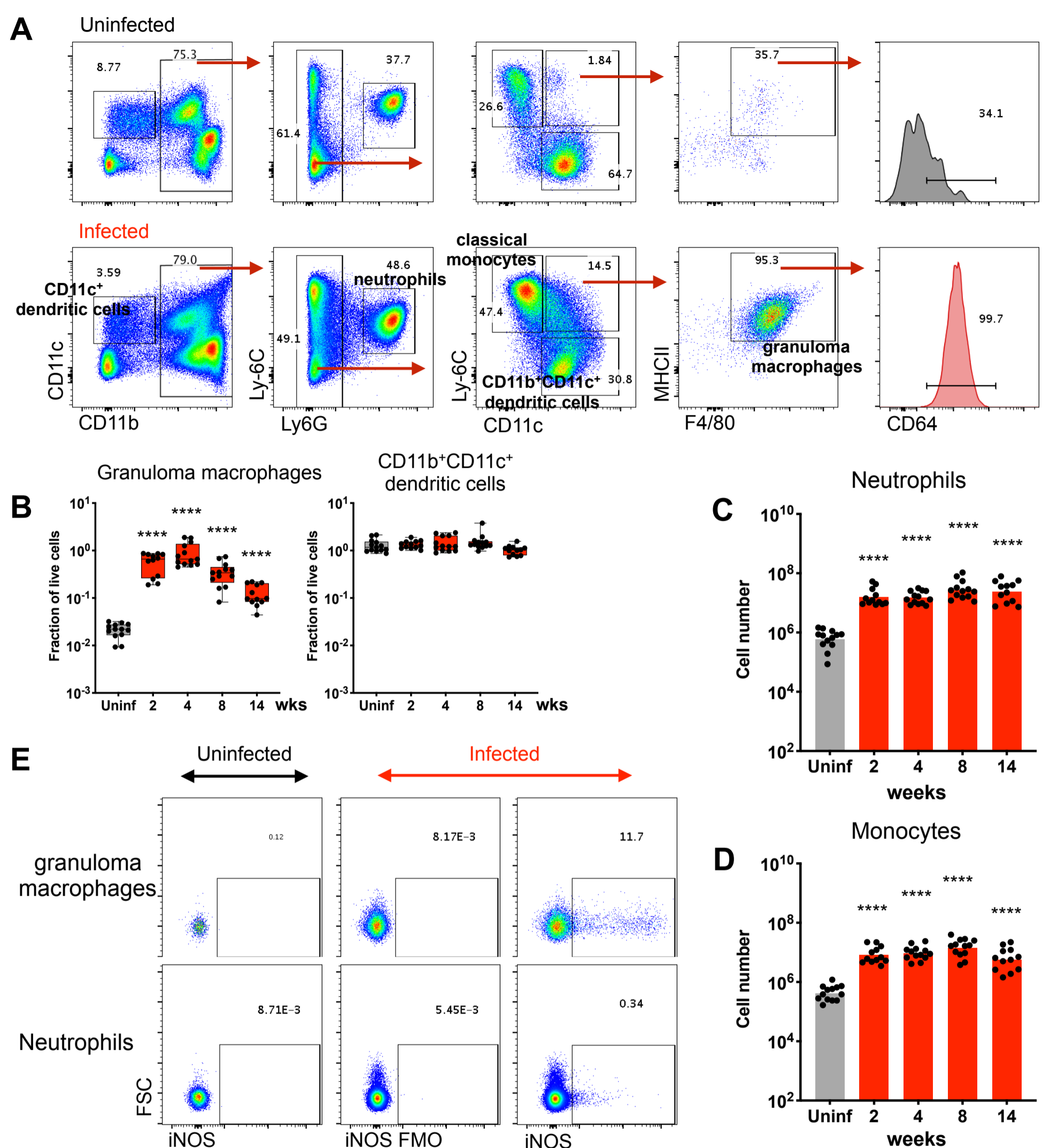
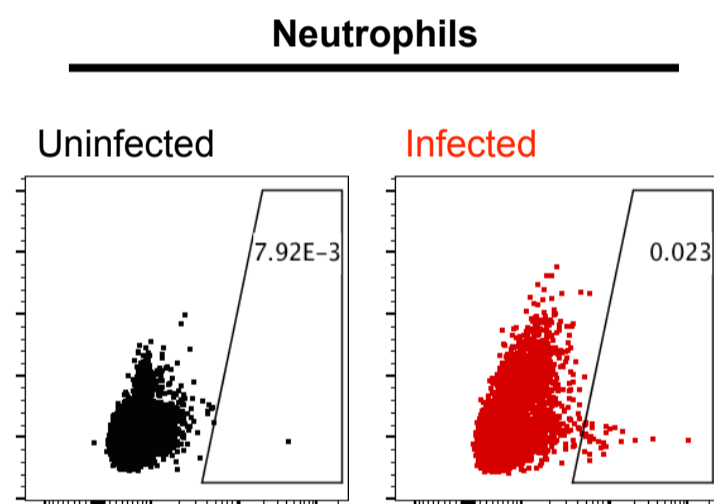
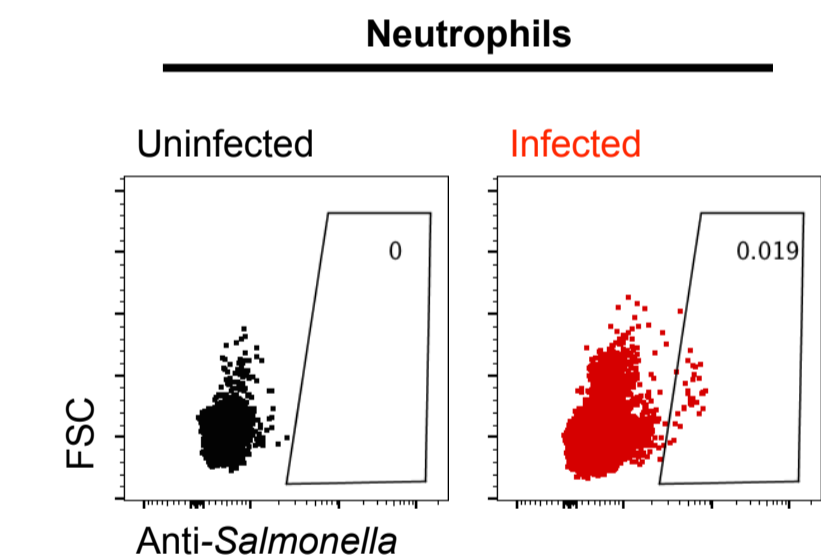
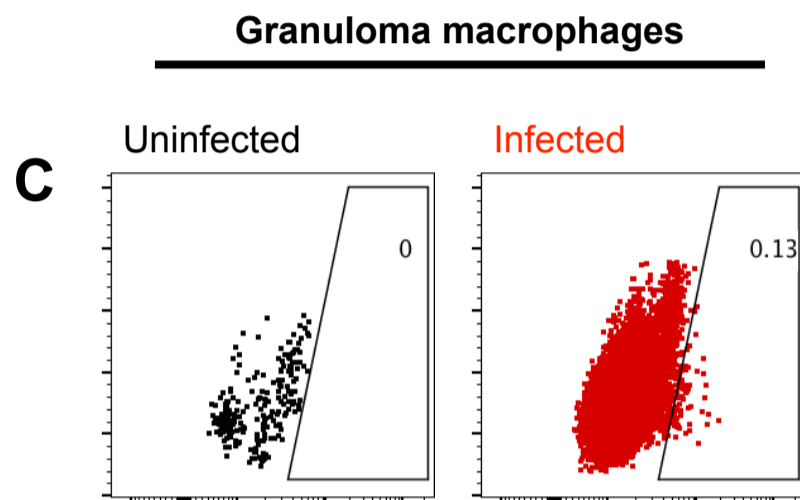
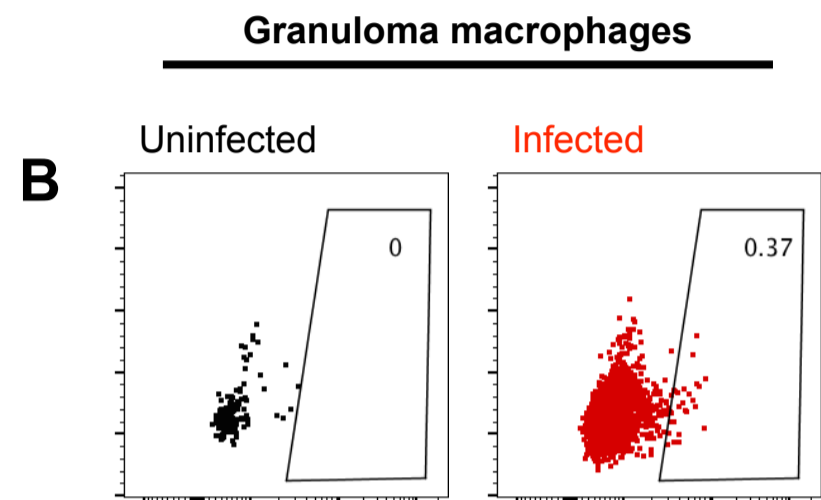
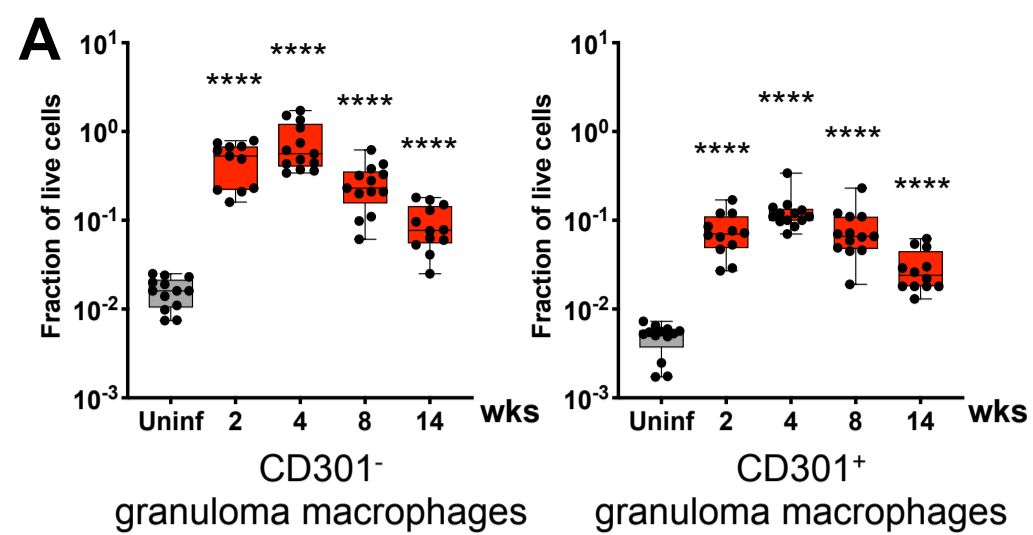


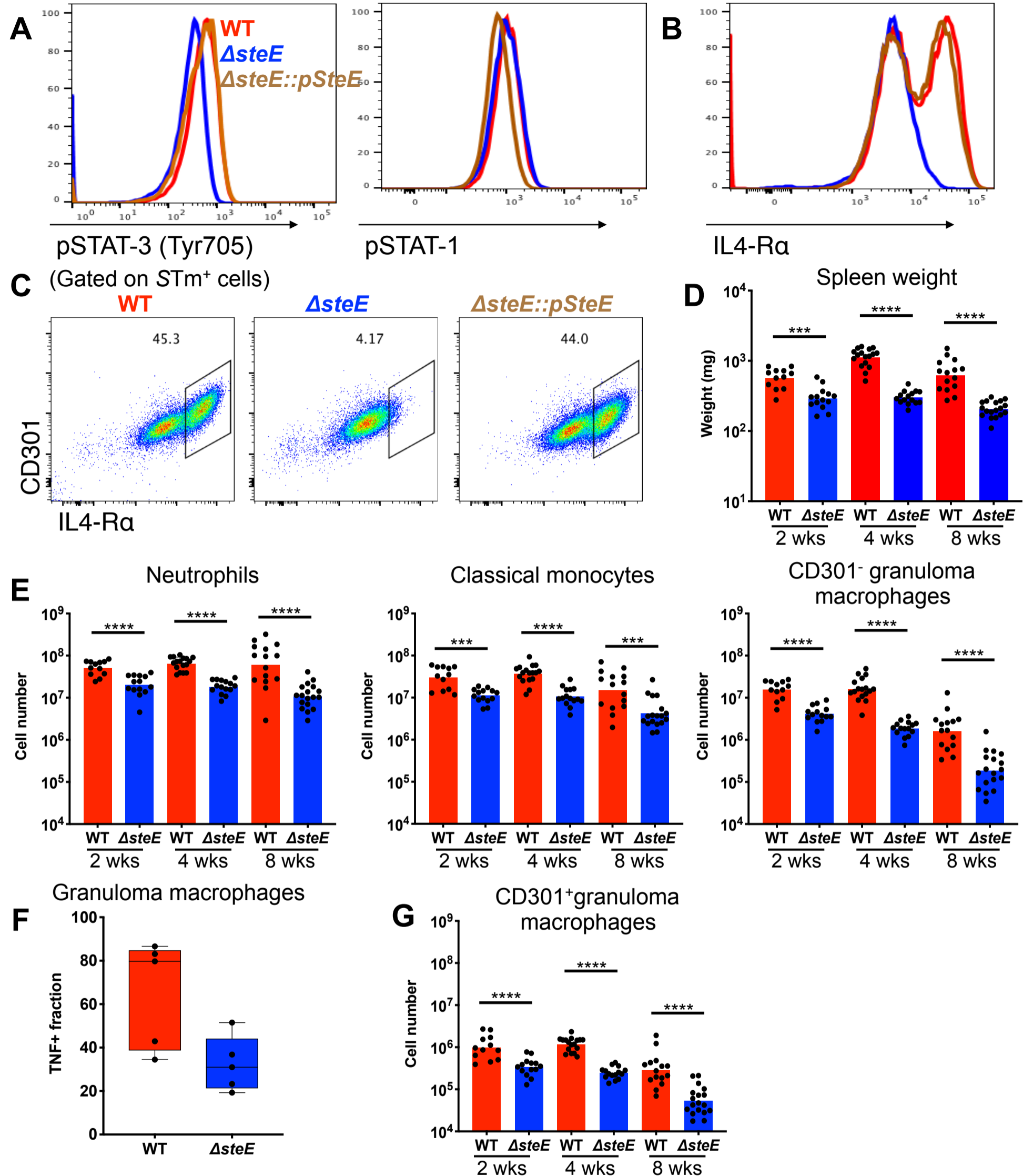
**Figure S1. Related to Figure 1:** (A) Gating scheme for quantitation of antigen experienced, IFN $\gamma$ <sup>+</sup> CD4<sup>+</sup> T cells in STm infected spleens. Samples were gated for size/scatter, living, and singlet population then further gated as displayed. Analysis of mice at 4 weeks post-infection shown. (B-C) Additional confocal microscopy showing immune cellular organization of splenic of STm granulomas. Analysis of 1 to 3-month infected animals shown. Scale bar: 50  $\mu$ m. White boundaries demarcate granulomas. Arrows indicate admixed neutrophils within granuloma.  $n > 10$ , multiple sections per mouse.



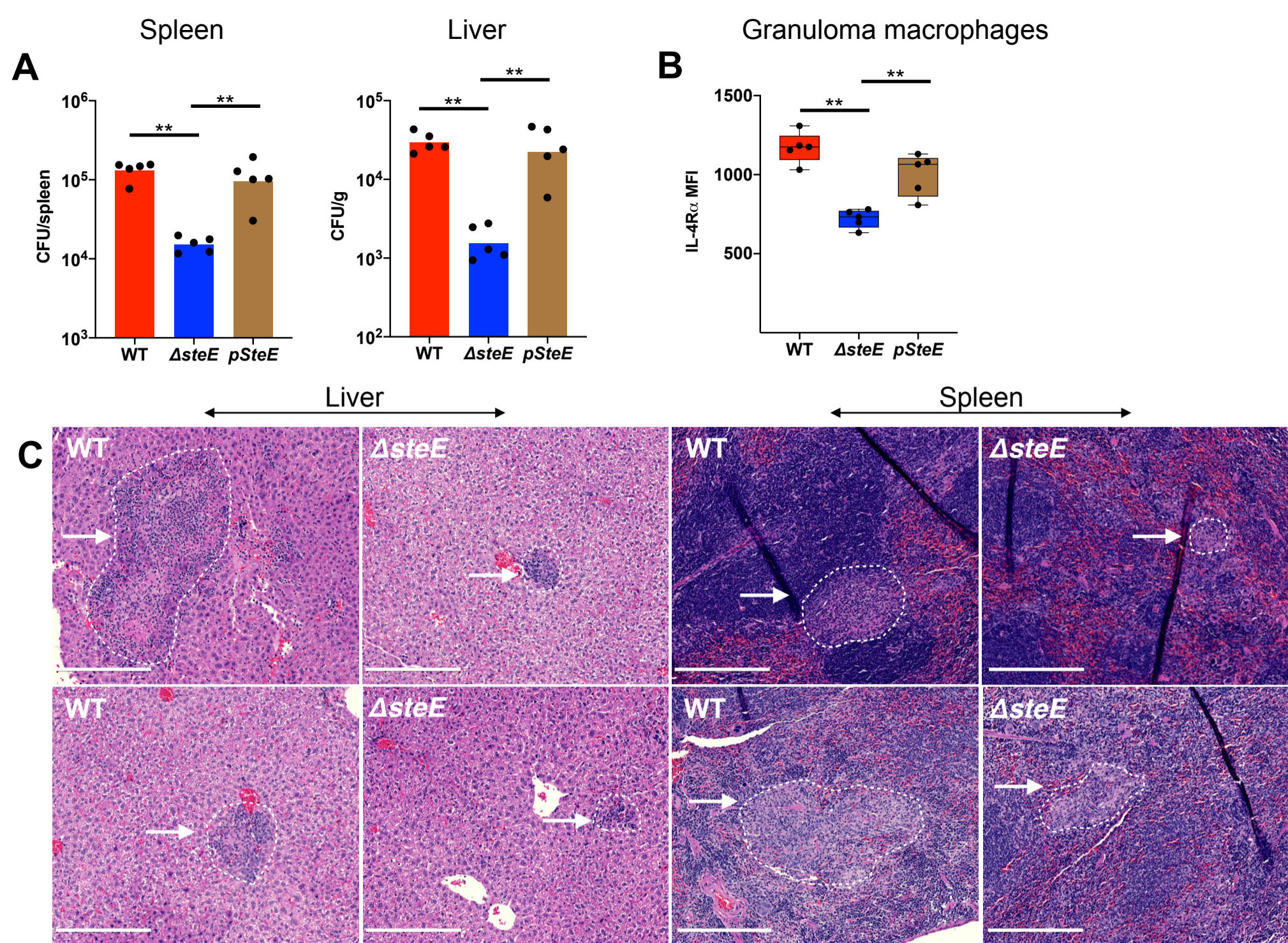
**Figure S2. Related to Figure 2:** (A) Gating scheme to identify and quantify CD11b<sup>+</sup>CD11c<sup>+</sup>Ly6C<sup>+</sup> granuloma macrophages. Samples were gated for size/scatter, living, and singlet population then further gated as displayed. Analysis of mice at 4 weeks p.i. shown. (B) Frequencies of granuloma macrophages and CD11b<sup>+</sup>CD11c<sup>+</sup> dendritic cells, as gated in S2A, in uninfected and infected spleens at indicated time points p.i. (C-D) Quantitation of neutrophils (C) and classical monocytes (D) in uninfected and infected spleens at indicated time points p.i. Bars: geometric means; dots: individual mice. Significance derived from comparing infected animals at each time point to uninfected animals. (E) Examples of endogenous iNOS staining among myeloid cells from uninfected and STm infected spleens by flow cytometry. Granuloma macrophages and neutrophils were gated as in S2A and examined for iNOS expression as shown. FMO: fluorescence-minus-one staining control. Significance calculated using a two-tailed Mann-Whitney test. \*\*\*\* p < 0.0001. A-E, at least 3 independent experiments, 4-5 mice per group per experiment.



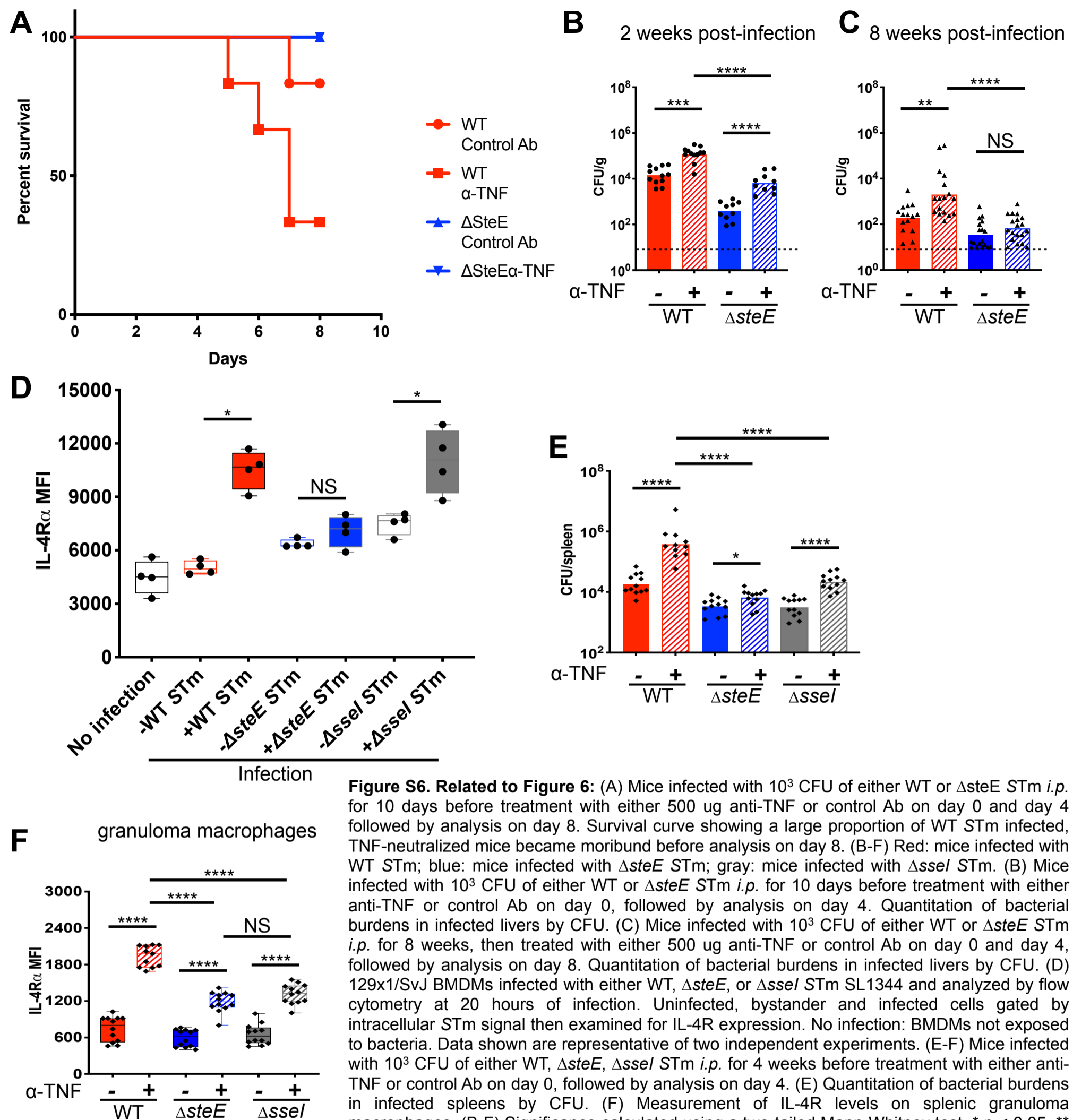
**Figure S3. Related to Figure 3:** (A) Frequencies of CD301<sup>-</sup> and CD301<sup>+</sup> granuloma macrophages in uninfected and infected spleens at indicated time points p.i. Significance derived from comparing infected animals at each time point to uninfected animals. (B) Splenocytes analyzed by flow cytometry were first gated for live, singlet, CD19<sup>-</sup>CD3<sup>-</sup>NK1.1<sup>-</sup> population, followed by gating for granuloma macrophages and other major myeloid cell populations as shown in figure S2A, then examined for intracellular STm using an anti-*Salmonella* antibody. Numbers indicated fractions of gated events within the parent cell population. Black: uninfected, red: infected. (A) Mice orally infected with 10<sup>8</sup> *S. Typhimurium* SL1344 for 2 weeks. (B) Mice infected with 10<sup>3</sup> CFU STm *i.p.* for 2 weeks. Significance calculated using a two-tailed Mann-Whitney test. \*\*\*\*  $p < 0.0001$ .



**Figure S4. Related to Figure 5:** (A-C) 129x1/SvJ BMDMs infected with either WT,  $\Delta$ steE, or  $\Delta$ steE::pSteE STm SL1344 and analyzed by flow cytometry at 20 hours of infection. Infected cells gated for positive intracellular STm then examined for pSTAT3, pSTAT1, IL-4R, and CD301 levels. (A) Intracellular levels of pSTAT3 and pSTAT1. (B) Surface expressions of IL-4R. (C) Frequencies of CD301<sup>+</sup>, IL-4R<sup>hi</sup> infected BMDMs. (D) Spleen weights of  $\Delta$ steE and WT STm infected mice at indicated time points p.i. (E) Quantitation of CD301<sup>-</sup> granuloma macrophages, neutrophils, and classical monocytes in  $\Delta$ steE and WT STm-infected spleens at indicated time points p.i. (F) Mice infected with 10<sup>3</sup> CFU of either WT or  $\Delta$ steE STm *i.p.* for 8 weeks. Measurement of intracellular TNF levels of granuloma macrophages following 3 hours of stimulation *ex vivo* with HKST. (G) Quantitation of CD301<sup>+</sup> granuloma macrophages in  $\Delta$ steE and WT STm-infected spleens at indicated time points p.i. (D-G) Significance calculated using a two-tailed Mann-Whitney test. \*\*\* p < 0.001, \*\*\*\* p < 0.0001.



**Figure S5. Related to Figure 5:** (A-B) Mice infected with either WT,  $\Delta steE$ , or  $\Delta steE::psteE$  STm SL1344 and analyzed on day 10 p.i. (A) Quantitation of bacterial burdens in infected spleens and livers using CFU plating assays. (B) Measurements of IL-4R levels on granuloma macrophages from infected spleens. (C) Additional examples of granuloma development defect in  $\Delta steE$  STm-infected animals at 4 weeks p.i.. Scale bar: 200  $\mu$ m. Significance calculated using a two-tailed Mann-Whitney test. \*  $p < 0.05$ , \*\*  $p < 0.01$ . Data shown are representative of at least two independent experiments.



**Figure S6. Related to Figure 6:** (A) Mice infected with  $10^3$  CFU of either WT or  $\Delta$ steE STm *i.p.* for 10 days before treatment with either 500 ug anti-TNF or control Ab on day 0 and day 4 followed by analysis on day 8. Survival curve showing a large proportion of WT STm infected, TNF-neutralized mice became moribund before analysis on day 8. (B-F) Red: mice infected with WT STm; blue: mice infected with  $\Delta$ steE STm; gray: mice infected with  $\Delta$ sseI STm. (B) Mice infected with  $10^3$  CFU of either WT or  $\Delta$ steE STm *i.p.* for 10 days before treatment with either anti-TNF or control Ab on day 0, followed by analysis on day 4. Quantitation of bacterial burdens in infected livers by CFU. (C) Mice infected with  $10^3$  CFU of either WT or  $\Delta$ steE STm *i.p.* for 8 weeks, then treated with either 500 ug anti-TNF or control Ab on day 0 and day 4, followed by analysis on day 8. Quantitation of bacterial burdens in infected livers by CFU. (D) 129x1/SvJ BMDMs infected with either WT,  $\Delta$ steE, or  $\Delta$ sseI STm SL1344 and analyzed by flow cytometry at 20 hours of infection. Uninfected, bystander and infected cells gated by intracellular STm signal then examined for IL-4R expression. No infection: BMDMs not exposed to bacteria. Data shown are representative of two independent experiments. (E-F) Mice infected with  $10^3$  CFU of either WT,  $\Delta$ steE,  $\Delta$ sseI STm *i.p.* for 4 weeks before treatment with either anti-TNF or control Ab on day 0, followed by analysis on day 4. (E) Quantitation of bacterial burdens in infected spleens by CFU. (F) Measurement of IL-4R levels on splenic granuloma macrophages. (B-F) Significance calculated using a two-tailed Mann-Whitney test. \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , \*\*\*\*  $p < 0.0001$ .