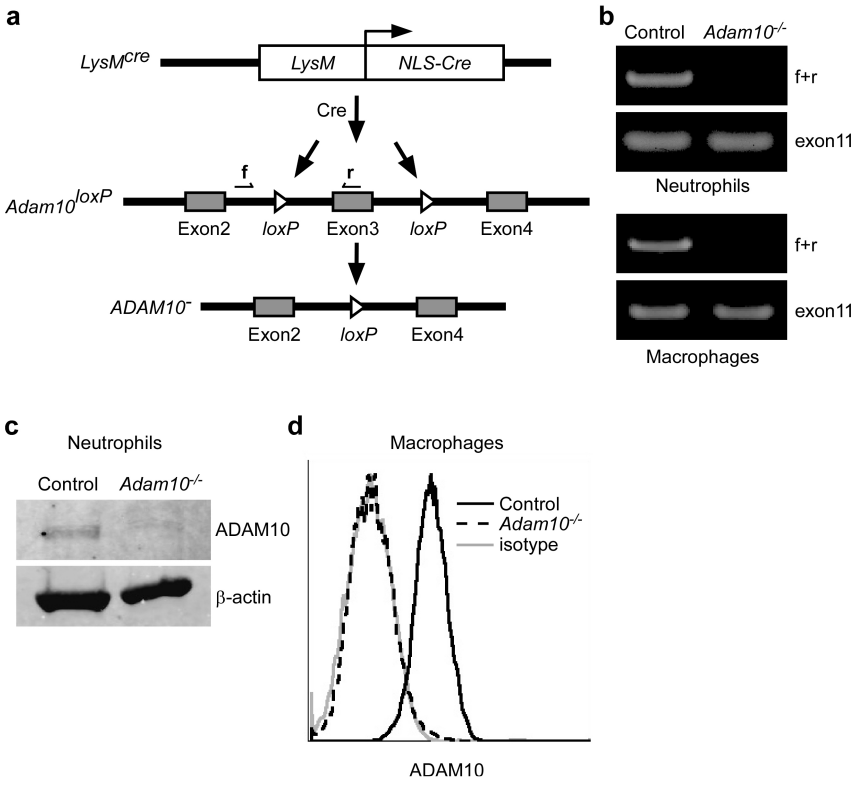
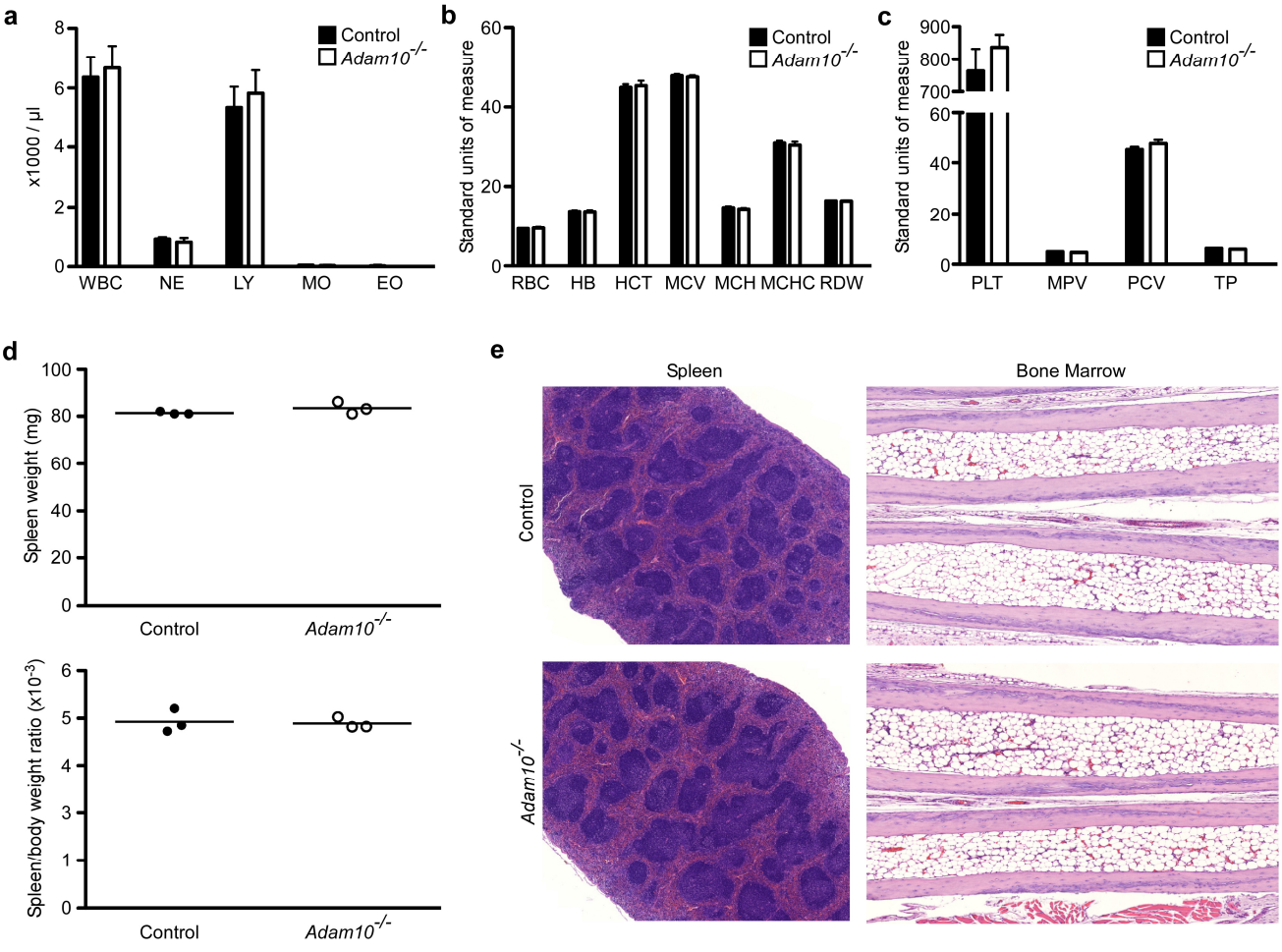
Online Suppl. Fig. 1



Online Suppl. Fig. 1. Generation and analysis of myeloid-lineage specific ADAM10 conditional knockout mice. (**a**) Schematic demonstrating the breeding strategy to derive mice harboring deletion of *Adam10*$^{-/-}$ in the myeloid hematopoietic lineage under the control of the *LysM* promoter. Labels "f" and "r" indicate sites of forward and reverse PCR primers utilized to document Cre recombinase-dependent excision of exon 3 in (**b**). (**b**) PCR-based analysis performed on genomic DNA from primary Gr-1$^+$ neutrophils and bone marrow-derived macrophages to demonstrate excision of exon 3 in mice harboring the *LysM*^{cre} *ADAM10*$^{loxP/loxP}$ genotype (*Adam10*$^{-/-}$). A control PCR product was generated from exon 11 of the *Adam10* gene to document integrity of the genomic DNA prepared from *Adam10*$^{-/-}$ mice. (**c**) Western blot analysis performed on lysates prepared from primary Gr-1$^+$ neutrophils harvested from control and *Adam10*$^{-/-}$ mice to document loss of neutrophil ADAM10 expression. (**d**) Flow cytometric analysis of ADAM10 expression on the surface of bone marrow-derived macrophages from control and *Adam10*$^{-/-}$ mice to document loss of macrophage ADAM10 expression.

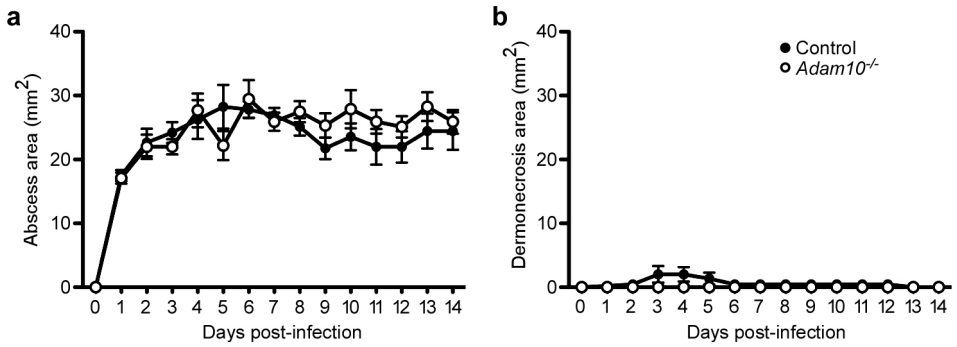
Online Suppl. Fig. 2



Online Suppl. Fig. 2. Myeloid lineage *Adam10*$^{-/-}$ mice display normal hematopoiesis. (**a**-**c**) Complete peripheral blood count analysis from 7-week old female control (black bars) or *Adam10*$^{-/-}$ (white bars) mice. (**a**) Differential white blood cell counts in thousands per microliter; WBC, total white blood cells; NE, neutrophils; LY, lymphocytes; MO, monocytes; EO, eosinophils. (**b**) Erythrocyte counts and indices in control and *Adam10*$^{-/-}$ mice: RBC, total erythrocyte counts in millions per microliter; HB, total hemoglobin in grams per deciliter; HCT, hematocrit; MCV, mean corpuscular volume in femtoliters; MCH, mean corpuscular hemoglobin in picograms; MCHC, mean corpuscular hemoglobin concentration in grams per deciliter; RDW, red cell distribution width. (**c**) Platelet counts and indices in control and *Adam10*$^{-/-}$ mice: PLT, total platelet counts in thousands per microliter; MPV, mean platelet volume in femtoliters; PDW, platelet distribution width; PCV, packed cell volume; TP, total protein. (**d**)

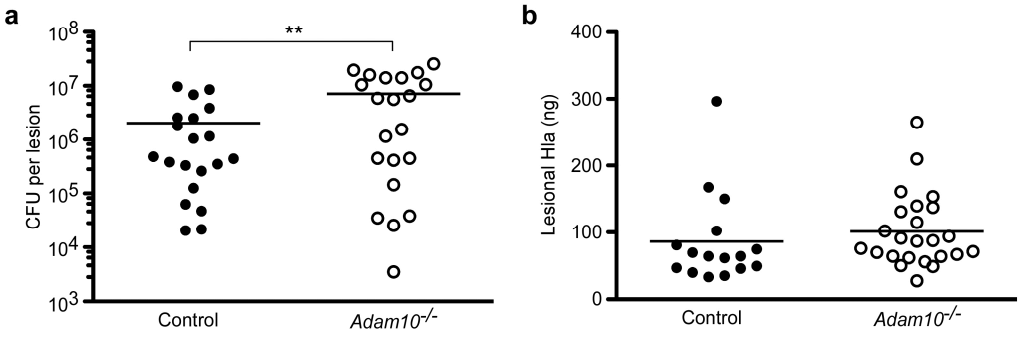
Spleens from 16- to 20-week-old female mice were weighed and compared to body weight to test for splenomegaly. (**e**) Architecture and cellularity of the spleen and metatarsal marrow compartment were evaluated by hematoxylin and eosin staining of samples harvested from adult control and *Adam10*$^{-/-}$ mice.

Online Suppl. Fig. 3.



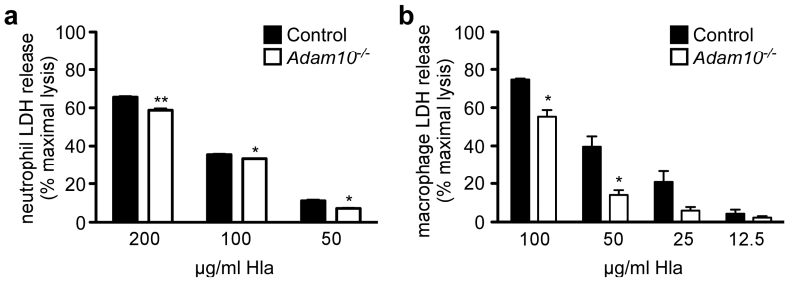
Online Suppl. Fig. 3. Lesion size phenotype of *Adam10*$^{-/-}$ mice is dependent on Hla-ADAM10 toxin-receptor interaction. Control and *Adam10*$^{-/-}$ animals were infected subcutaneously with 1.5x10^{7} CFU of the Hla-deficient isogenic USA300/LAC mutant *S. aureus hla::erm*, and areas of abscesses (**a**) and dermonecrosis (**b**) were monitored as in figure 1 ($p>0.05$ for all days in both (**a**) and (**b**), analyzed by Student's t-test).

Online Suppl. Fig. 4.



Online Suppl. Fig. 4. Aggregate data from multiple replicate experiments corresponding to Figure 1d and 1e. (**a**) Pooled CFU recovery data from three experiments in which skin lesions were harvested 7 days post-infection as in Figure 1d (**p<0.01, analyzed by Student's t-test). (**b**) Pooled lesional Hla data from two experiments in which skin lesions were harvested 24 hours post-infection as in Figure 1e (p=0.45, analyzed by Student's t-test).

Online Suppl. Fig. 5.



Online Suppl. Fig. 5. Primary murine neutrophils and macrophages resist lytic injury by Hla. Primary neutrophils (**a**) and bone marrow-derived macrophages (**b**) were treated with varying concentrations of Hla and resulting cytotoxicity was measured by LDH release assay performed after 3 hours of toxin treatment. Quantification represents percentage of a detergent lysis control for the indicated cell type (*$p<0.05$, **$p<0.01$, analyzed by Student's t-test).