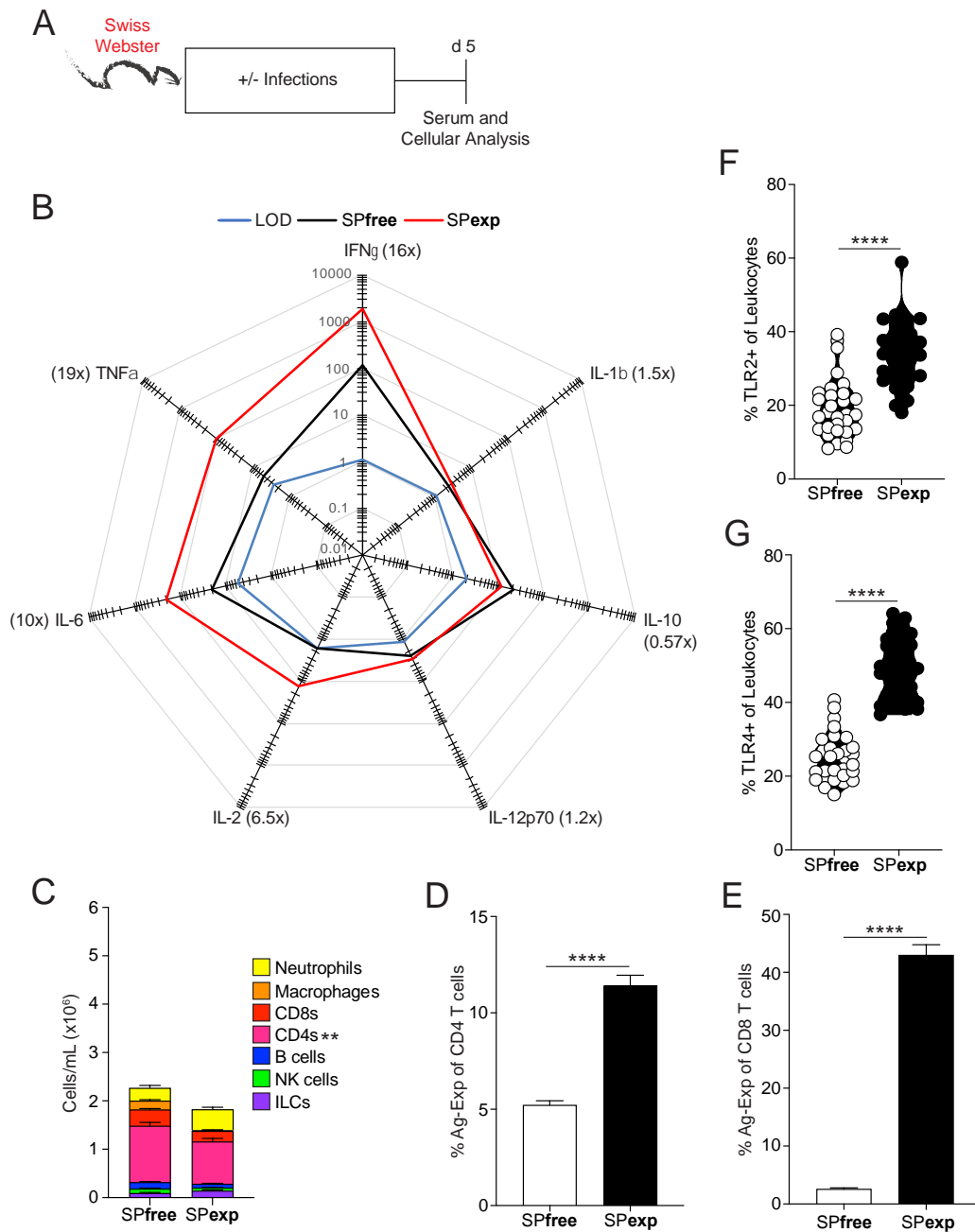
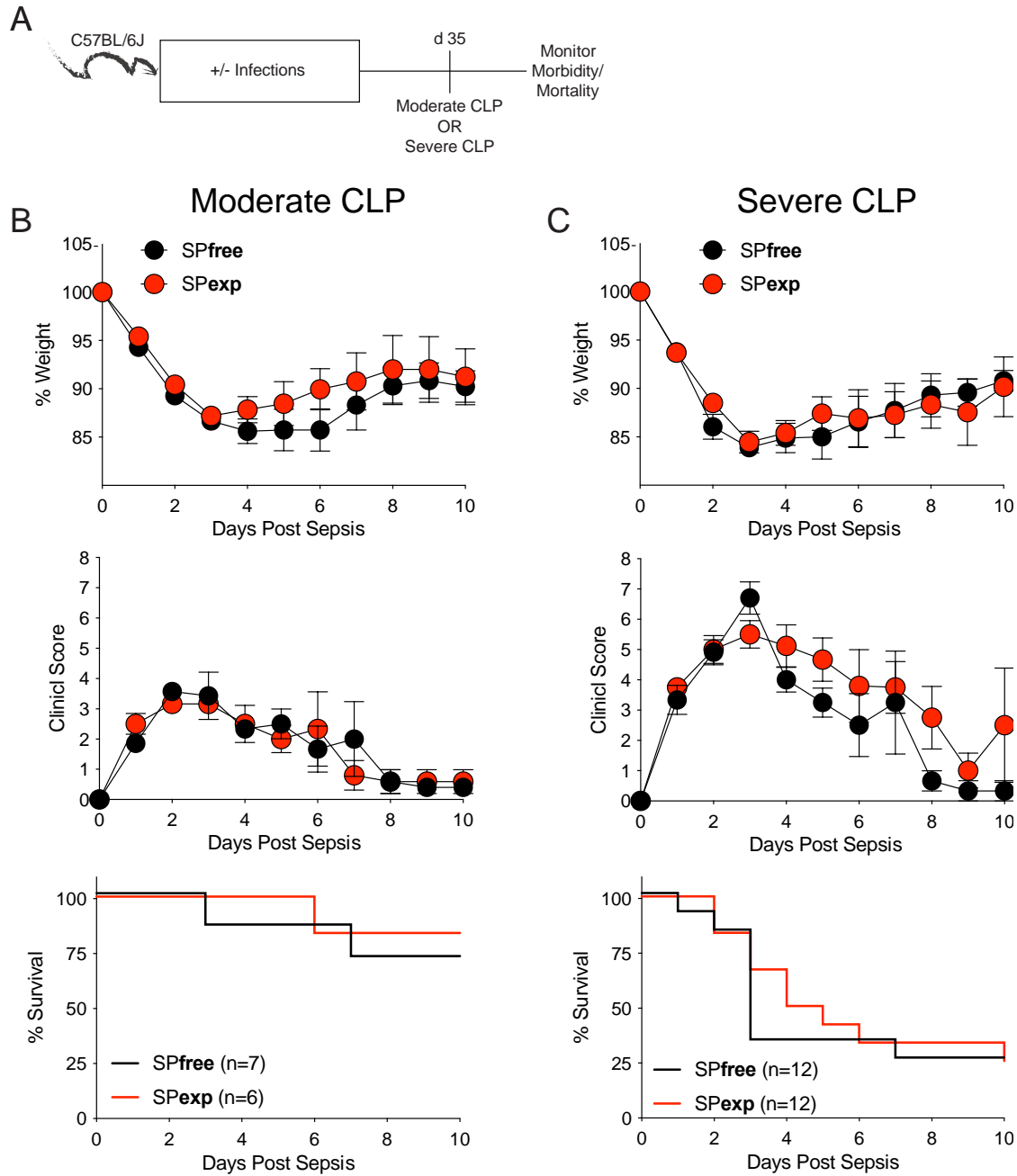


Supplemental Figure 1

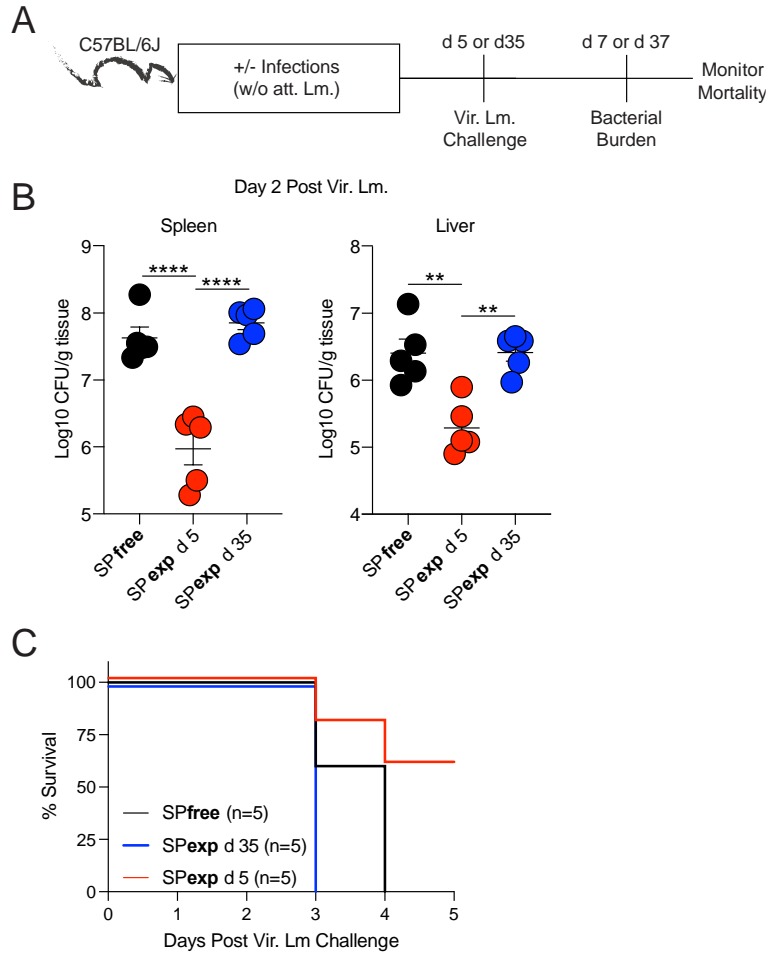


**Supplemental Figure 1. Irrespective of host genetics, sequential infection leads to experienced immune status.** **A)** Experimental design. Serum and PBL were collected from Swiss Webster SPexp mice, 5 d after last infection. **B)** Summary data of analyte concentrations (pg/mL) 5 d post last infection. **C)** Number of cells per mL of PBL, frequency of Ag-experienced **D)** CD4 and **E)** CD8 T cells, and **F)** frequency of TLR2- and **G)** TLR4-expressing leukocytes 5 days after last infection. Data are representatives from at least three independent experiments with 20 mice per group. Error bars represent SEM. \*\*\*:  $p < 0.01$ , \*\*\*\*:  $p < 0.0001$ .



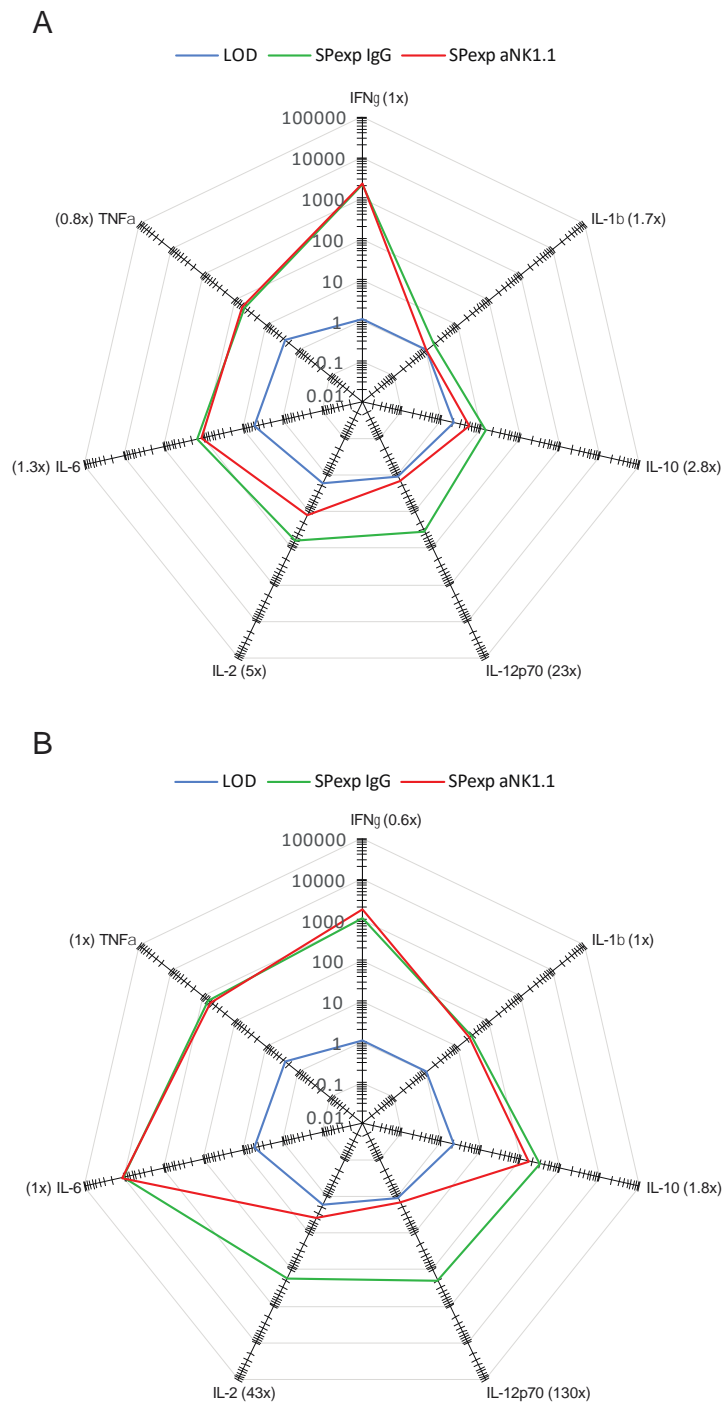
**Supplemental Figure 2. Equivalent survival between SPfree and SPexp mice when severe septic event is 35 dpli. A)** Experimental design. Moderate or severe CLP (~10-20% or ~50% mortality in SPfree mice, respectively (23)) was performed 35 days post-last infection in SPexp and age-matched SPfree B6 mice. Body weight and mortality were monitored over time. **B)** Weight, clinical score, and survival of mice following moderate CLP. **C)** Weight, clinical score, and survival of mice following severe CLP. Data are representatives from at least two independent experiments with 6-12 mice per group.

Supplemental Figure 3



**Supplemental Figure 3. Enhanced anti-Listerial response in immune-experienced hosts correlates with basal inflammation. A)** Experimental design. SPfree and SPexp mice (without attenuated *Lm.* infection) were challenged with  $8 \times 10^4$  CFU virulent *Lm.* 5 or 35 d post last infection and mortality was monitored. Bacterial burden was assessed within spleen and liver 2 d after virulent *Lm.* challenge. **B)** *Lm.* CFU per gram of (left) spleen and (right) liver 2 d post challenge. **C)** Mortality of mice following challenge. Data are representatives from at least one independent experiments with 5 mice per group. Error bars represent SEM. \*\*:  $p < 0.01$ , \*\*\*\*:  $p < 0.0001$ .

Supplemental Figure 4



**Supplemental Figure 4. NK cells contribute to basal and cytokine storm inflammation in SPexp mice. A) Summary data of analyte concentrations (pg/mL) 12 hr prior to CLP. B) Summary data of analyte levels 12 hr post CLP. Data are representatives from two independent experiments with 9-10 mice per group.**