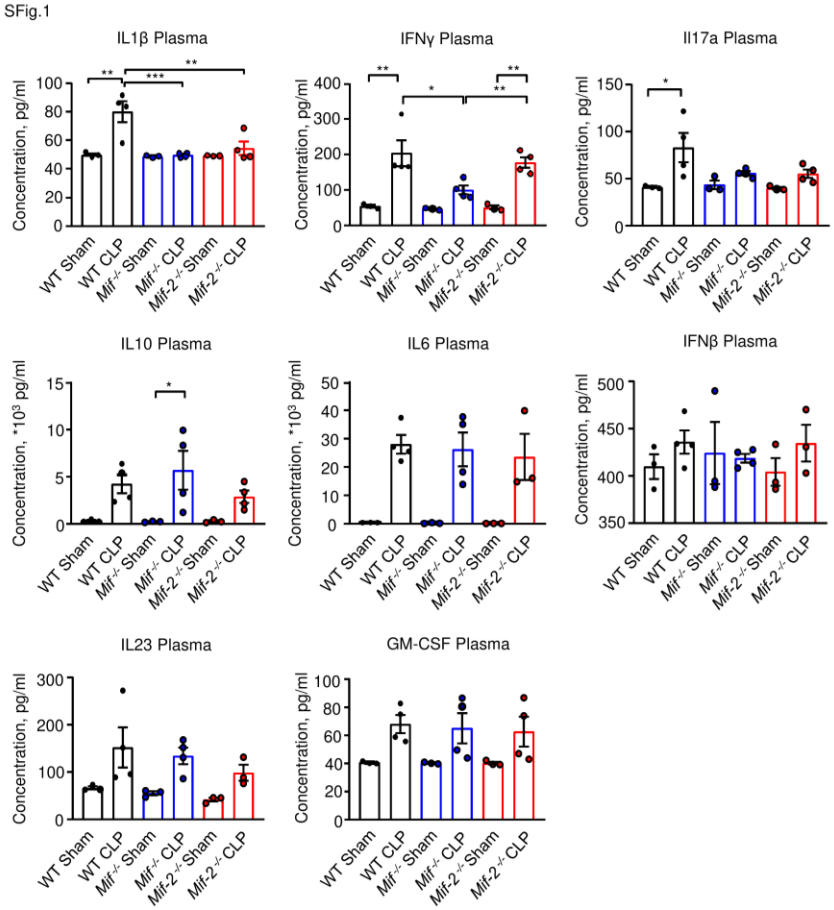
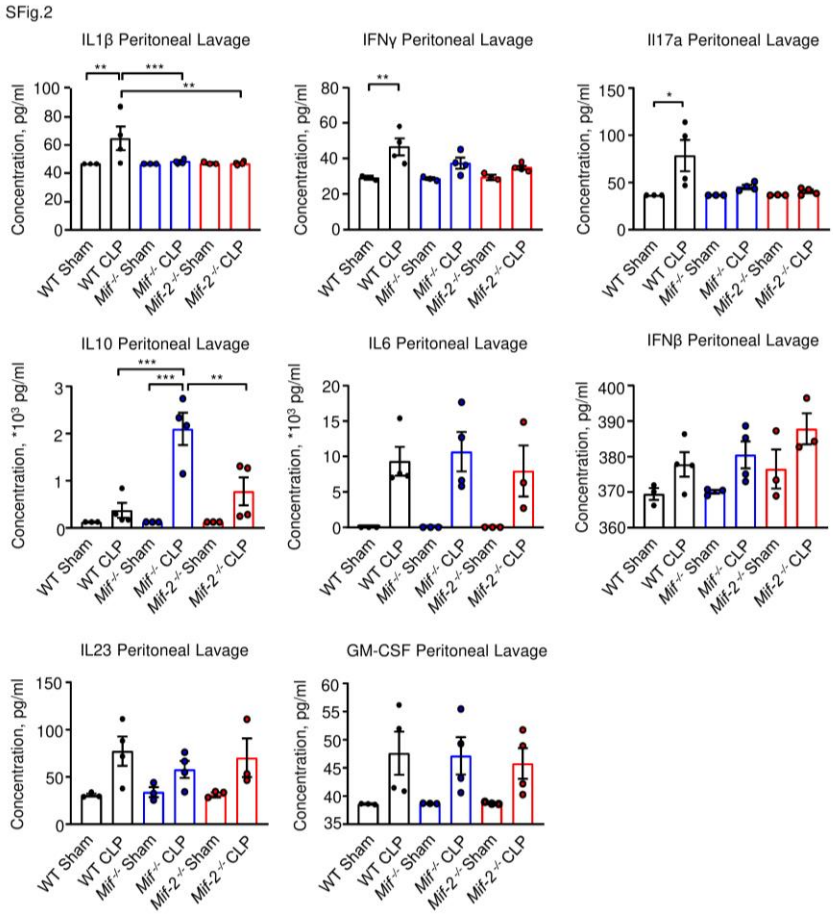
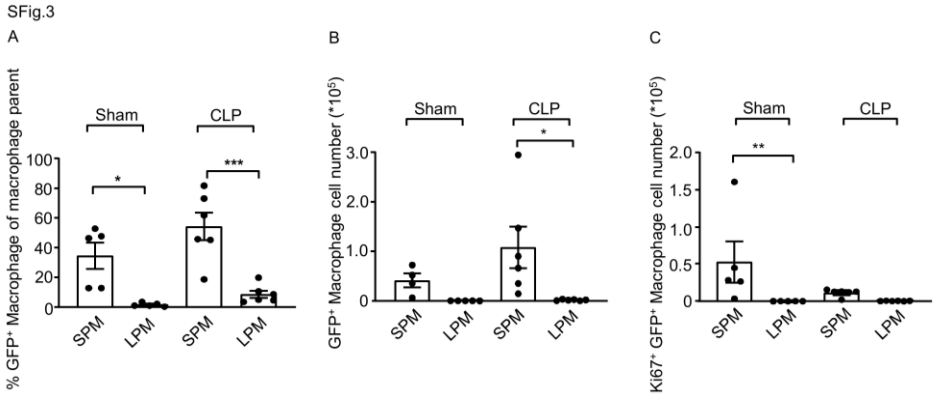
Supplemental Figures



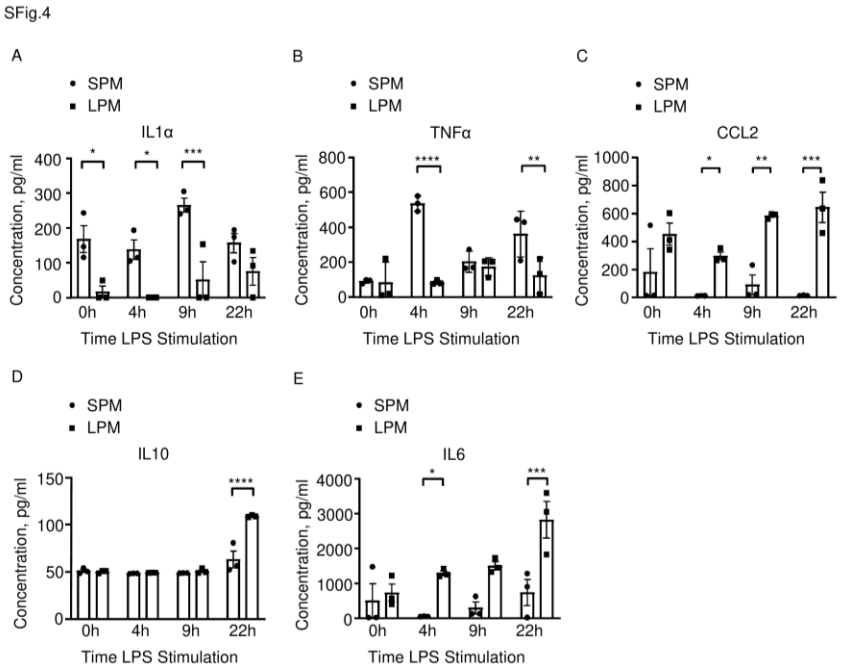
Supplemental Figure 1: *Mif* $^{-/-}$ mice exhibit reduced levels of circulating inflammatory cytokines. Plasma cytokine and chemokine concentrations in WT, *Mif* $^{-/-}$ and *Mif-2*$^{-/-}$ mice after CLP and Sham surgery. Cytokine/chemokine levels were measured by flow cytometry using the Biolegendplex Multi Analyte Flow Assay Kit. n=3-4 mice per group, one-way ANOVA with Tukey´s multiple comparison. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.



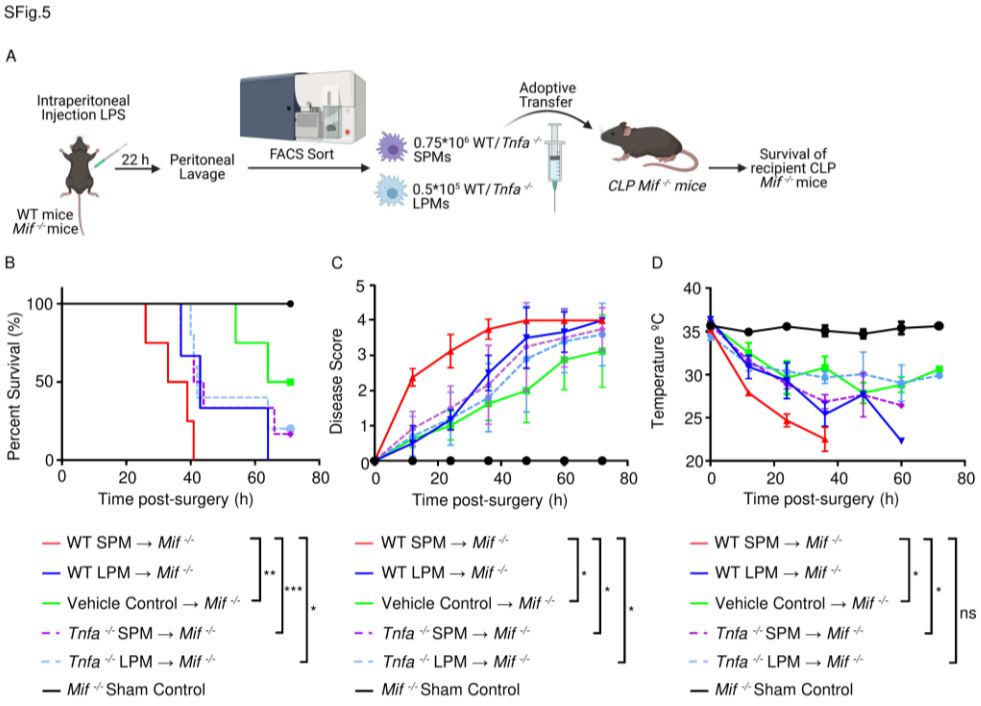
Supplemental Figure 2: *Mif* $^{-/-}$ mice exhibit reduced levels of inflammatory cytokines in the peritoneal fluid. Peritoneal fluid cytokine and chemokine concentrations in WT, *Mif* $^{-/-}$ and *Mif-2*$^{-/-}$ mice after CLP and Sham surgery. Cytokine/chemokine levels were measured by flow cytometry using the Biolegendplex Multi Analyte Flow Assay Kit. n= 3-4 mice per group, with replication, one-way ANOVA with Tukey´s multiple comparison. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.



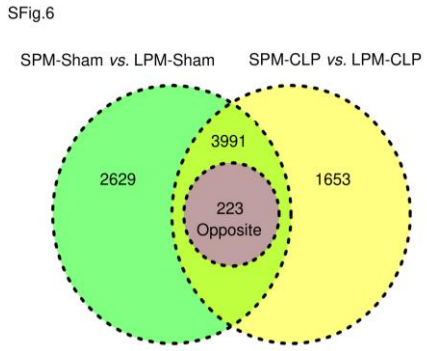
Supplemental Figure 3: SPMs originate from circulating GFP$^+$CX3CR1$^+$ monocytes. *Cx3cr1*^{GFP} mice were subjected to CLP or sham surgery. Peritoneal cells were obtained 22 h post-CLP for measurement by flow cytometry of **(A)** % GFP$^+$ macrophages, (**B**) GFP$^+$ macrophage content, and **(C)** proliferating (Ki67$^+$) GFP$^+$ macrophage number. CountBright absolute counting beads were used to determine the absolute cell count. n=5-6 mice studied, Kruskal-Wallis with Dunn's multiple comparisons. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.



Supplemental Figure 4: Inflammatory cytokine production by SPMs and LPMs. **(A)** IL1α, **(B)** TNFα, **(C)** CCL2, **(D)** IL10 and **(E)** IL6 cell supernatant levels from cultured FACS-sorted SPMs and LPMs ($1x10^5$ cells/well) after 100 ng/ml LPS stimulation. Levels were measured by flow cytometry using Biolegendplex Multi Analyte Flow Assay Kit. n=3 with 6 mice pooled per data point, Two-way ANOVA with Sidak's multiple comparisons test. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.



Supplemental Figure 5: TNFα deficiency reduces SPM induced mortality in *Mif* $^{-/-}$ CLP mice. **(A)** Experimental scheme for the adoptive transfer of WT and *Tnfa* $^{-/-}$ SPMs or LPMs into *Mif* $^{-/-}$ recipients. Image created with Biorender.com **(B)** Kaplan-Meier survival plots, **(C)** disease scores, and **(D)** surface body temperature of *Mif* $^{-/-}$ CLP mice after adoptive transfer of WT SPM (red), WT LPM (blue), PBS as vehicle control (green), *Tnfa*$^{-/-}$ SPM (purple dotted line) and *Tnfa* $^{-/-}$ LPM (light blue dotted line). A sham control was additionally included (black). Data are from 3-6 mice per group and representative of three independent experiments. *p* values determined by **(B)** Log-rank (Mantel-Cox) test, **(C,D)** with Kruskal Wallis test with Dunn's multiple comparisons test. Significance for **C,D** was determined at 36 h post-injection. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.



Supplemental Figure 6: Venn diagram of differentially expressed gene lists for SPMs versus LPMs under sham and CLP conditions. The numbers shown are for genes with a q-value of <0.05 and compare significant genes from SPM-sham vs LPM-sham to significant genes from SPM-CLP vs LPM-CLP. Comparison of SPM-sham vs LPM-sham revealed 2629 genes to be differentially regulated under sham condition, and comparison of SPM-CLP vs LPM-CLP revealed 1653 genes to be differentially regulated only under CLP condition. 3991 genes are differentially expressed in SPM vs LPM and are shown in both sham and CLP conditions. 223 genes are differentially expressed between SPM vs LPM but are regulated in opposite directions when comparing sham or CLP conditions (*e.g.*, upregulated in SPM-sham but downregulated under SPM-CLP).