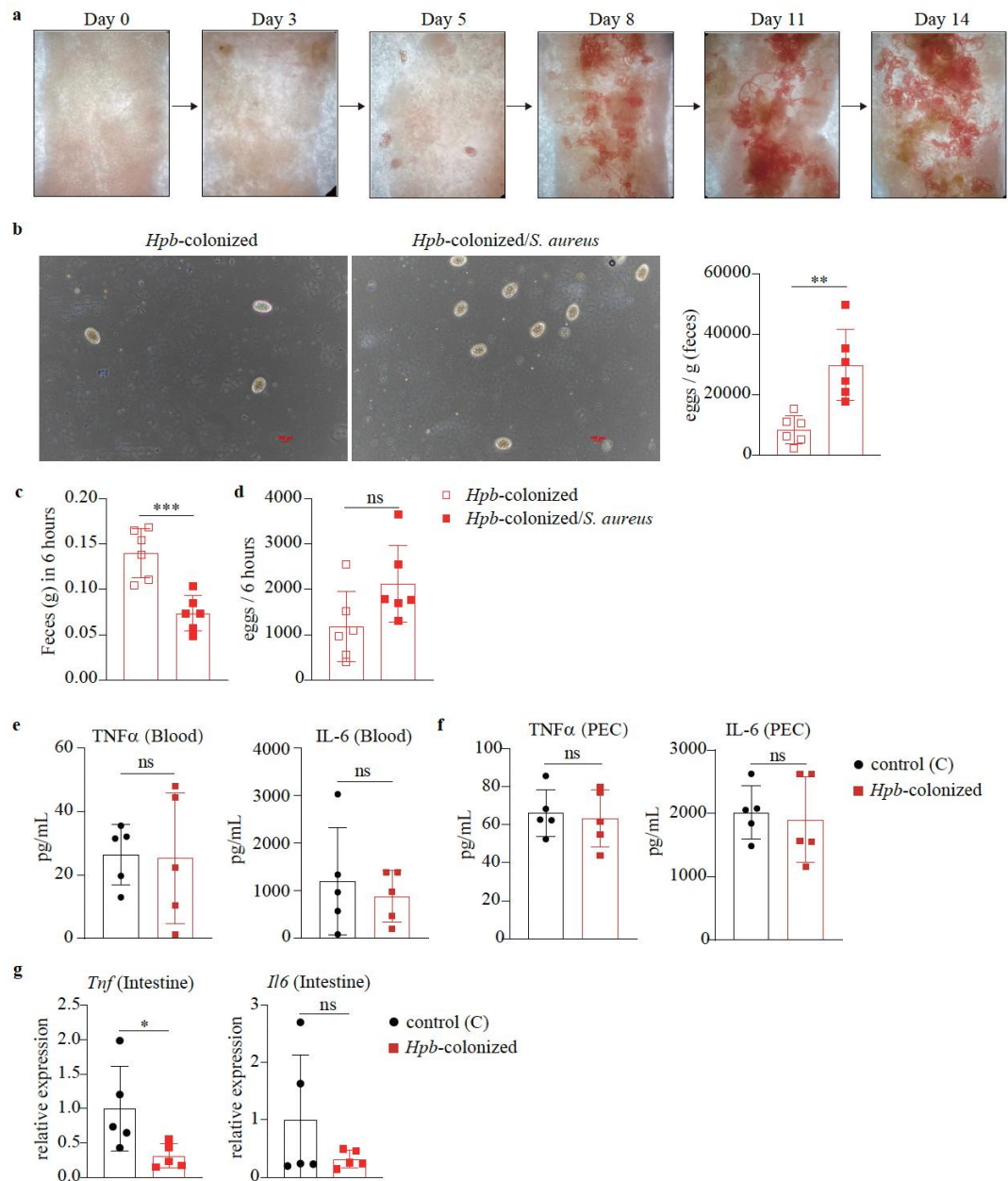
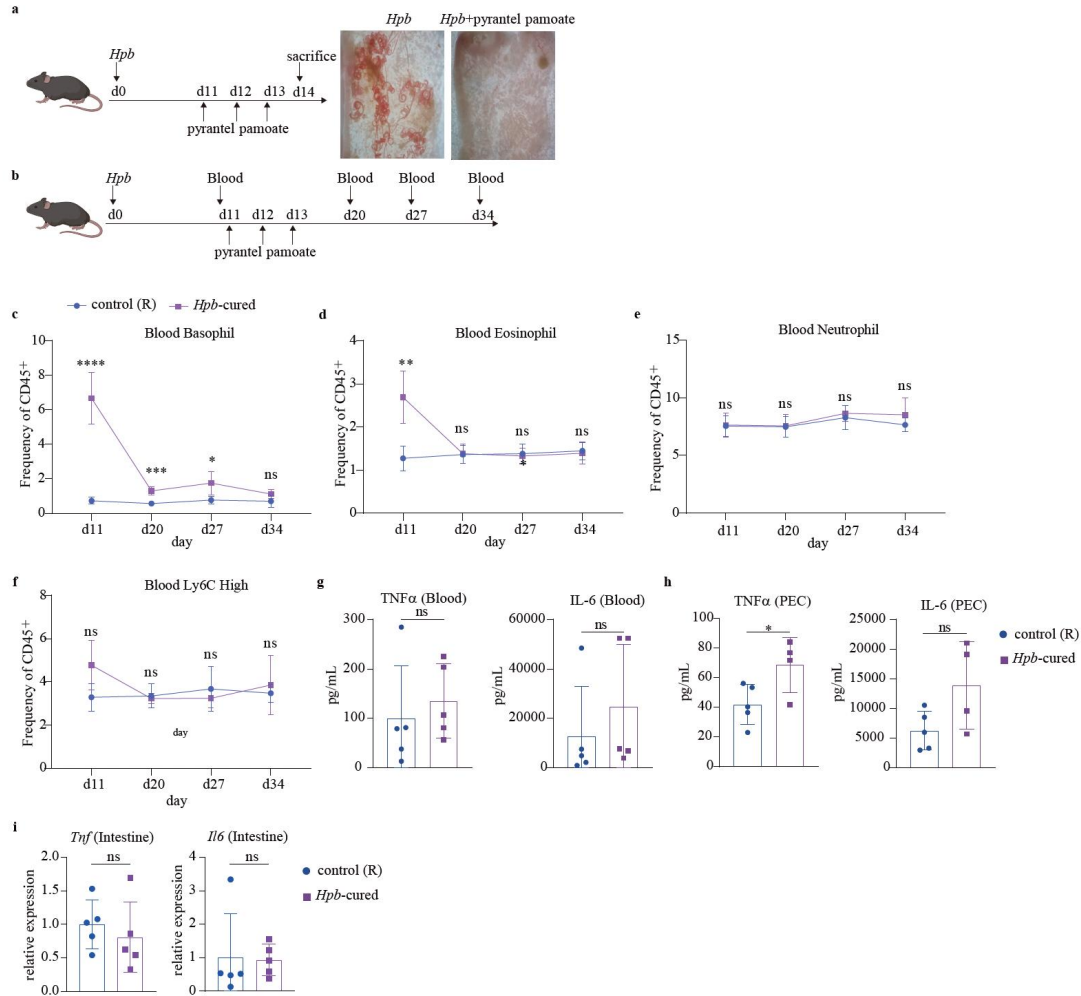


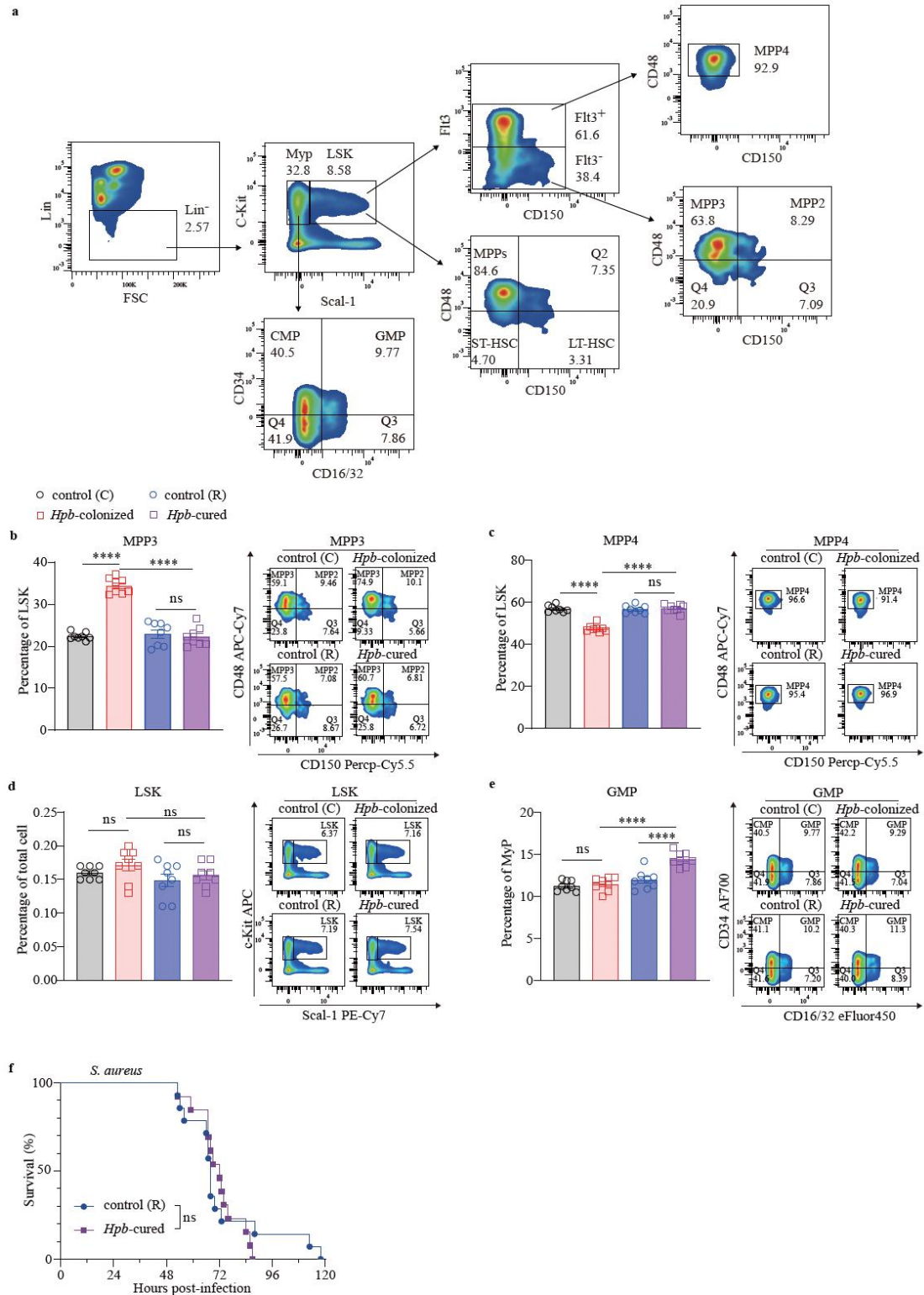


Extended Data Fig. 1 *Hpb* administration unaffecteds the levels of TNF α and IL-6 post *S. aureus* challenge. **a**, Representative images illustrating the presence of adult worms within the duodenal lumen at specified time points following *Hpb* infection. **b–d**, Fecal pellets were collected over a 6 h period from *Hpb*-only-infected and coinfected mice then weighed (**c**). The representative images of *Hpb* eggs were showed (**b**, left panel) and *Hpb* eggs per gram of feces (**b**, right panel) were determined. The estimated total number of eggs (**d**) produced during the feces collection period was determined. Student's *t* test, ns $p > 0.05$; ** $p < 0.01$; *** $p < 0.001$; $n = 6$ mice per group. Data are pooled from two independent experiments. **e**, **f**, The concentrations of TNF α and IL-6 in both blood (**e**) and peritoneal cavity (**f**) were measured using ELISA following 16 hours of stimulation with 5×10^3 CFU *S. aureus* in mice, either infected or uninfected with *Hpb*. Student's *t* test, ns $p > 0.05$; $n = 5$ per group. Representative data were shown. **g**, Intestinal *Tnf* and

Il6 mRNA levels were assessed in *Hpb*-colonized and control (C) mice following *S. aureus* challenge for 16h. Student's *t* test, ns $p > 0.05$; $*p < 0.05$; $n = 5$ mice per group. Representative data were shown.

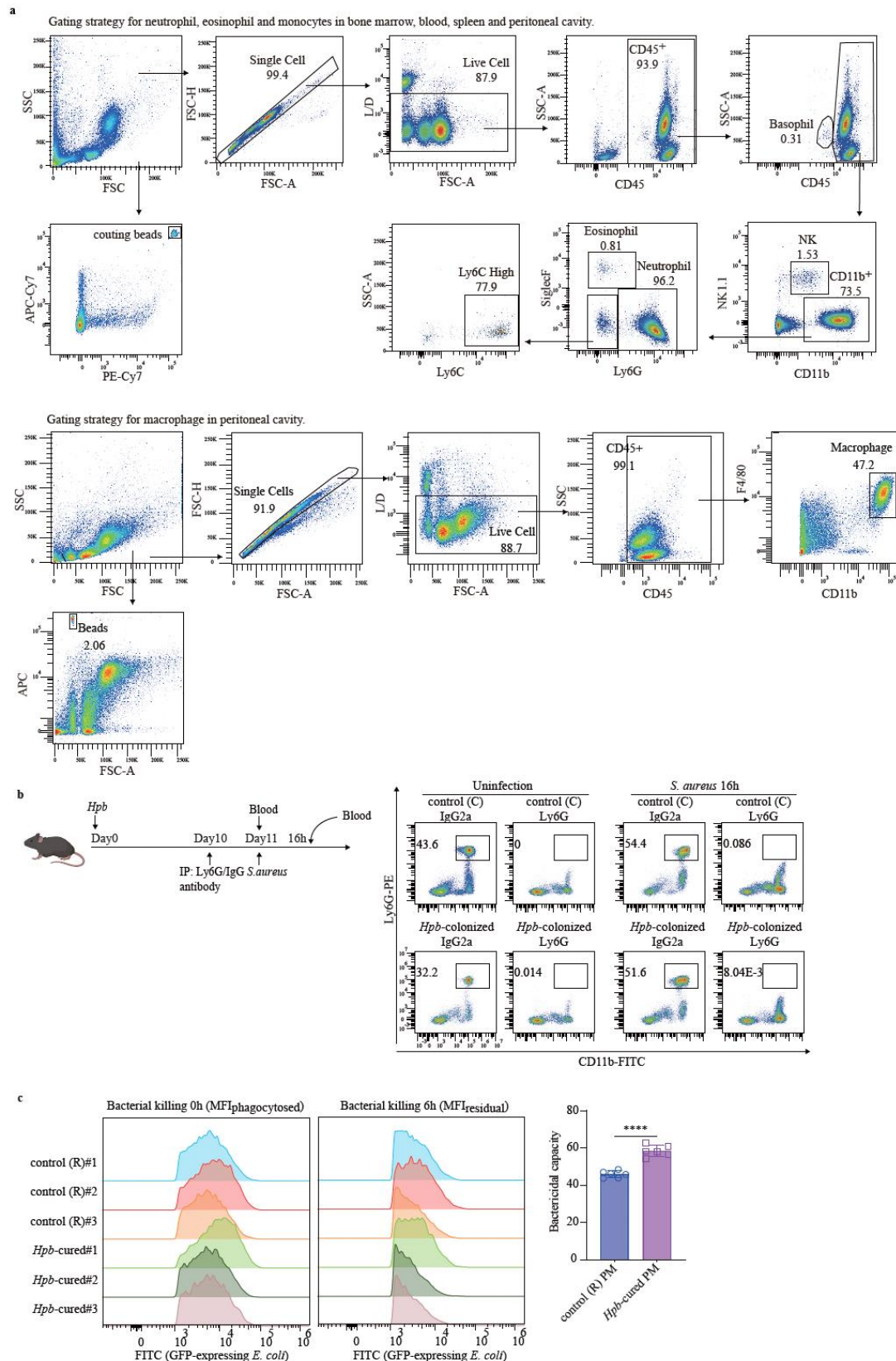


Extended Data Fig. 2 Th2 response in the peripheral blood of *Hpb*-colonized mice restores to homeostasis after receiving anthelmintic treatment and a subsequent 3-week rest period. **a**, The experimental setup of anthelmintic treatment (left). Representative images within duodenal lumen confirming the deworming capacity after administration with anthelmintic (right). **b**, Experimental workflow for blood harvest via tail vein in dewormed mice. **c-f**, The frequencies of basophils (**c**), eosinophils (**d**), neutrophils (**e**) and Ly6C high monocytes (**f**) in blood of mice following *Hpb* infection and deworming treatment at respective time points. Data are mean ± SD. Student's t test, ns $p > 0.05$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$; n=5 per group. Data are from one representative experiment. **g, h**, TNFα and IL-6 concentrations in blood (**g**) and peritoneal cavity (**h**) were determined after 16 hours of infection with 5×10^3 CFU *S. aureus*, in the presence or absence of *Hpb* exposure. Student's t test, ns $p > 0.05$; n=5 per group. Data are from one representative experiment. **i**, Intestinal *Tnf* and *Il6* mRNA levels were assessed in *Hpb*-cured and control (R) mice following *S. aureus* challenge for 16h. Student's t test, ns $p > 0.05$; n=5 mice per group. Data are from one representative experiment.



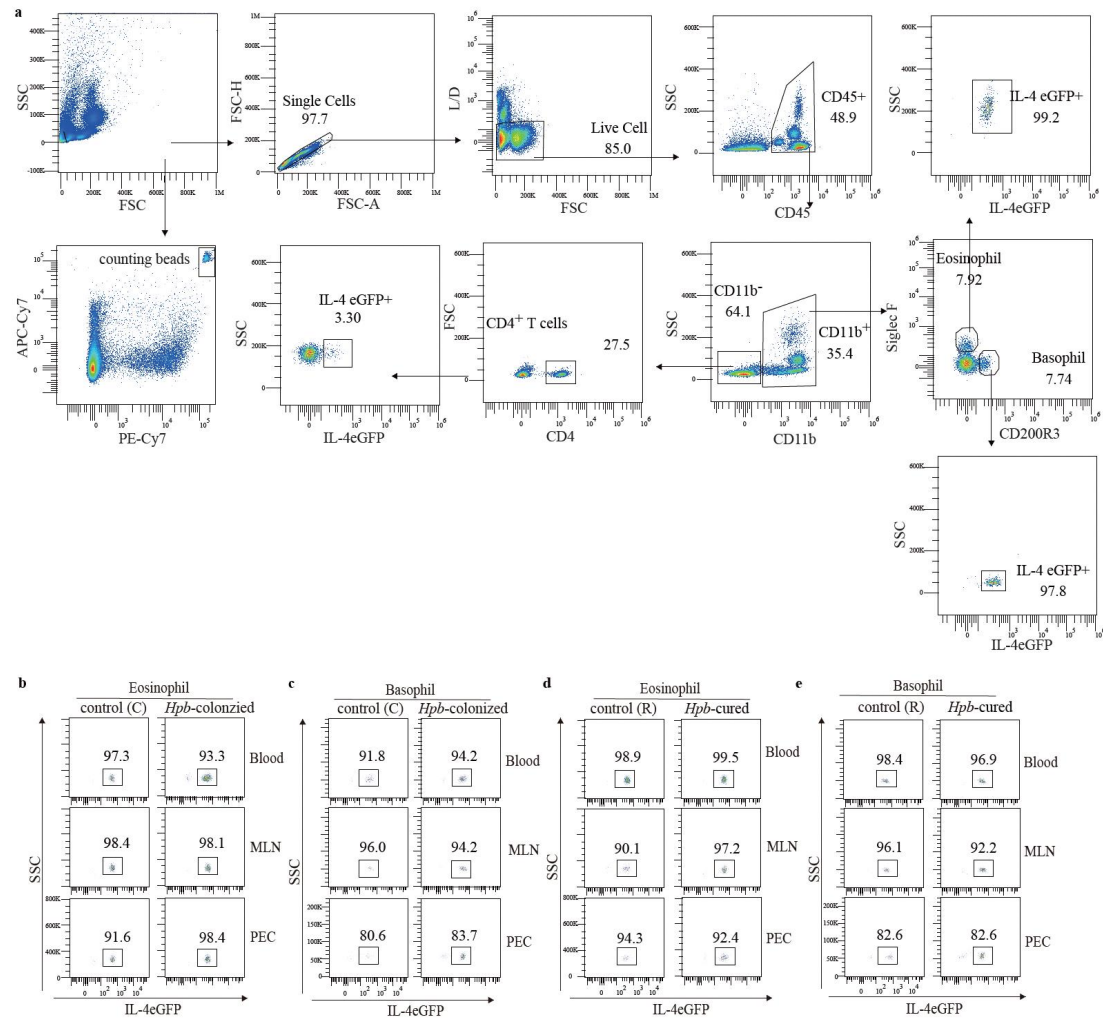
Extended Data Fig. 3 *Hpb* infection results in biased myelopoiesis. **a**, The gating strategies involved in identification of hematopoietic progenitor cells. After gating for Lin⁻ cell populations, the MyP and LSK were characterized as Lin⁻cKit⁺Scal⁻ and Lin⁻cKit⁺Scal⁺, respectively. MyP were identified as CMP (CD16/32⁻CD34⁺) and GMP (CD16/32⁺CD34⁺). LSK populations were profiled as MPPs (CD48⁺CD150⁻), LT-HSC (CD48⁻CD150⁺) and ST-HSC (CD48⁻CD150⁻). LSK was further defined as

MPP2 (CD48⁺Flt3⁻CD150⁺), MPP3 (CD48⁺Flt3⁻CD150⁻) and MPP4 (CD48⁺Flt3⁺CD150⁻). **b-e**, Frequencies of MPP3 (**b**), MPP4 (**c**), LSK (**d**) and GMP (**e**) were determined. Data are expressed as mean $\pm$ SD. Student's t test, ns $p>0.05$, * $p<0.05$, **** $p<0.0001$; n=5 per group. Data are pooled from two independent experiments. Representative flow cytometry plots were shown. (**f**) After 6 weeks BMT, the recipient mice were challenged with *S. aureus* and survival ratios were determined. Log-rank test, ns $p>0.05$; n=10 per group. Data are pooled from two independent experiments.

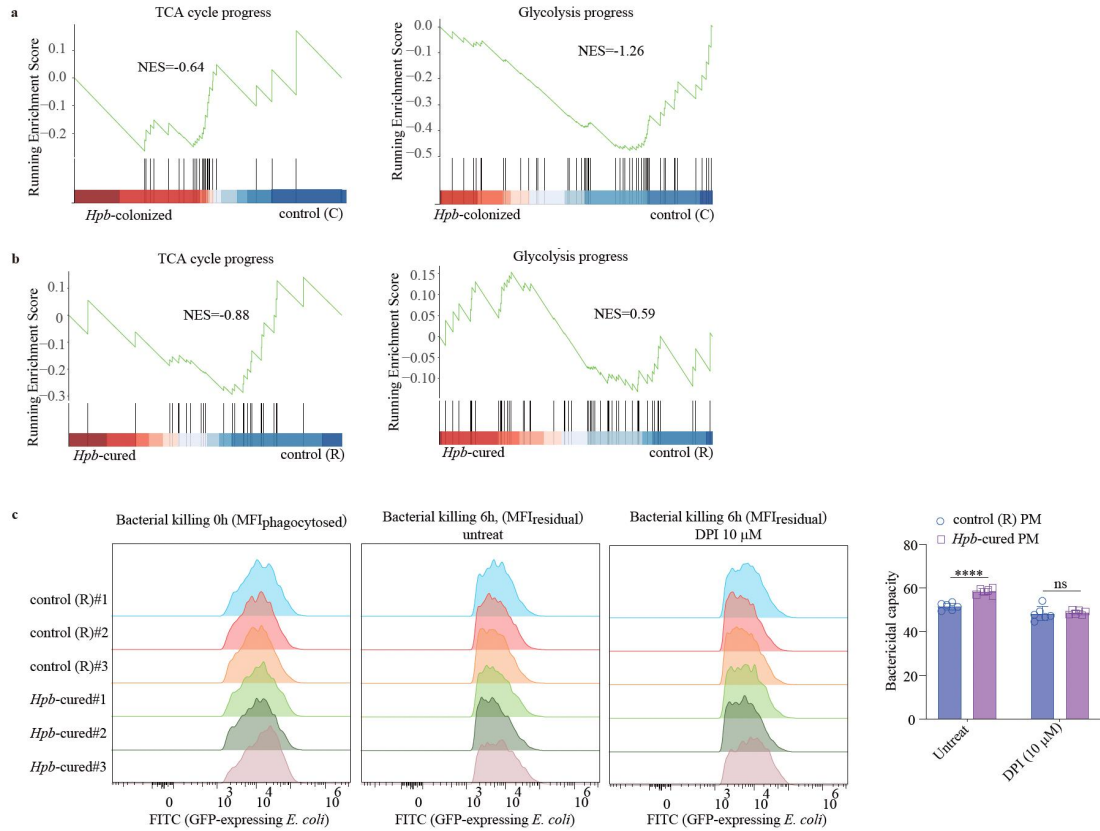


Extended Data Fig. 4 The gating strategies of innate immune cells, and the efficiency of neutrophil depletion with anti-Ly6G mAb. **a**, The gating strategies of innate immune cell populations in peripheral circulation system and tissues. **b**, The

workflow of collecting peripheral blood for validating the neutrophils depletion efficiency. *Hpb* colonized or control (C) mice were intraperitoneally administrated with anti-Ly6G mAb and rat IgG2a at 10 days. After 24 hours, these mice were challenged with *S. aureus*. The peripheral blood was collected both before and post infection 16 hours, respectively. Representative flow cytometry plots for identifying neutrophil depletion efficiency. **c**, Sorted peritoneal macrophages either from control (R) or *Hpb*-cured mice were cocultured with GFP-labelled *E.coli* and then in vitro bactericidal assay were performed. Student's t test, ns $p>0.05$, **** $p<0.0001$, n=6 per group. Data are pooled from two independent experiments (right panel). Representative flow cytometry plots were shown (left panel).



Extended Data Fig. 5 The expression of IL-4 in eosinophils and basophils were unmediated by *Hpb* colonization and training. **a**, The gating strategies of CD4⁺ T cells and IL-4eGFP⁺ immune cell populations in blood, MLN and peripheral cavity. **b-e**, The blood, spleen, MLN and peritoneal fluids in 4get mice with *Hpb* colonization or training were harvested, then the proportion of IL-4eGFP⁺ in eosinophils (**b**, **d**) and basophils (**c**, **e**) were determined. Representative flow cytometry plots from three independent experiments were shown.



Extended Data Fig. 6 Glycolysis and TCA cycle pathways were undisturbed by *Hpb* colonization and training. **a**, GSEA of RNA-Seq signals of genes related to glycolysis and TCA cycle process in *Hpb* colonized and its control (C) group. **b**, GSEA of RNA-Seq signals of genes related to glycolysis and TCA cycle process in *Hpb*-cured and its control (R) group. **c**, In vitro bactericidal assays were performed with or without DPI treatment in peritoneal macrophages sorted from control (R) and *Hpb*-cured mice. Student's t test, ns $p>0.05$, **** $p<0.0001$, $n=6$ per group. Data are pooled from two independent experiments (right panel). Representative flow cytometry plots were shown (left panel).