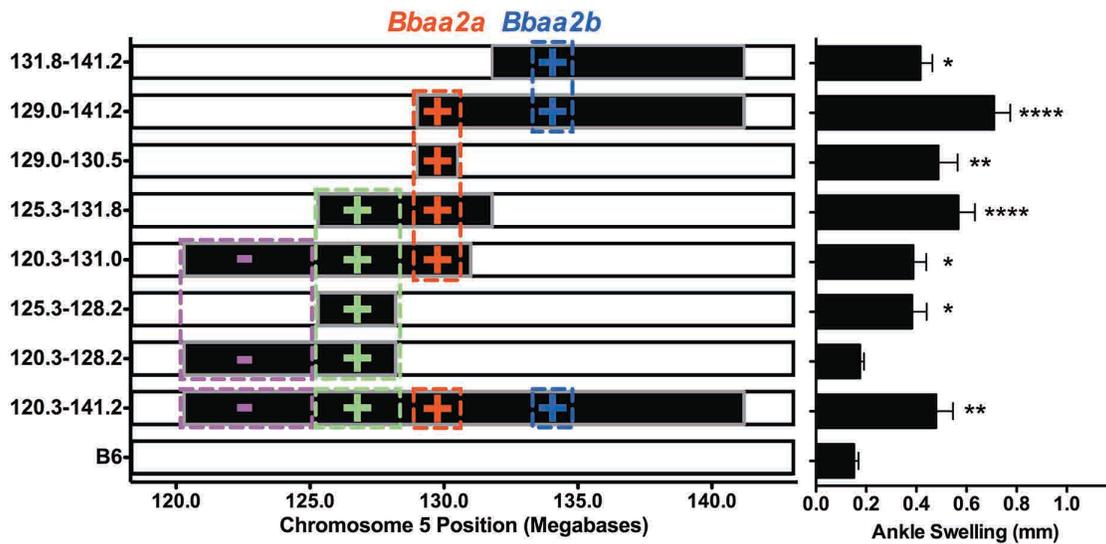
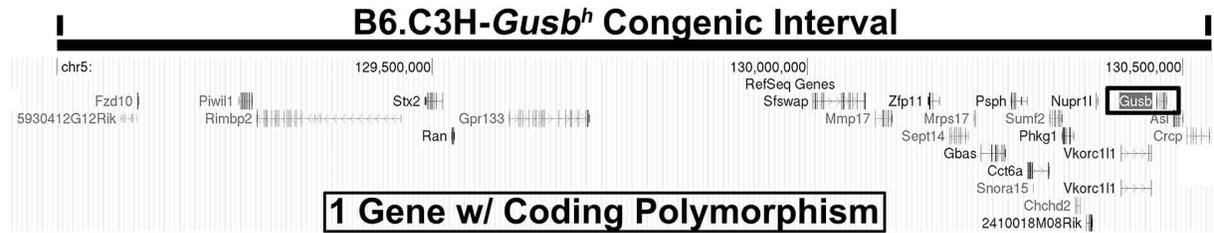


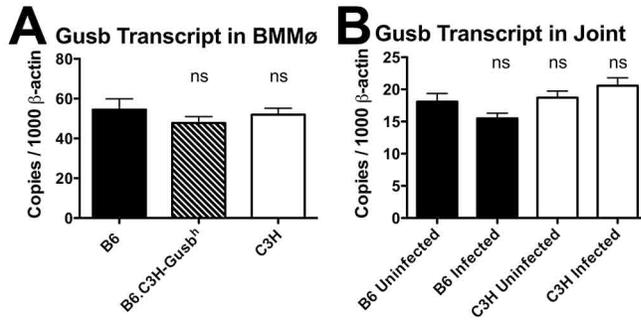
## Supplementary Materials



**Figure S1. Multiple regulators in *Bbaa2*.** The ankle swelling measurements of *Borrelia burgdorferi* infected B6.C3H-*Bbaa2* sub-interval congenic strains (as in Figure 1A) are most consistent with the presence of multiple positive regulators and one negative regulator within *Bbaa2*. A selected subset of congenic lines has been included in this figure to emphasize the contribution of each regulatory sub-interval. As noted, the ankle swelling conferred by *Bbaa2a* and *Bbaa2b* co-segregated with increased histopathology and neutrophil infiltration (Figure 1A). The lack of co-segregation by the green 125.3 to 128.2 sub-interval may reflect a difference in sensitivity between the continuous, quantitative variable of ankle swelling and the categorical nature of histology scores, or may reflect a true biological distinction between the disease processes that produce swelling and histopathology for this regulatory interval. The purple interval from 120.3 to 125.3 is proposed to contain a negative regulatory element that impacts both ankle swelling and histopathology (Figure 1A). Notably, previous analysis by Confidence Interval Mapping predicted the presence of multiple regulators within *Bbaa2* (17). Significance assessed by One-Way ANOVA followed by Dunnett's Multiple Comparison Test versus B6 (as in Figure 1A). (\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*\*  $p < 0.0001$ )

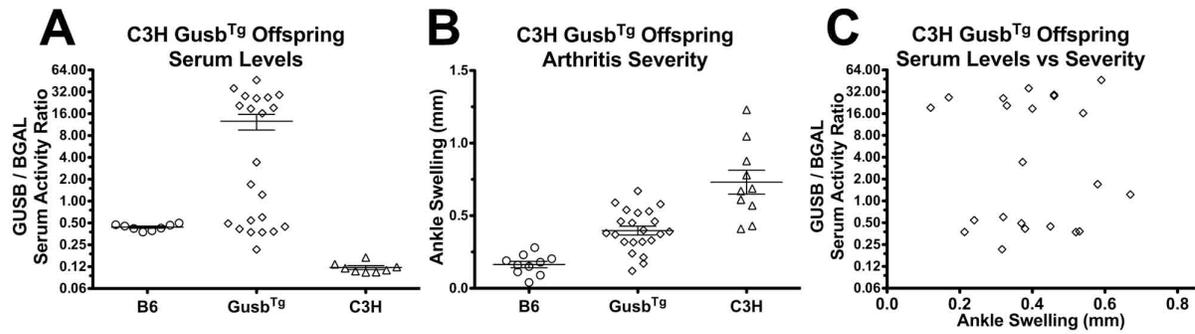


**Figure S2.** *Composition of the B6.C3H-Gusb<sup>h</sup> congenic interval.* The 129.0 - 130.5 interval contains 24 genes (RefSeq Genes, Mouse July 2007 [NCBI37/mm9] Assembly, <http://genome.ucsc.edu/>). The interval is highly conserved between the B6 and C3H strains with only one high confidence coding polymorphism, located in the *Gusb* gene.

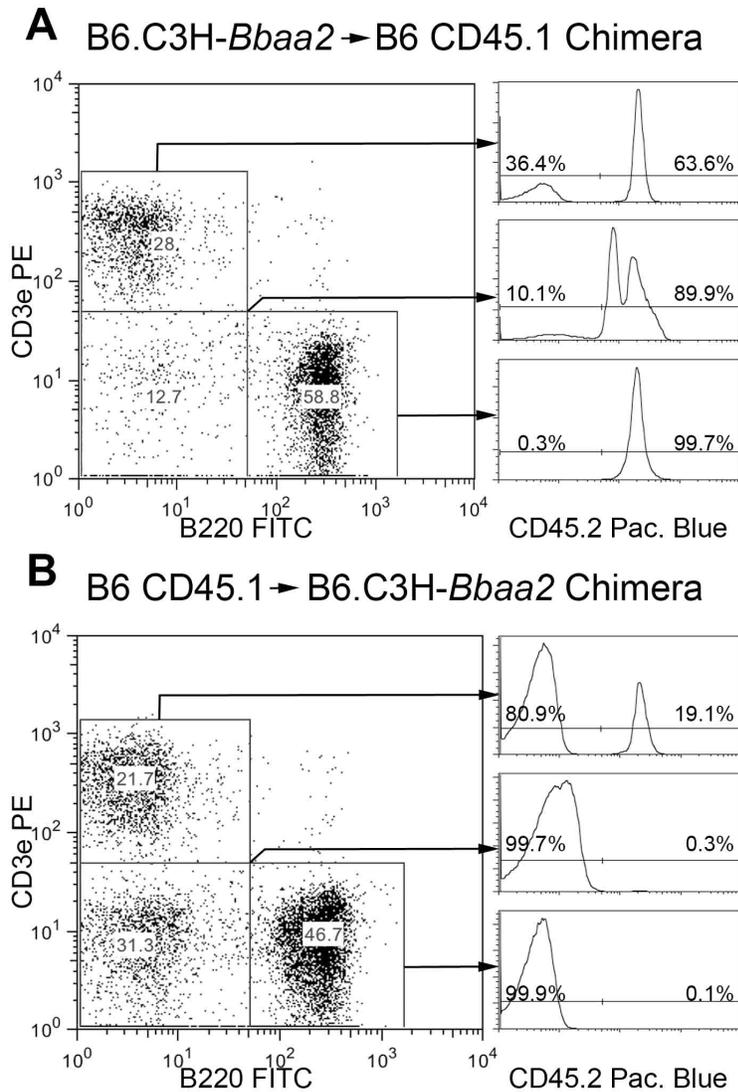


**Figure S3.** *Gusb* transcripts are stably expressed. **(A)** No significant differences in *Gusb* transcript levels were observed between strain-specific bone marrow derived macrophages (mean  $\pm$  SEM, n=6). **(B)** *Gusb* transcript levels did not change significantly within joints following *B. burgdorferi* infection (mean  $\pm$  SEM, n=5 to 6 for each group). Significance assessed by One-Way ANOVA followed by Dunnet's Multiple Comparison Test versus B6 (uninfected).





**Figure S5.** Correction of *GUSB* activity in C3H *Gusb<sup>Tg</sup>* offspring. **(A)** Scatter plot of the ratio between serum activities of GUSB and beta-galactosidase (internal control), showing that all 22 included C3H *Gusb<sup>Tg</sup>* offspring from four different founders had elevated serum activity levels. **(B)** Scatter plot of arthritis severity (as in Figure 4C). **(C)** There is no apparent correlation between very high-level transgenic overexpression of *Gusb<sup>b</sup>* and more or less severe Lyme arthritis, suggesting that expression above a threshold level is sufficient to confer resistance. This is consistent with the resistance conferred by intermediate GUSB levels in B6.C3H-*Bbaa2*, B6.C3H-*Gusb<sup>h</sup>*, and *Gusb<sup>Null</sup>* heterozygotes (Figure 2).



**Figure S6.** *Radiation chimera composition.* Measurement of CD45.2 positivity (right histograms) of circulating blood leukocytes at 3 weeks post-transplant indicates high-level ( $\geq 90\%$ ) engraftment was achieved for B cells (B220 positive, CD3e negative) and Myeloid lineages (CD3e, B220 double negative), with 60-80% engraftment of T cells (CD3e positive, B220 negative). A rapid reconstitution protocol was employed to allow infection of mice within the time frame associated with arthritis development (6-8 weeks of age). **(A)** High CD45.2 positivity measured for B6.C3H-*Bbaa2* (CD45.2) splenocyte donor transplanted into a B6 CD45.1 recipient. **(B)** Low CD45.2 positivity detected for a B6 CD45.1 splenocyte donor transplanted into a B6.C3H-*Bbaa2* recipient.