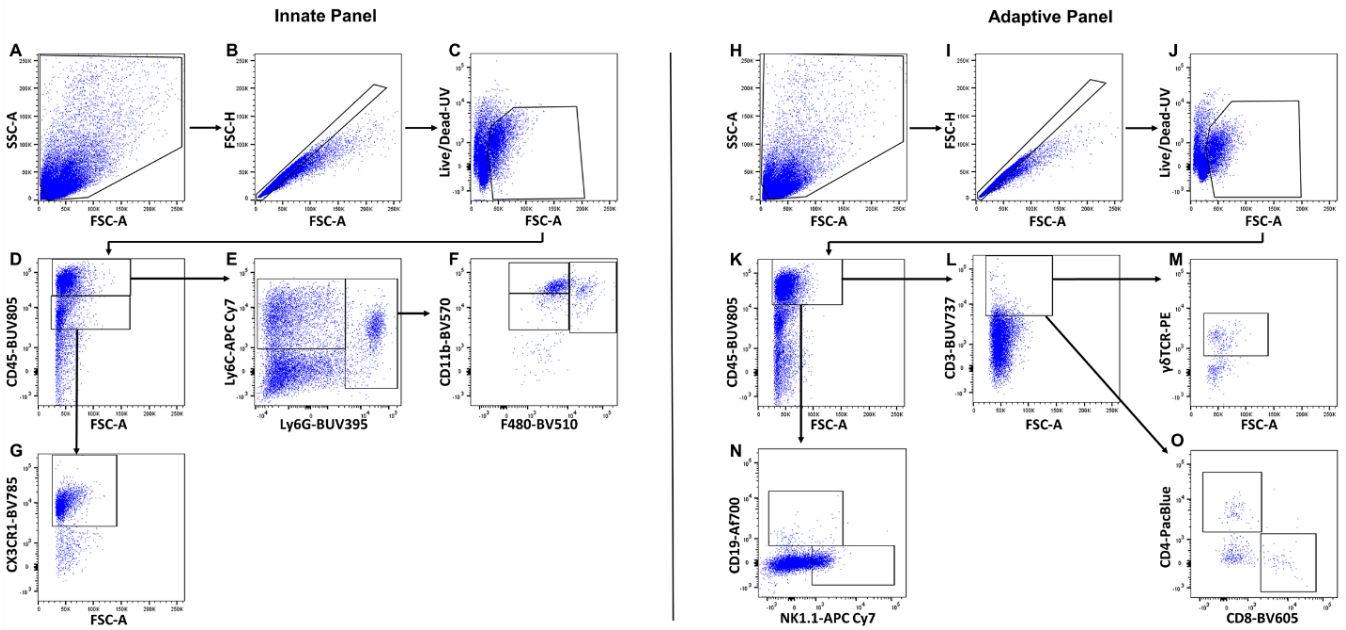
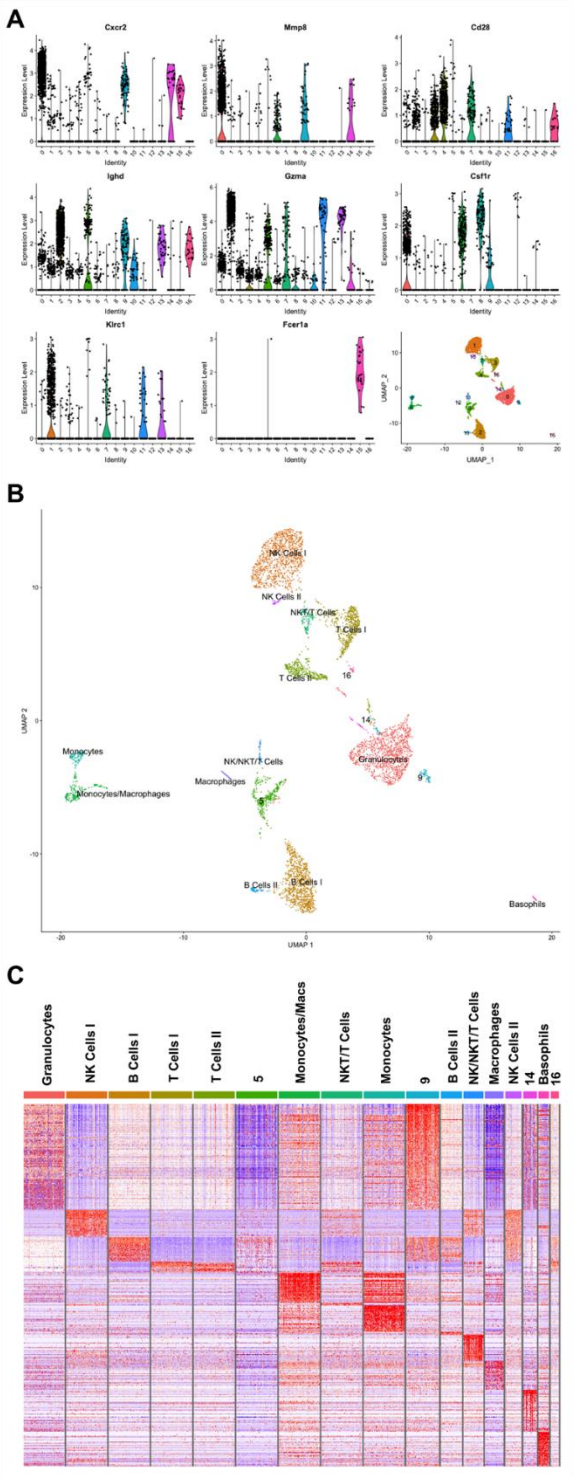
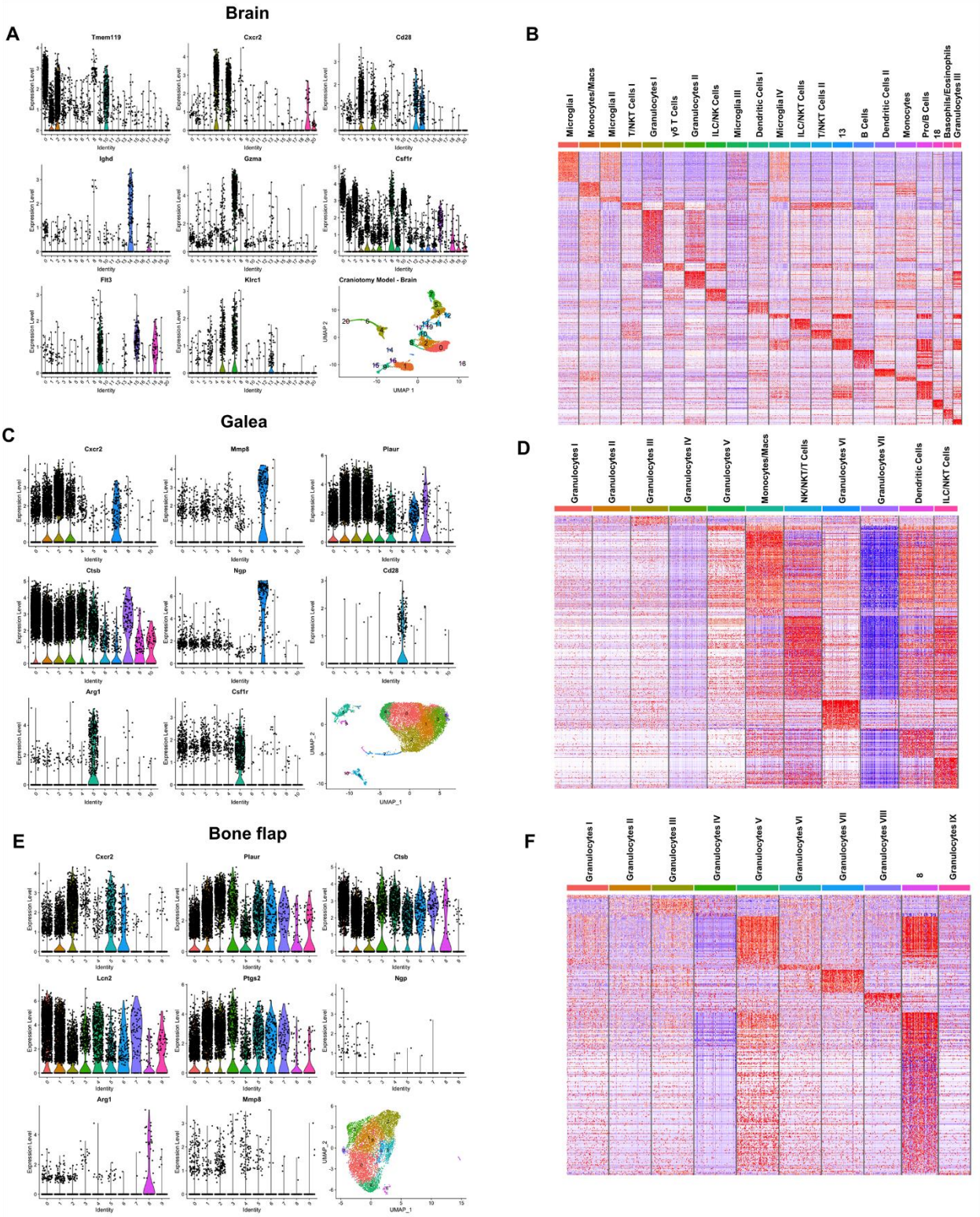



**Supplemental Figure 1. Gating strategy to quantify immune populations in the brain following *S. aureus* craniotomy infection.** From the (**A**, **H**) total events, (**B**, **I**) single cells were gated using FSC-A vs. FSC-H, followed by (**C**, **J**) exclusion of dead cells. For the innate immune panel, (**D**) Live, $CD45^{high}$ leukocytes were separated into (**E**) $Ly6G^{-}Ly6C^{+}$ monocytes vs. $Ly6G^{+}Ly6C^{+}$ cells, which were further identified as (**F**) MDSCs ($CD11b^{high}Ly6G^{+}Ly6C^{+}F4/80^{-}$) and neutrophils ($CD11b^{low}Ly6G^{+}Ly6C^{+}F4/80^{-}$) based on CD11b and F4/80 expression. Microglia were defined as (**D**) $CD45^{low}$ vs. FSC and (**G**) $CX3CR1^{+}$. Adaptive immune cells were subjected to the same initial steps (**H**-**J**) as described for the innate immune panel, where (**K**) live, $CD45^{high}$ leukocytes were separated into (**L**) $CD3^{+}$ cells that were further divided into (**M**) γδ T cells ($\gamma\delta TcR^{+}$) and (**O**) $CD4^{+}$ and $CD8^{+}$ T cells. (**N**) NK cells ($NK1.1^{+}$) and B cells ($CD19^{+}$) were identified from the $CD45^{high}$ population.




**Supplemental Fig. 2. Transcriptional profile of peripheral blood leukocytes during *S. aureus* craniotomy infection.** Viable CD45$^{+}$ cells were isolated from the blood (n= 4,914 cells) of mice (n=10) at day 7 following *S. aureus* craniotomy infection by FACS and processed for scRNA-seq. (**A**) Violin plots of select genes across the various clusters to facilitate cluster identification. (**B**) Transcriptional clusters were identified by SingleR and are presented as UMAP plots. (**C**) Heatmap of blood leukocyte clusters demonstrating the transcriptional heterogeneity across and within a given leukocyte type. Clusters that could not be accurately identified because they lacked a dominant transcriptional signature or included a mix of multiple leukocyte types were left as cluster numbers.




**Supplemental Fig. 3. scRNA-seq reveals predominant granulocyte infiltrates in the galea and bone flap following *S. aureus* craniotomy infection.** Viable CD45$^{+}$ cells were isolated from the (**A** and **B**) brain (n= 9,233 cells), (**C** and **D**) galea (n= 11,771 cells), and (**E** and **F**) bone flap (n= 6,672 cells) of mice (n=10) at day 7 following *S. aureus* craniotomy infection by FACS and processed for scRNA-seq. (**A**, **C**, and **E**) Violin plots of select genes across the various clusters, which were identified by SingleR and are presented as UMAP plots. (**B**, **D**, and **F**) Heatmaps of clusters demonstrating the transcriptional heterogeneity across and within a given cell type. Clusters that could not be accurately identified because they lacked a dominant transcriptional signature or included a mix of multiple leukocyte types were left as cluster numbers.