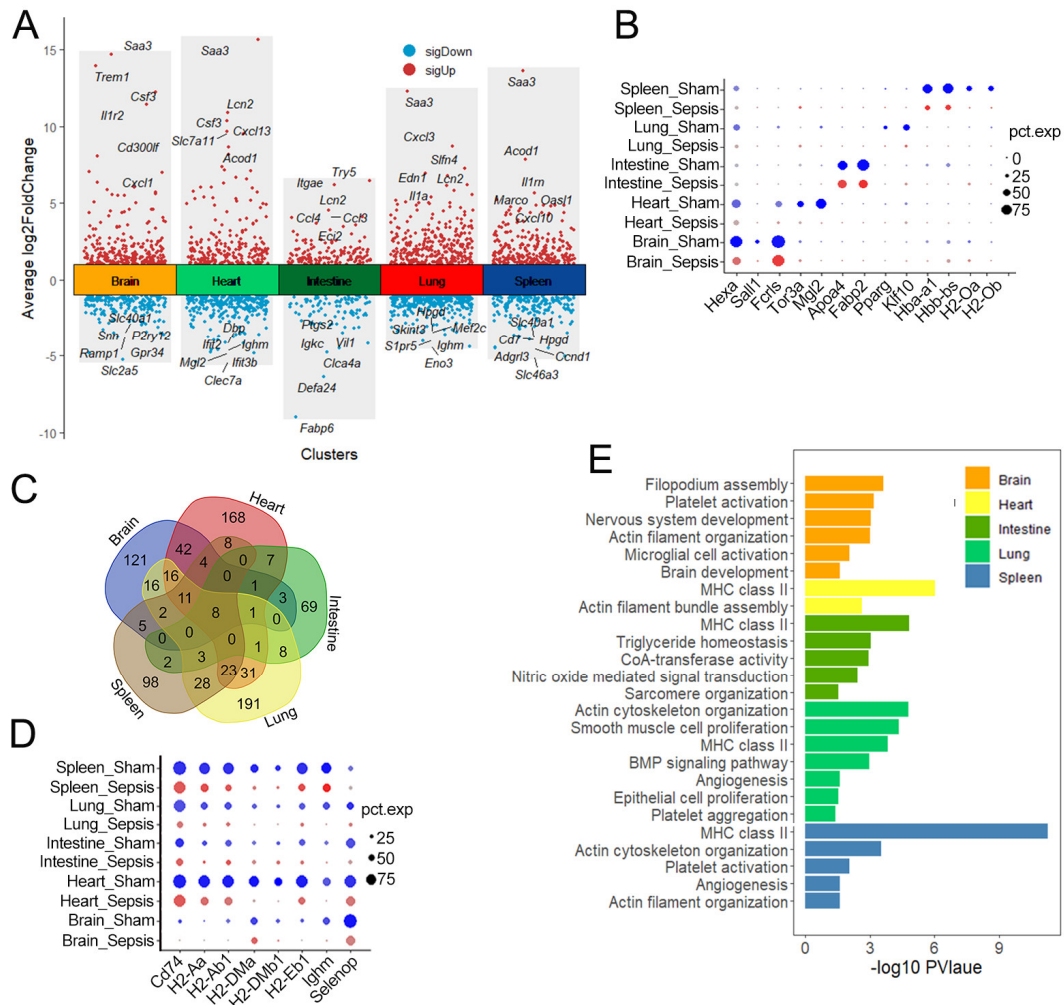


Figure S6. The differentially expressed genes of tissue-resident macrophages after sepsis. (A) The differentially expressed genes of resident macrophages in each tissue after sepsis. (B) Tissue-specifically downregulated genes. (C) Venn plot shows the down-regulated in different tissues. (D) 8 genes consistently down-regulated in different tissues after sepsis. (E) Functional enrichment analysis of the down-regulated genes in resident macrophages of each tissue.

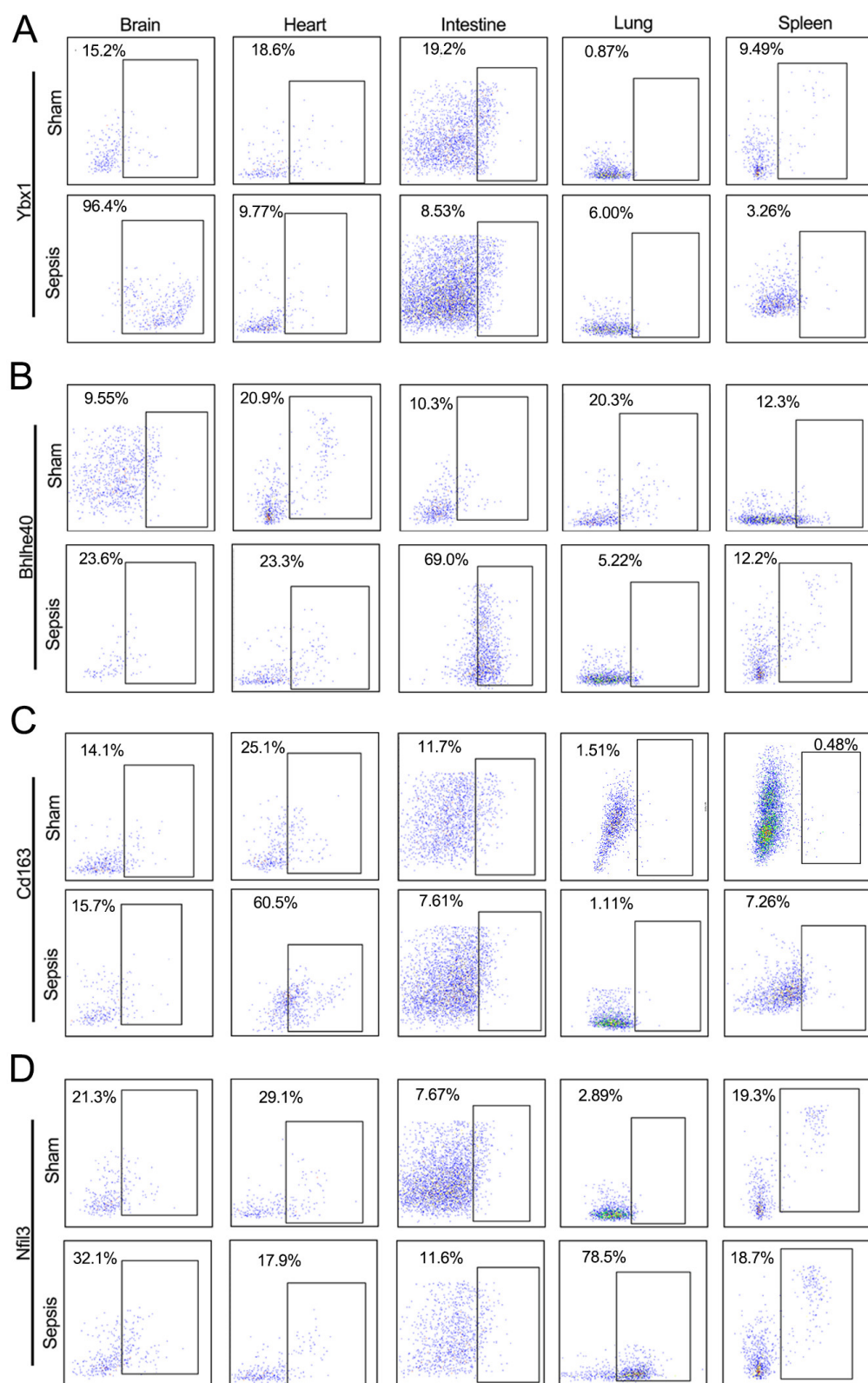


Figure S7. Flow cytometry revealed the proportions of Ybx1⁺ (A), Bhlhe40⁺ (B), Cd163⁺ (C) and Nfil3⁺ (D) cells in resident macrophages of different tissues from mice with sham and sepsis.

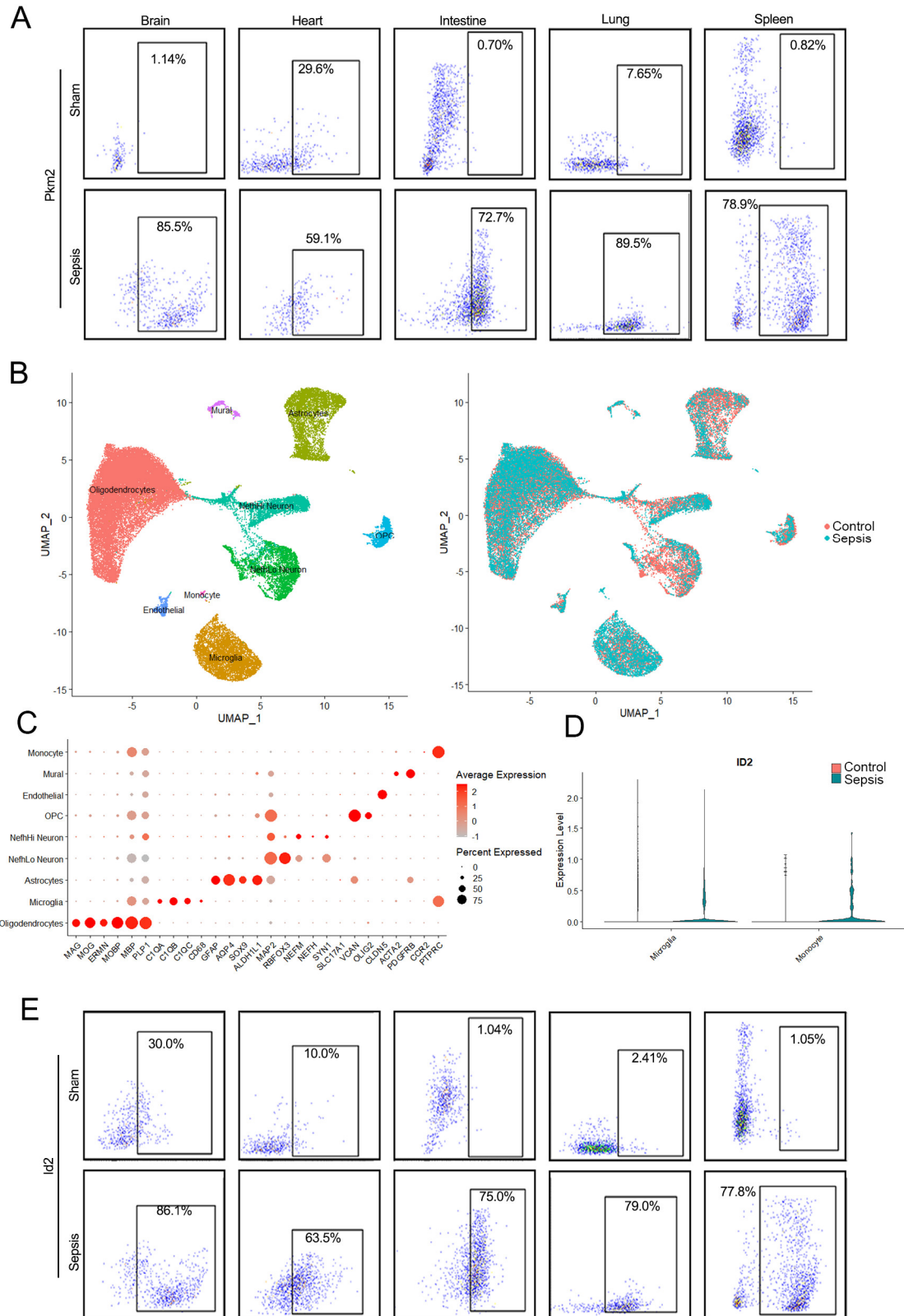


Figure S8. (A) Flow cytometry revealed the proportions of Pkm2⁺ cells in resident macrophages of different tissues from mice with sham and sepsis. (B) UMAP plots show the cell types of hippocampus from septic patients and age-matched controls. (C) DotPlot show the expression of marker genes in each cell type. (D) The expression of

ID2 in microglia and monocytes. (E) Flow cytometry revealed the proportions of *Id2*⁺ cells in resident macrophages of different tissues from mice with sham and sepsis.

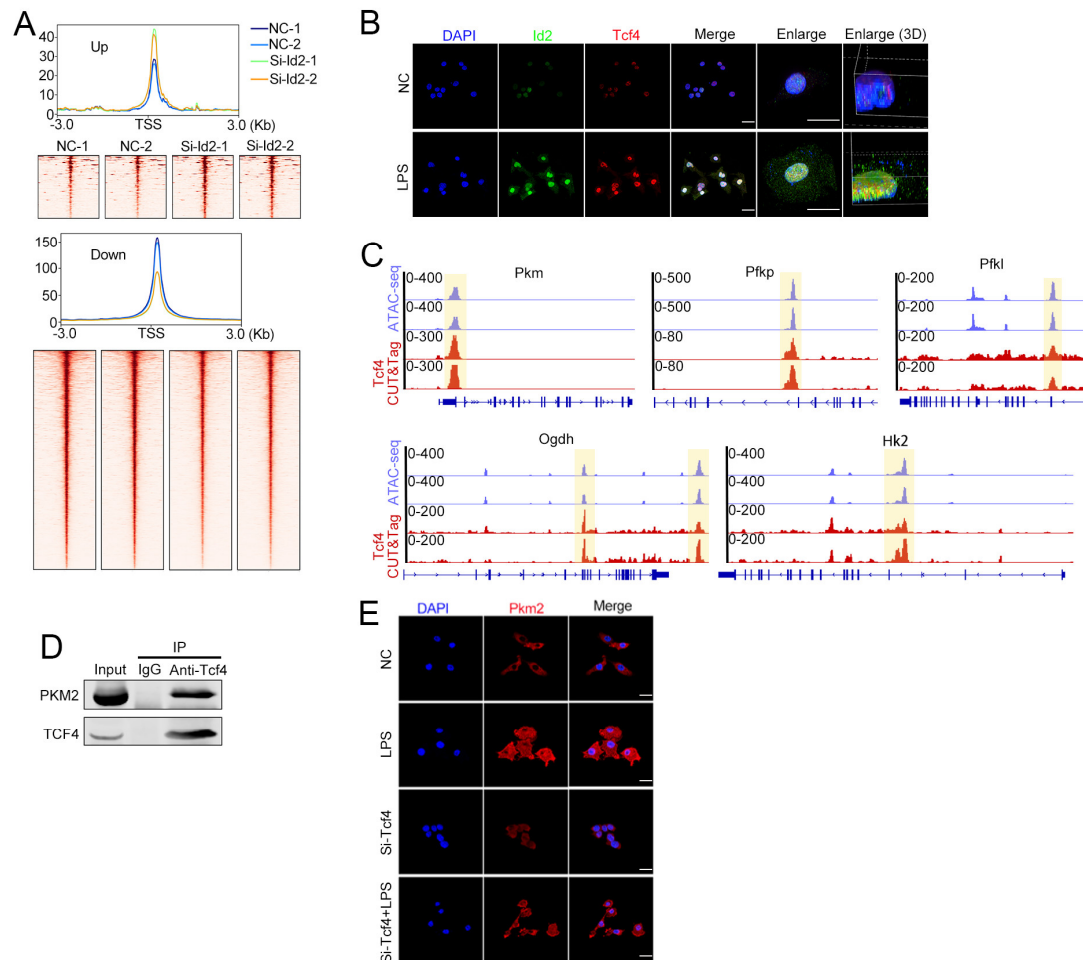


Figure S9. *Id2* cooperates with *Tcf4* to promote chromatin accessibility of *Pkm* and regulate its expression. (A) Peaks with increased (up) and decreased (down) chromatin accessibility. (B) Representative images illustrating *Id2* (green) and *Tcf4* (red) colocalize in RAW264.7 cells with DAPI-stained nuclei (blue) under normal control and 1 μ g/mL LPS-treated. Each dot represents one experiment, scale bar, 10 μ m, n = 3. (C) Integrative Genomics Viewer tracks display ATAC-seq reads and Anti-*Tcf4* CUT&Tag reads along the indicated genes. (D) Coimmunoprecipitation assay of the *Tcf4*-*Pkm2* interaction in RAW264.7 cells. (E) Representative images illustrating the expression of *Pkm2* after siRNA-mediated knockdown of *Tcf4*. Each dot represents one experiment, scale bar, 10 μ m, n = 3.