**Supplemental Figure 1. LPS induces TLR4 dependent HSPC expansion. A)** Representative flow plots of BM LSK 24 hours after PBS or LPS injection. % of **B)** LSK and **C)** LT-HSC ($CD150^{+}CD135^{-}$LSK) and ST-HSC ($CD150^{-}CD135^{+}$ LSK) expansion in C3H/HeOuJ and C3H/HeJ mice following intraperitoneal injection of 5 μg of LPS; **D)** % LSK expansion in B6, $MyD88^{-/-}$, and $TRIF^{-/-}$ mice; or **E)** SEV129 mice and $IFNAR^{-/-}$ mice 24 hours following intraperitoneal injection of 5 μg of LPS. *$p<0.05$ for PBS vs LPS. ** $p<0.05$ for wild type LPS treated versus knockout LPS treated mouse. Experiments were performed at least 3 separate times with an n=3-4 per group.

**Supplemental Figure 2. LT-HSCs from septic mice are capable of long term reconstitution. A)** Schema for identification of $Lineage^{-}$c-$kit^{+}$$sca\text{-}1^{+}$ LSK and $CD150^{+}CD135^{-}$ LT-HSCs and $CD150^{-}CD135^{+}$ activated ST-HSCs 36 hours after sham or CLP surgery. **B)** Gating schema for sorting of LT-HSCs 36 hours after sham or CLP for long term reconstitution experiment with FACSAria following magnetic sorting for lineage-depletion showing pre-sort (top panels) and **C)** post-sort purities. **D)** Survival of lethally irradiated mice following transfer of ten $CD150^{+}CD135^{-}$LSK cells from sham (n=7) or CLP (n=7) mice with $5x10^{5}$ $Lineage^{+}$ cells for radioprotection, or $5x10^{5}$ $Lineage^{+}$ cells without $CD150^{+}CD135^{-}$LSK cells (n=10).

**Supplemental Figure 3. CLP-induced bone marrow reprogramming of hematopoiesis involves depletion of B cells and increased myeloid differentiation of hematopoietic progenitors. A)** Time course of bone marrow B cell depletion following CLP. Representative flow plots of $AA4.1^{+}B220^{low}$ pre-B cells 36 hours after sham treatment (left panels) and CLP treatment (right panels) in **B)** B6 control and **C)** $MyD88^{-/-}$ mice with graphical representations (bottom panels) of % pre-B cells in bone

marrow at 36 hours or Day 7 following sham or CLP treatment. D) 36 hours following sham or CLP treatment, total Lineage$^-$ hematopoietic stem and progenitor cells were isolated by magnetic bead sorting and 1x$10^4$ Lineage$^-$ cells were cultured in methylcellulose with the indicated cytokines. 14 days later, colonies were counted with a light microscope. Each point represents Lineage$^-$ cells from two mice of the same treatment group. All experiments were performed at least twice with an n=4 per group.

**Supplemental Figure 4. Blockade of inflammatory factors that regulate hematopoiesis have no effect on CLP induced LSK expansion**. 36 hours following sham or CLP procedure BM was analyzed for LSK expansion. **A)** C57BL/6, IL1R$^{-/-}$ and IL-6$^{-/-}$ animals. **B)** Sham or CLP mice with or without treatment with pegylated soluble TNFR1 (100 mg/kg). **C)** C57BL/6 sham and CLP mice with or without treatment with apocynin (apo-5mg/kg) and n-acetyl cysteine (NAC-100mg/kg). **D)** C57BL/6 sham and CLP mice treated with or without indomethicin (5mg/kg). All treatments were given i.p. 2 hours prior to surgery. Apo+NAC and TNFR1 were also given 24 hours following CLP.

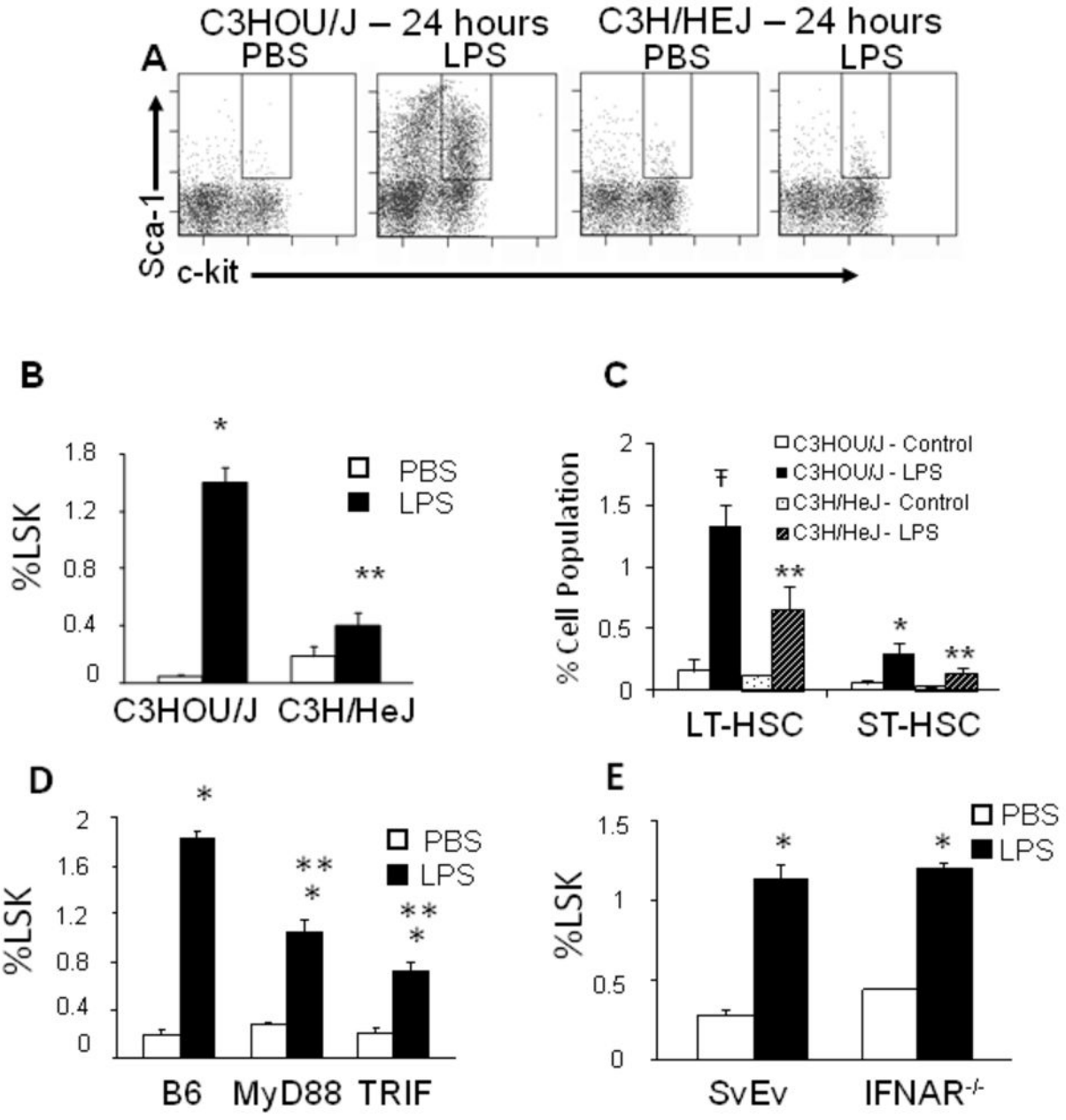
**Supplemental Figure 5. Staphylococcal superantigen induces HSPC expansion and S. aureus sepsis induces a temporary leukopenia. A)** Expansion of LSK, LT-HSCs and ST-HSCs in B6 mice treated IP with 10μg of Staphylococcal enterotoxin B (SEB) or same volume of PBS as control. **B)** represents peripheral blood total leukocyte counts.

**Supplemental Figure 6. Time course of BM repopulation following CLP.** Mice were subjected to Sham or CLP and at different time points hind limb bones were harvested

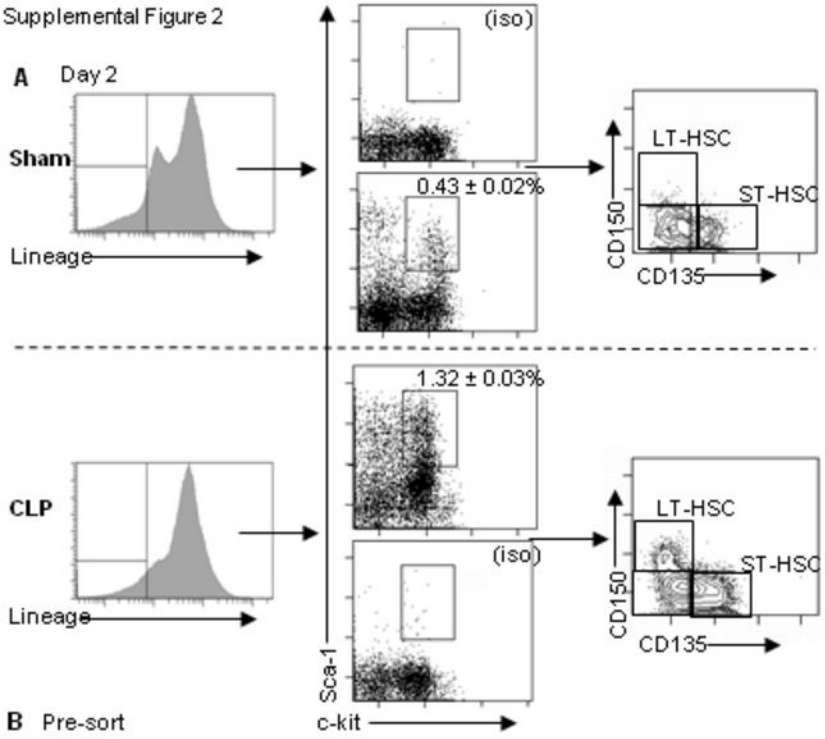
for H&E staining. All micrographs are 100x magnification. **A)** At 12 hours, there is increased dilatation of BM vasculature and increased space from cell loss is beginning. **B)** By 36 hours after CLP, BM space is maximal and there is continued dilatation of the BM vasculature. **C)** 96 hours after CLP, there is continued BM space but the BM vasculature has returned to normal. **D)** By Day 7, the BM has completely regained cellularity with dramatically increased myeloid elements. **E)** Time course of the total BM cellularity following sham or CLP * $p<0.05$ control vs treatment by Student's t-test. Experiments were performed three independent times with at least n=3 per group. Figure represents data from one experiment.

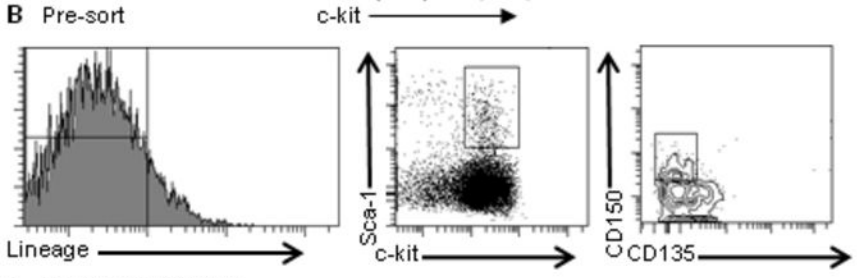
**Supplemental Figure 7. Expansion of total cell numbers in response to CLP or *S. aureus* from selected experiments.** Total cell counts for LSK, LT-HSC, and ST-HSCs were calculated. **A)** Total cell number expansion of LT-HSC and ST-HSC in Sham and CLP treated WT (C57BL/6) mice, 36 hours after surgery (experiment from Figure 1 B and C). **B)** Total cell number expansion of LSK, LT-HSC and ST-HSC in WT, $MyD88^{-/-}$ and $TRIF^{-/-}$ mice 36 hours after Sham or CLP (experiment from Figure 2B). C) Total cell number expansion of LSK, LT-HSC and ST-HSC in WT versus $MyD88^{-/-}TRIF^{-/-}$ (DKO) mice 36 hours after IV infection with $5x10^6$ SA (experiment from Figure 2D). D) Total cell number expansion of LSK, LT-HSC and ST-HSC in $Rag1^{-/-}$ mice 36 horus after IV infection with $5x10^6$ SA (experiment from Figure 2E). * $p<0.05$, ∓ $p<0.001$ by Student's t test or one way ANOVA.

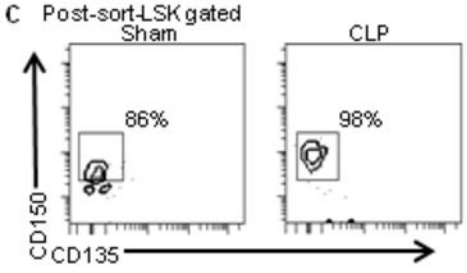
Supplemental Figure 1

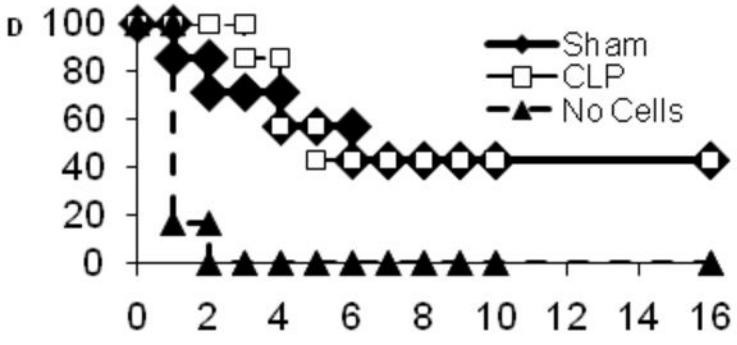


Supplemental Figure 2



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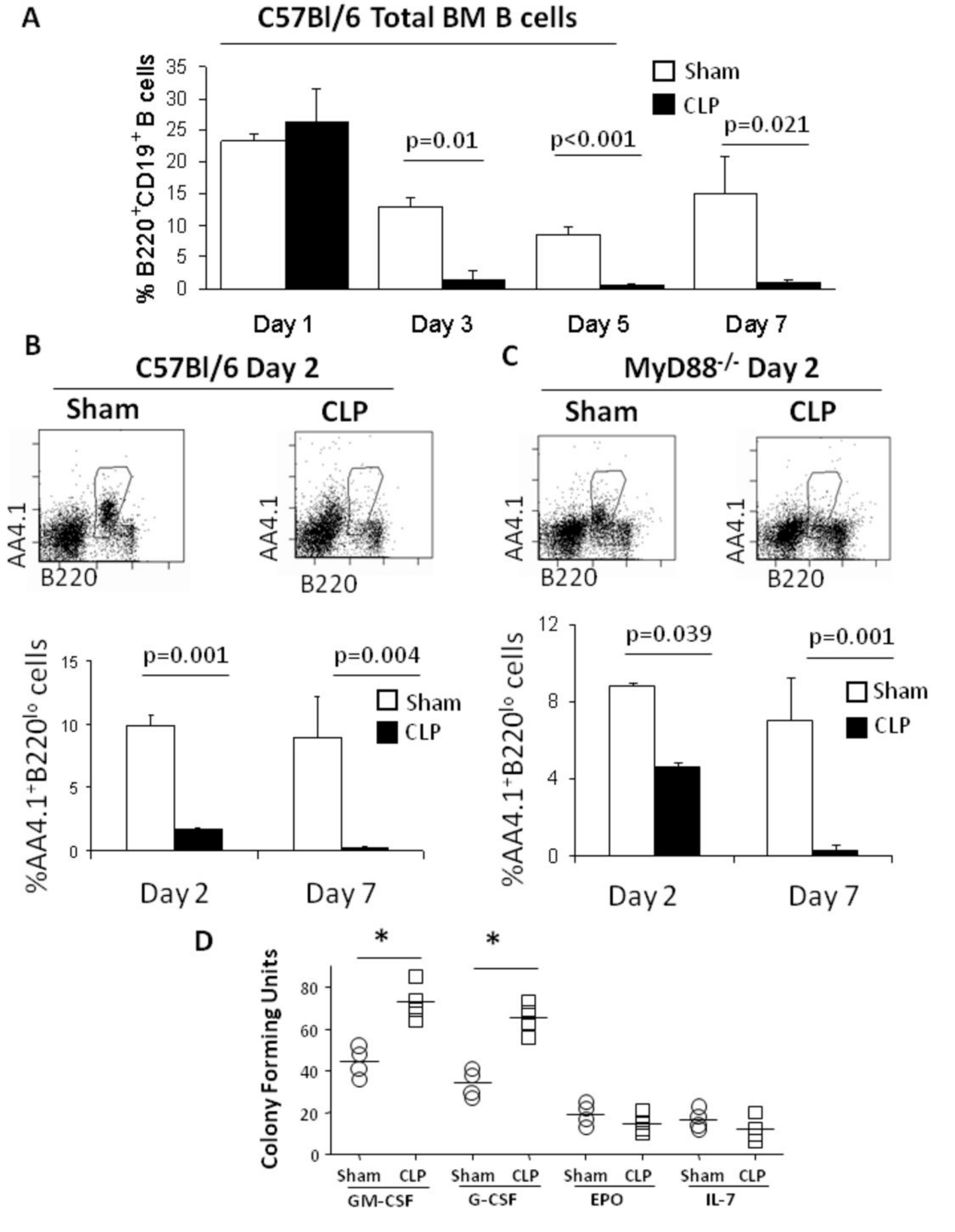

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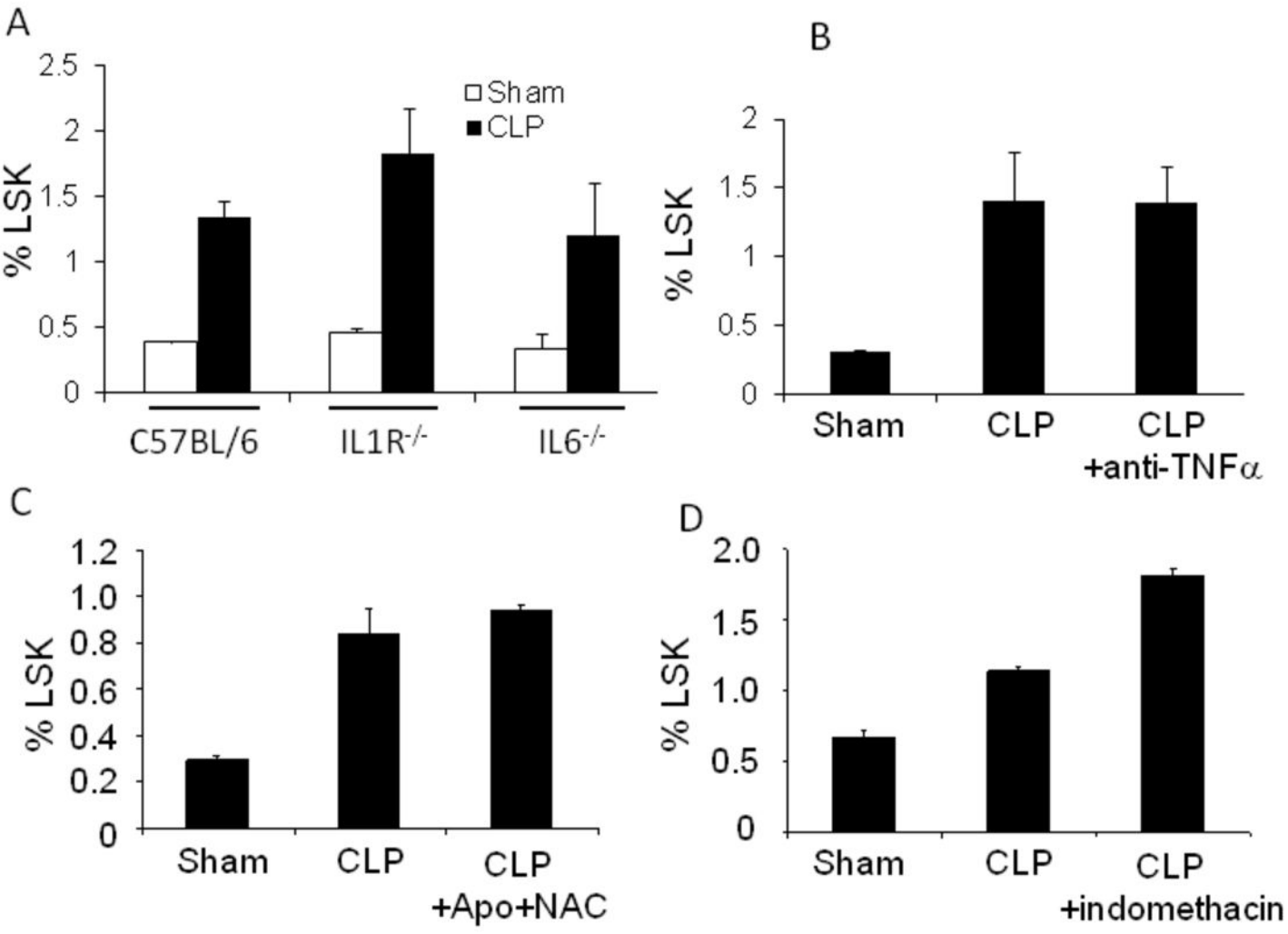

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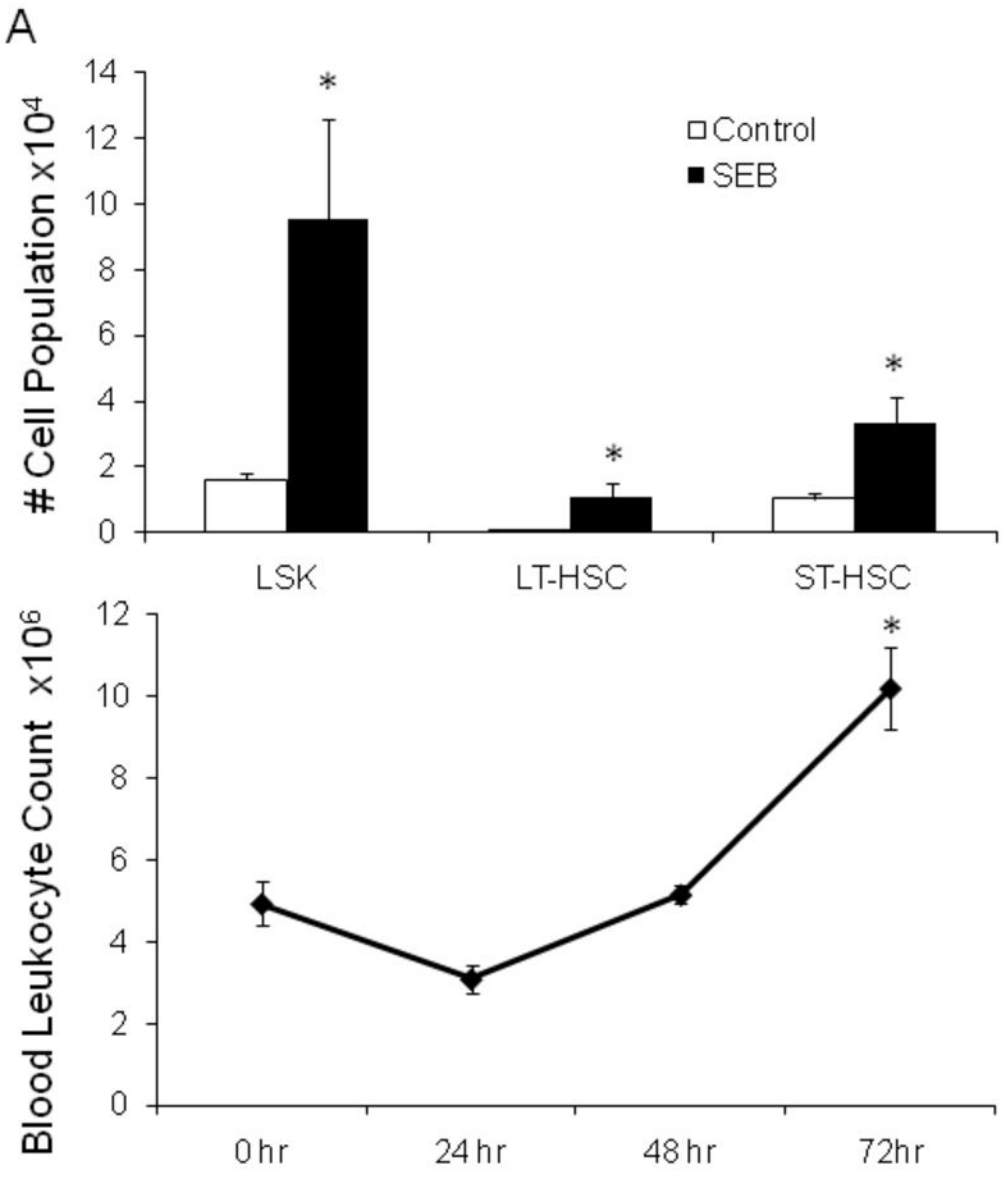
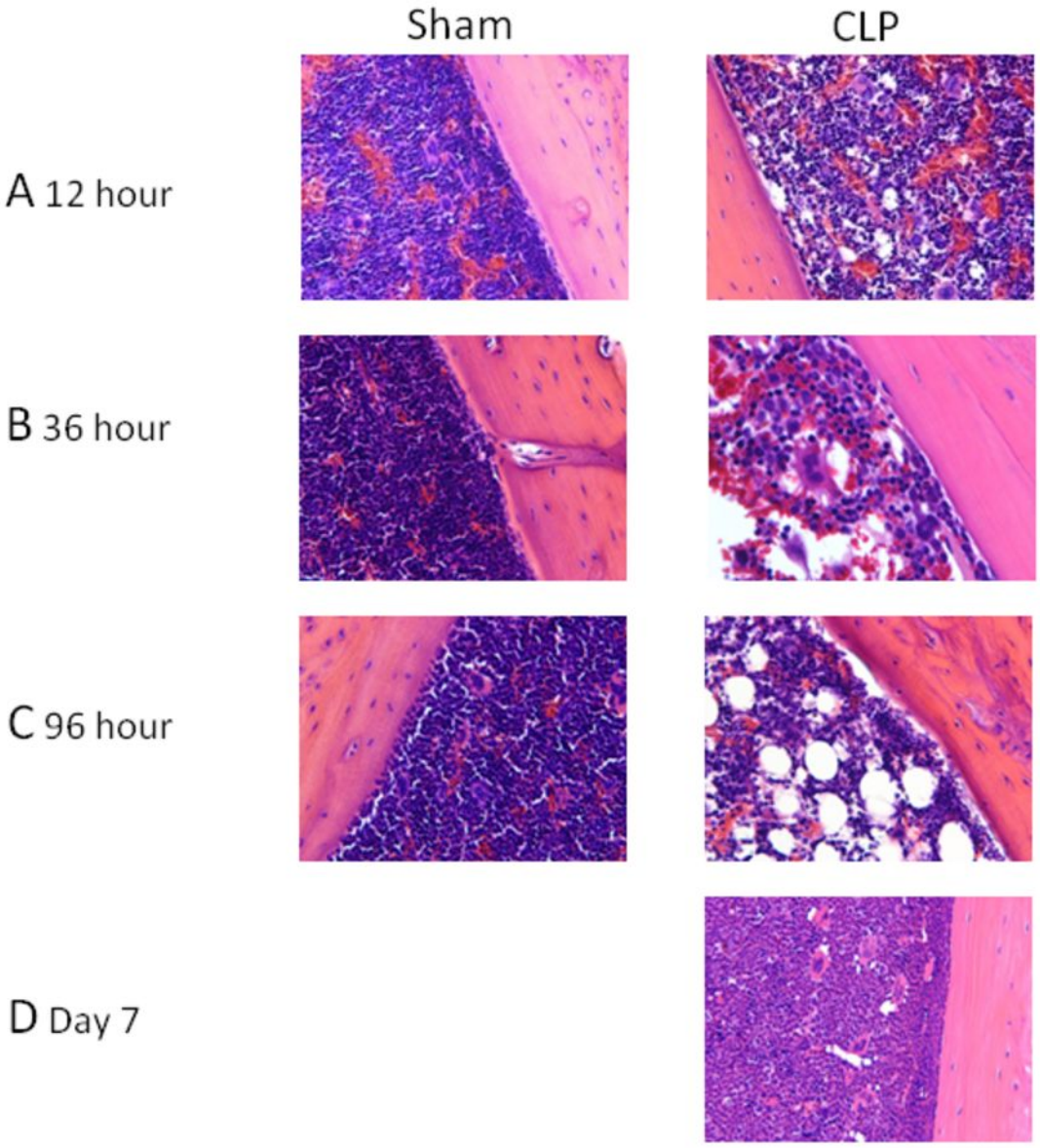
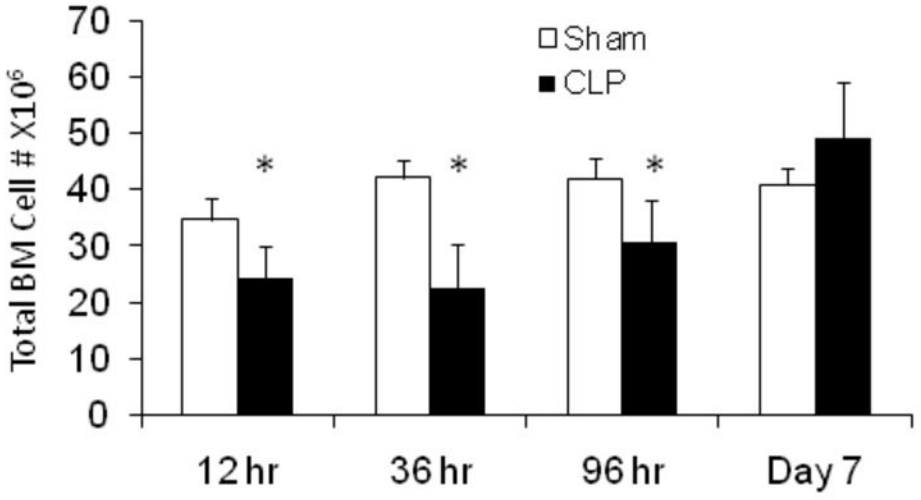


Supplemental Figure 6



Supplemental Figure 7