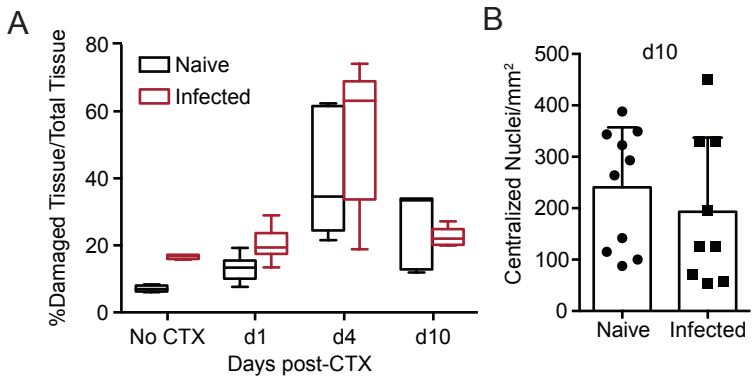
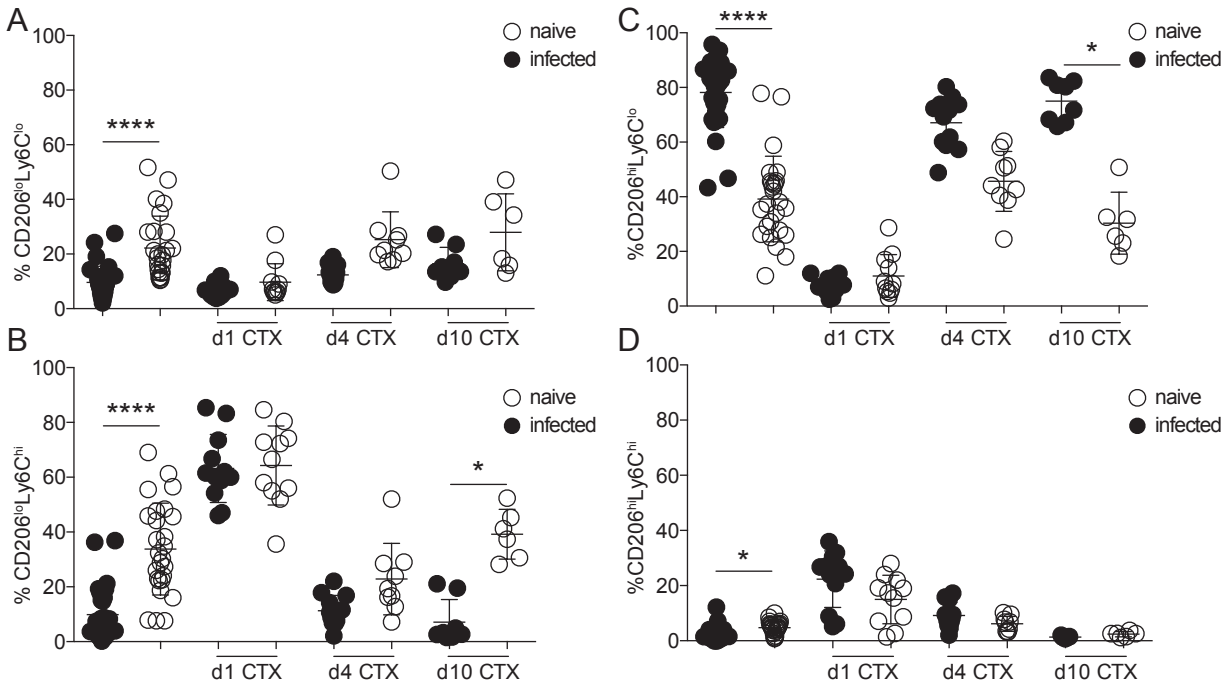
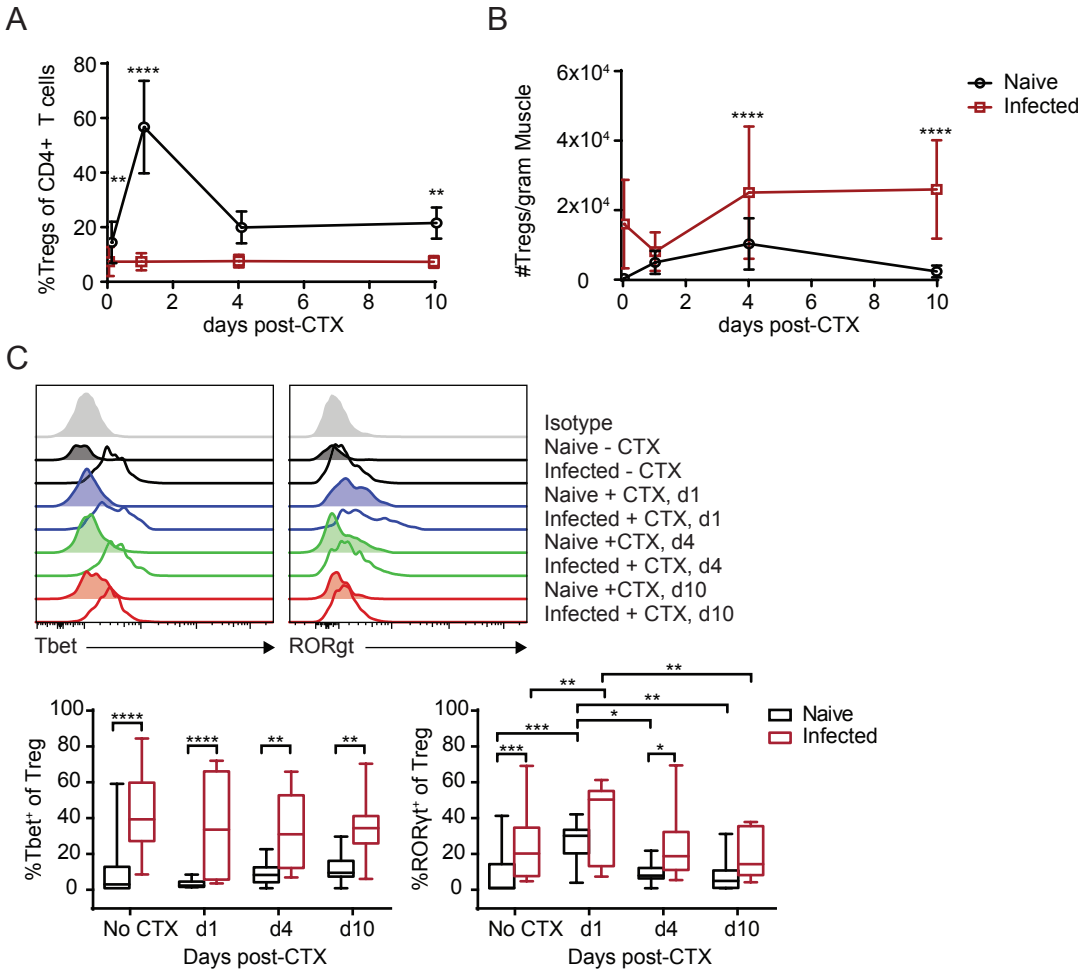


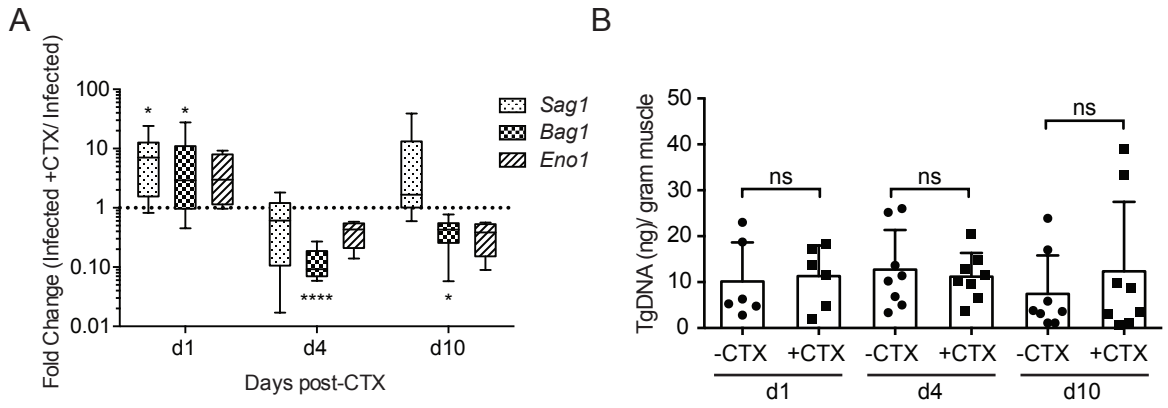
Supplemental Figure 1 – Skeletal muscle damage and regenerating fibers in uninfected and infected skeletal muscle following CTX-injury.(A) Percent damaged tissue area relative to total tissue area throughout CTX-injury. (n ≥ 5/group). **(B)** Number of centrally nucleated myofibers per mm2 in naïve and infected skeletal muscle 10 days-post CTX injury. (n = 9/group). Results are cumulative of three experiments of n = 3-4/group/experiment; error bars represent SD. Kruskal-Wallis with Dunnett's multiple-comparison test **(A),** Student's t test **(B).**



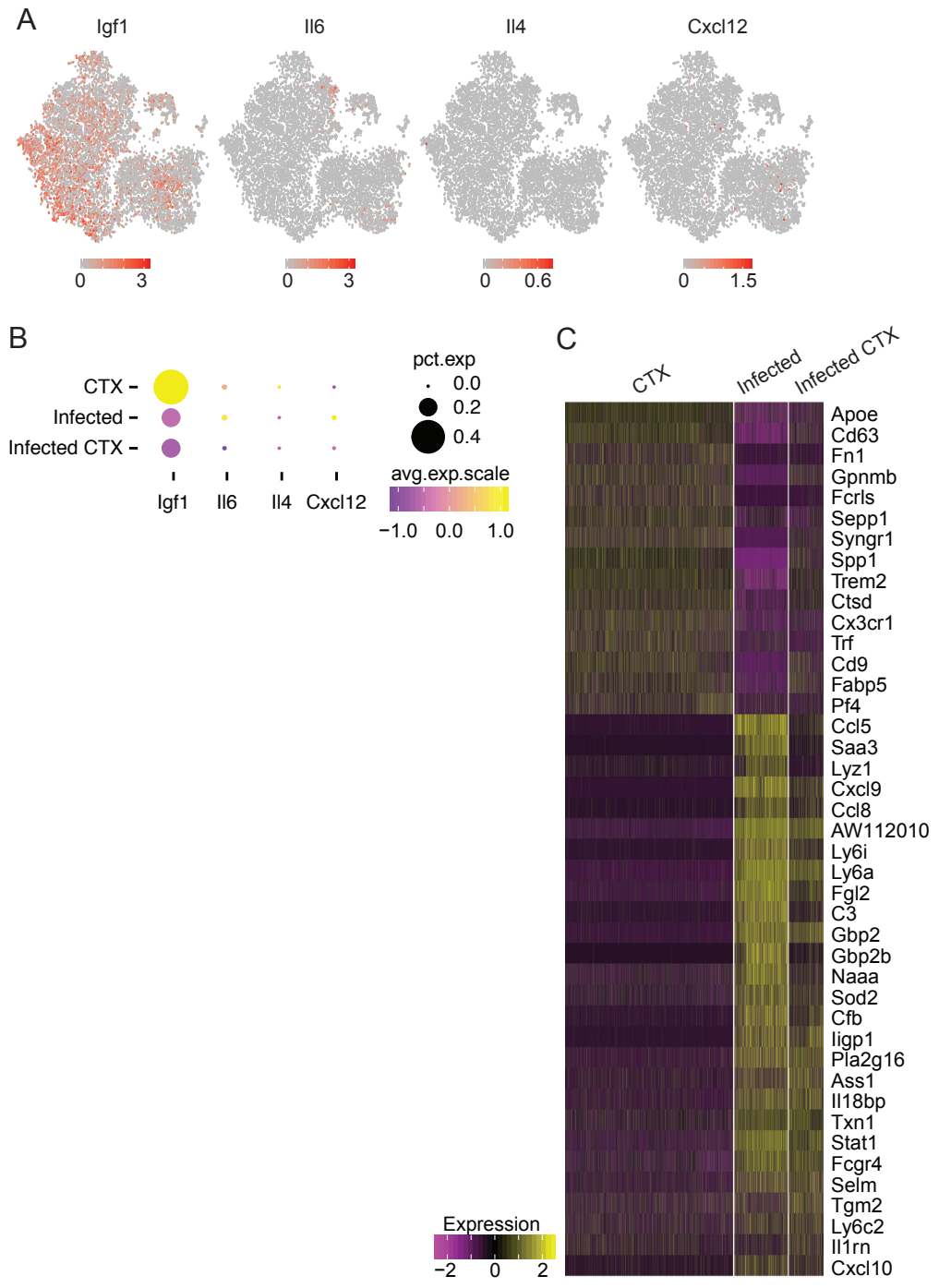
Supplemental Figure 2 – Distribution of Macrophage subsets. Graphical summary of Macrophage subsets **(A)** CD206^{lo}Ly6C^{lo} **(B)** CD206^{lo}Ly6C^{hi} **(C)** CD206^{hi}Ly6C^{lo} and **(D)** CD206^{hi}Ly6C^{hi} Results are cumulative of three experiments of n = 10-12/group/experiment; error bars represent SD. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001Kruskal-Wallis with Dunn's multiple-comparison test.



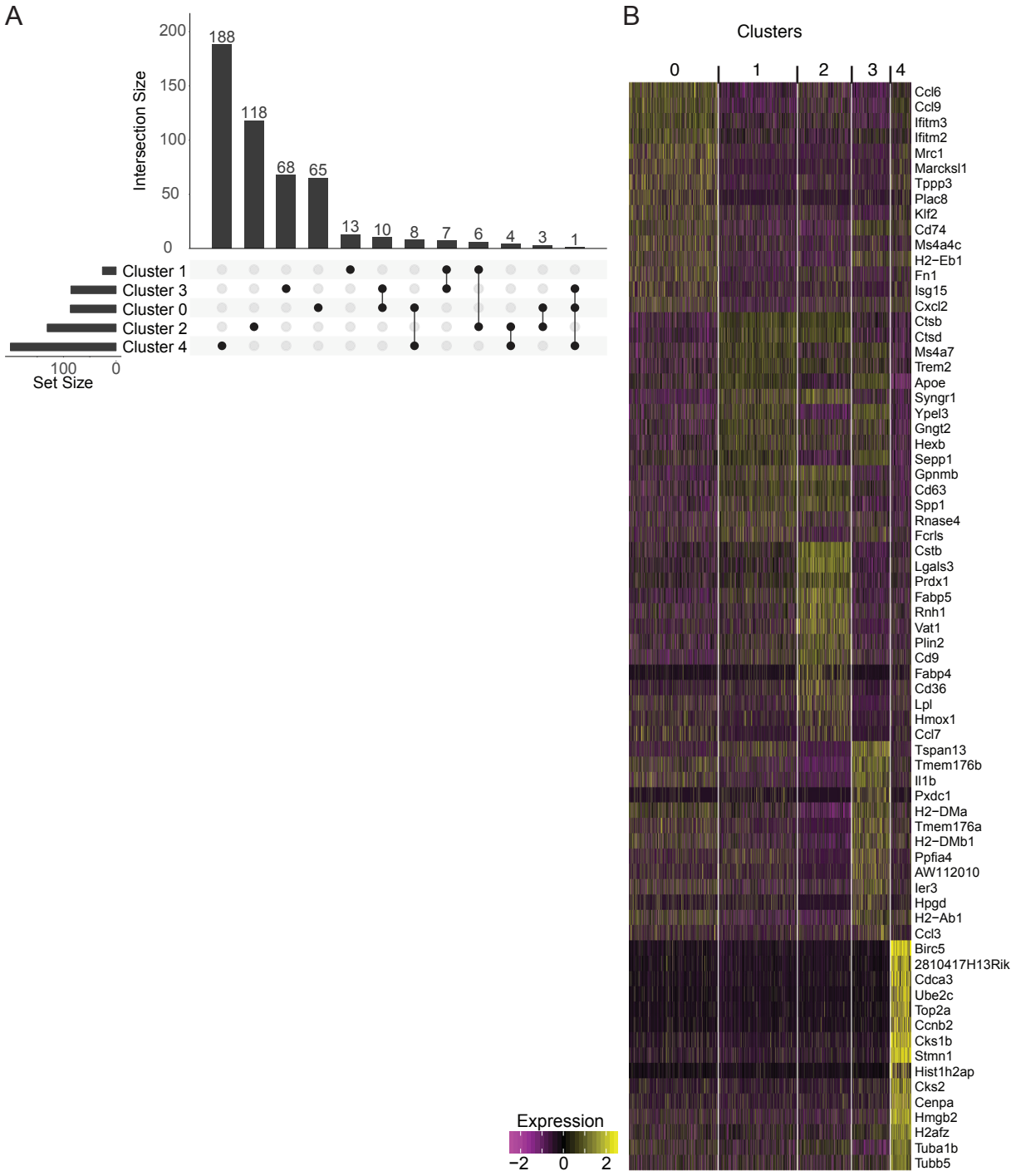
Supplemental Figure 3 – Skeletal muscle Tregs undergo different dynamics and phenotypic changes in infected muscle following CTX injury. (A) Frequency and **(B)** absolute number of skeletal muscle Tregs (TCRβ$^+$CD4$^+$Foxp3$^+$) at 0, 1, 4, and 10 days post-CTX injury. (n = 10 mice/group) **(C)** Representative flow plots and graphical summary of Tbet and RORγt expression in Tregs during CTX-injury response (n = 10 mice/group). Results are representative of three experiments of n = 3-4/group/experiment; error bars represent SD. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001, Kruskal-Wallis test **(A, C)**, ANOVA with Tukey's multiple-comparison test **(B)**.



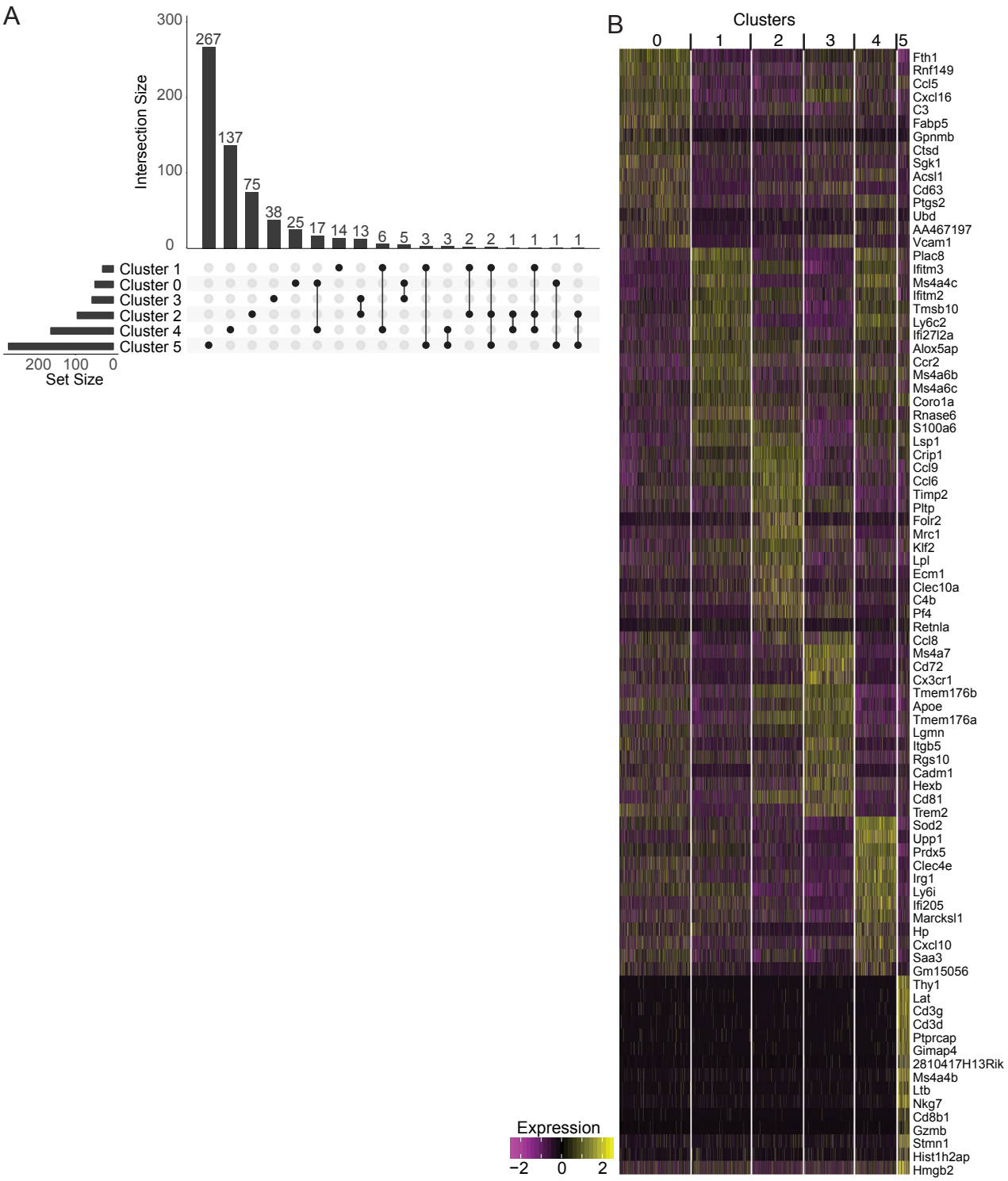
Supplemental Figure 4 - Assessment of Parasite Burden during CTX-injury (A) Quantification of *T. gondii* stage-specific transcripts *Sag1*, *Bag1*, and *Eno1* in skeletal muscle at 1, 4 and 10 days post-CTX injury normalized to *TgActin* and relative to contralateral uninjured infected skeletal muscle control. (n ≥ 5 mice/group). Statistics performed on log-transformed values. **(B)** Total parasite burden quantified by *T. gondii* specific gene B1. (n = 5-8 mice/group) Results are representative of two experiments of n = 3-4/group/experiment; error bars represent SD. *p < 0.05, ****p < 0.0001, ANOVA with Tukey's multiple-comparison test **(A)**, Students *t* test **(B)**.



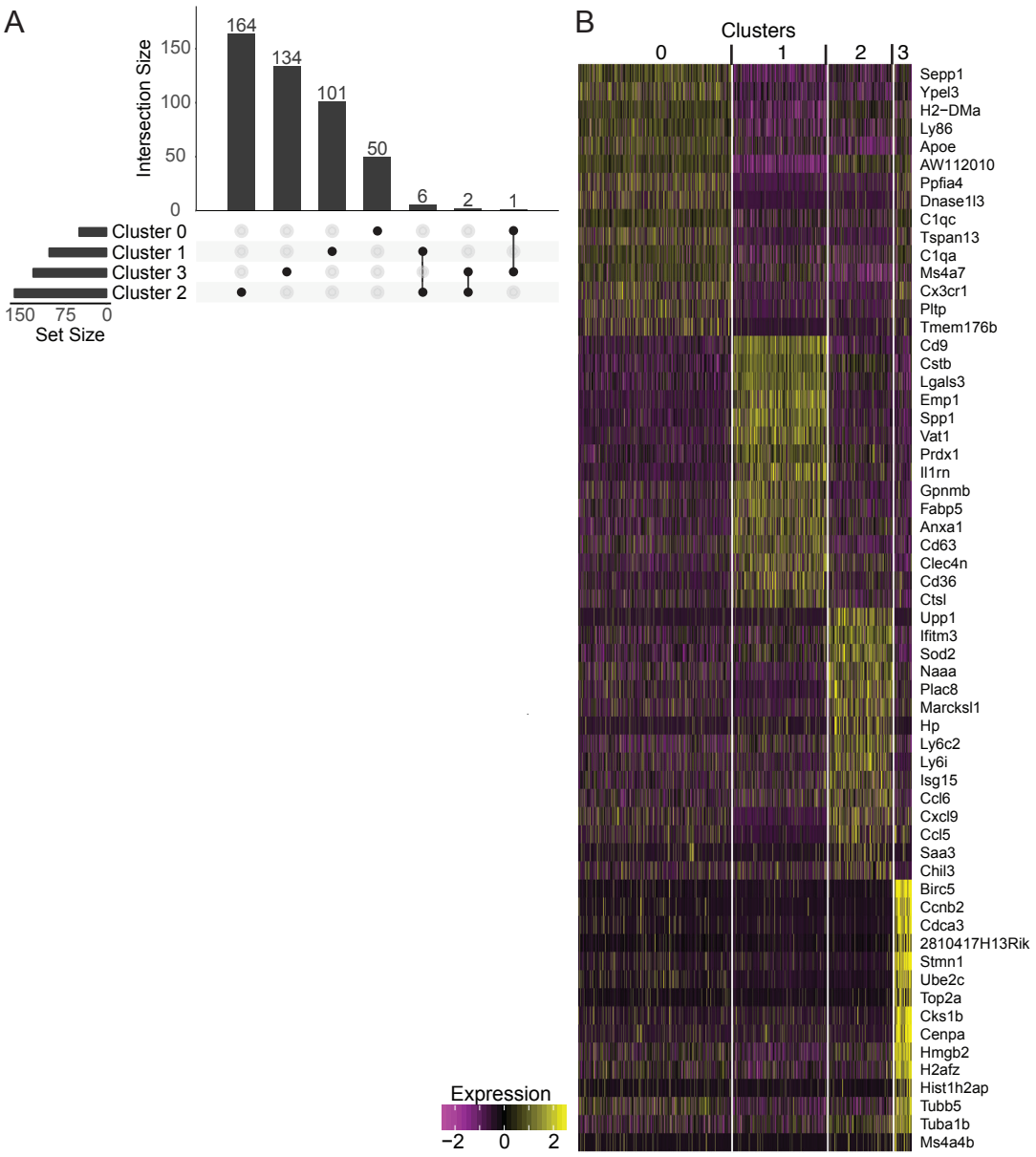
Supplemental Figure 5 – Analysis and visualization of expression of myogenic factors and top DEGs by experimental group. (A) Scaled expression of Igf1, Il6, Il4, and Cxcl12 overlayed on t-SNE plot of aggregated dataset. **(B)** Dotplot representation of Igf1, Il6, Il4, and Cxcl12 segregated by treatment group. Percent expression of marker in each treatment group is represented by dot size. Average expression level in expressing cells is represented by color scale. **(C) H**eatmap of top 15 differentially regulated genes in macrophages from each treatment group. Differentially regulated genes were identified by a fold change ≥ 2 at an adjusted p-value ≤ 0.05.



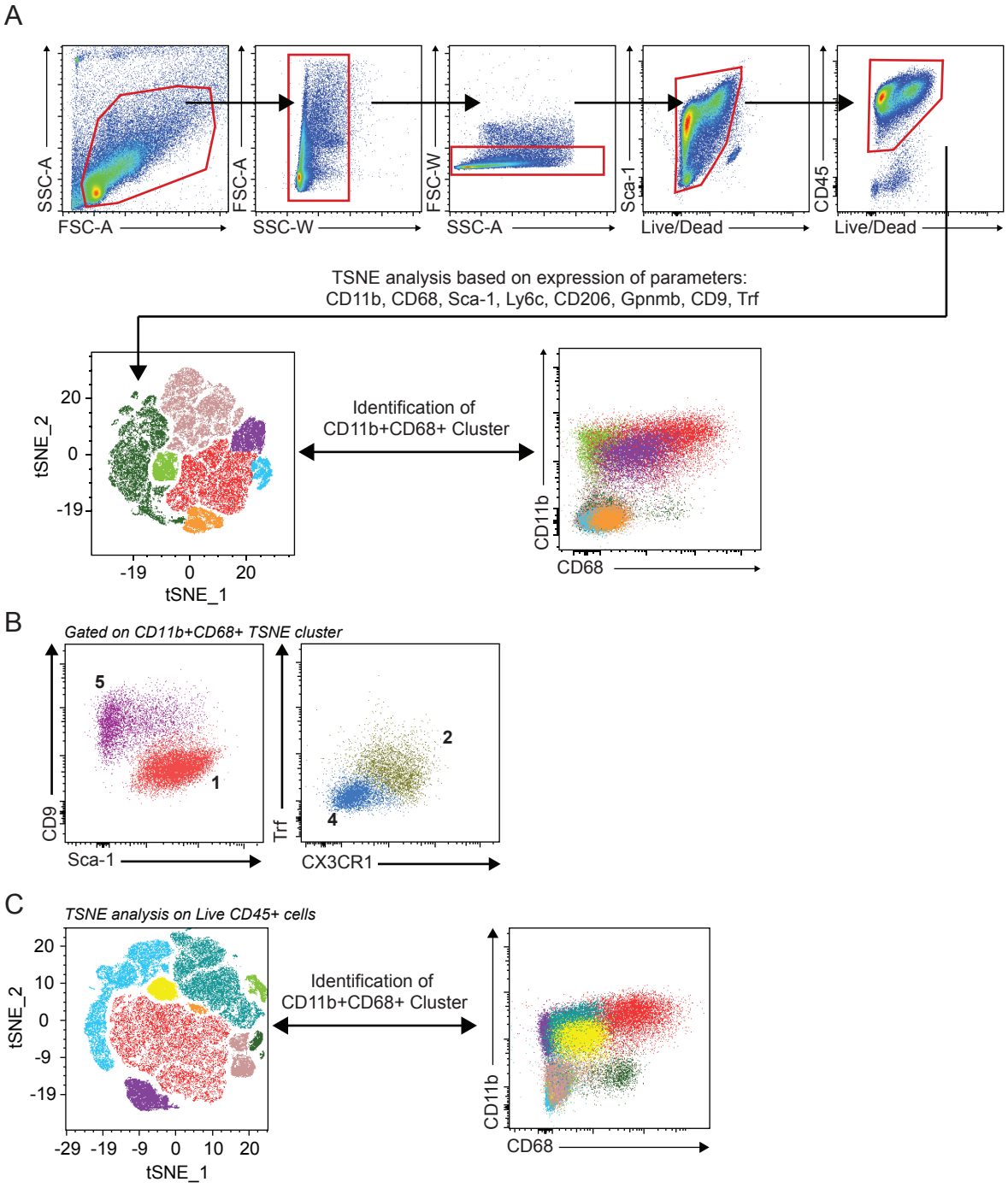
Supplemental Figure 6 – Top DEGs in CTX experimental group by cluster. (A) UpSet plot representing overlap in differentially regulated gene lists between the 5 transcriptionally unique clusters identified. Differentially regulated genes were identified by a fold change ≥ 2 at an adjusted p-value ≤ 0.05. **(B)** Heatmap representation of top 15 differentially regulated genes in each cluster



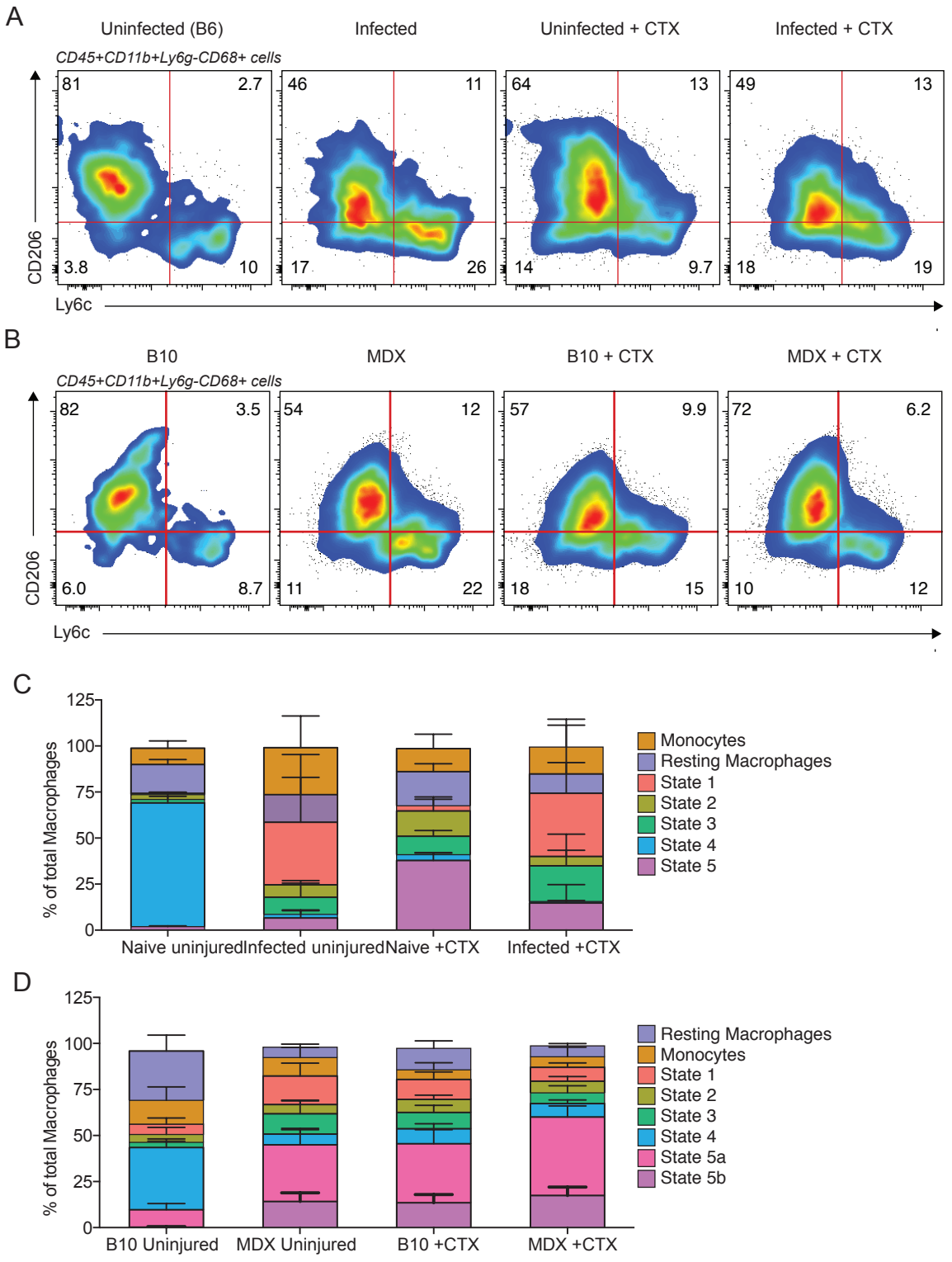
Supplemental Figure 7 – Top DEGs in Infected experimental group by cluster. (A) UpSet plot representing overlap in differentially regulated gene lists between the 6 transcriptionally unique clusters identified. Differentially regulated genes were identified by a fold change ≥ 2 at an adjusted p-value ≤ 0.05. **(B)** Heatmap representation of top 15 differentially regulated genes in each cluster.



Supplemental Figure 8 – Top DEGs in Infected + CTX experimental group by cluster. (A) UpSet plot representing overlap in differentially regulated gene lists between the 4 transcriptionally unique clusters identified. Differentially regulated genes were identified by a fold change ≥ 2 at an adjusted p-value ≤ 0.05. **(B)** Heatmap representation of top 15 differentially regulated genes in each cluster.



Supplemental Figure 9 – Analytical workflow for t-SNE analysis of flow cytometric data to identify CD11b^{+}CD68^{+} cells. (A) Gating scheme to identify live CD45+ cells (top). t-SNE analysis was performed on concatenated, downsampled (3000 cells/sample) live CD45+ skeletal muscle cells from uninfected, infected, uninfected + CTX, and infected + CTX samples 4-days post injury (n = 7-8 samples/group/experiment, 2 independent experiments). Parameters for t-SNE dimensional reduction included expression of markers: CD11b, CD68, Sca-1, Ly6c, CD206, Gpnmb, CD9, and Trf. Density-rich, spatially distinct clusters plotted on the two calculated t-SNE dimensions were identified, gated, and overlayed on a flow cytometric plot to determine their expression of CD11b and CD68. Gating of clusters was fine-tuned and iterated until the cluster of CD11b+CD68+ cells (red/purple) was identified. **(B)** Representative flow cytometric plots overlaying of cells from different monocle states identified through t-SNE analysis based on a panel of monocle distinguishing markers. (n = aggregated data of all groups, 7-8 samples/group) **(C)** t-SNE plot of cumulative cells from uninjured and CTX-injured (4 days-post injury) live CD45+ skeletal muscle cells. Parameters for t-SNE analysis were as in (**A**). Iterative gating was performed until the cluster of CD11b+CD68+ cells was identified on the TSNE plot. (n = aggregated data of all groups, 10 samples/group). Results are cumulative of two independent experiments.



Supplemental Figure 10 – Subsetting macrophages by CD206 and Ly6c expression during CTX-injury in naïve, infected, and mdx mice. (A) Representative flow plots macrophage subsets (CD206hi/loLy6chi/lo) in naïve and infected skeletal muscle with no CTX and 4 days post-CTX injury. (n = 7-8 samples/group). **(B)** Representative flow plots macrophage subsets (CD206hi/loLy6chi/lo) in B10 and mdx skeletal muscle with no CTX and 4 days post-CTX injury. (n = 10 samples/group). (C-D) Graphical summary of the percent of macrophages in monocytes, resting macrophages, and states 1-5. Results are cumulative of two independent experiments.