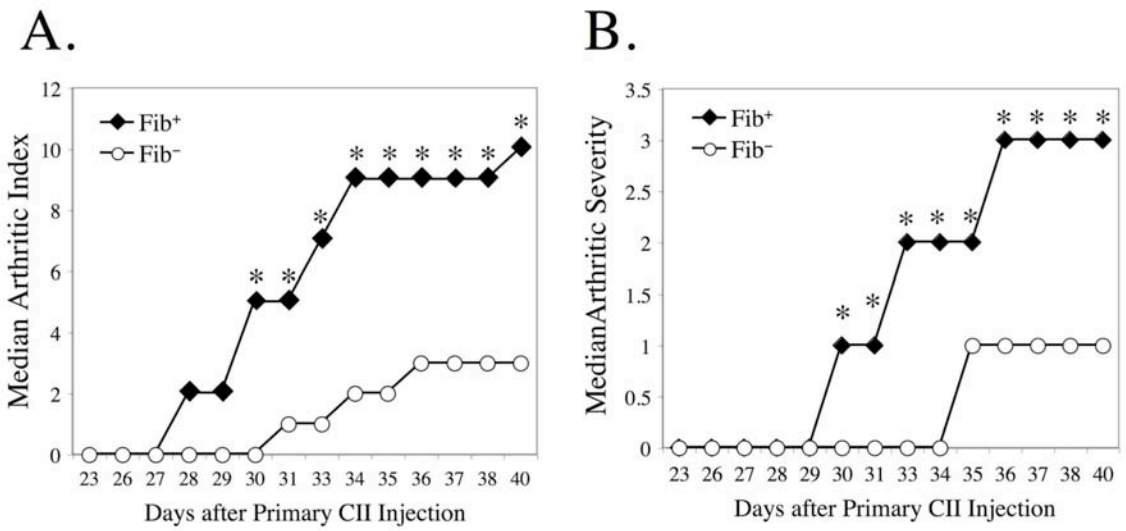
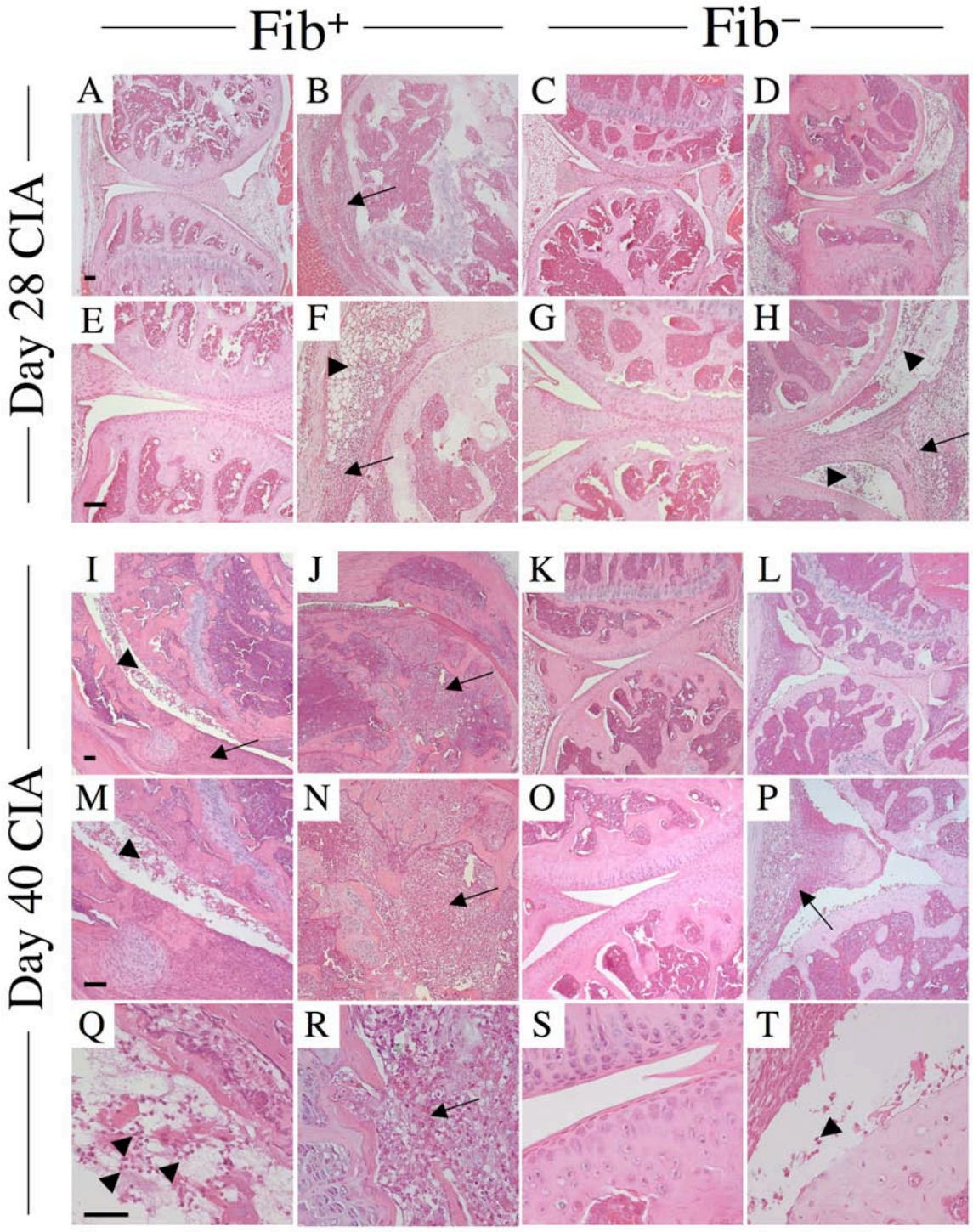
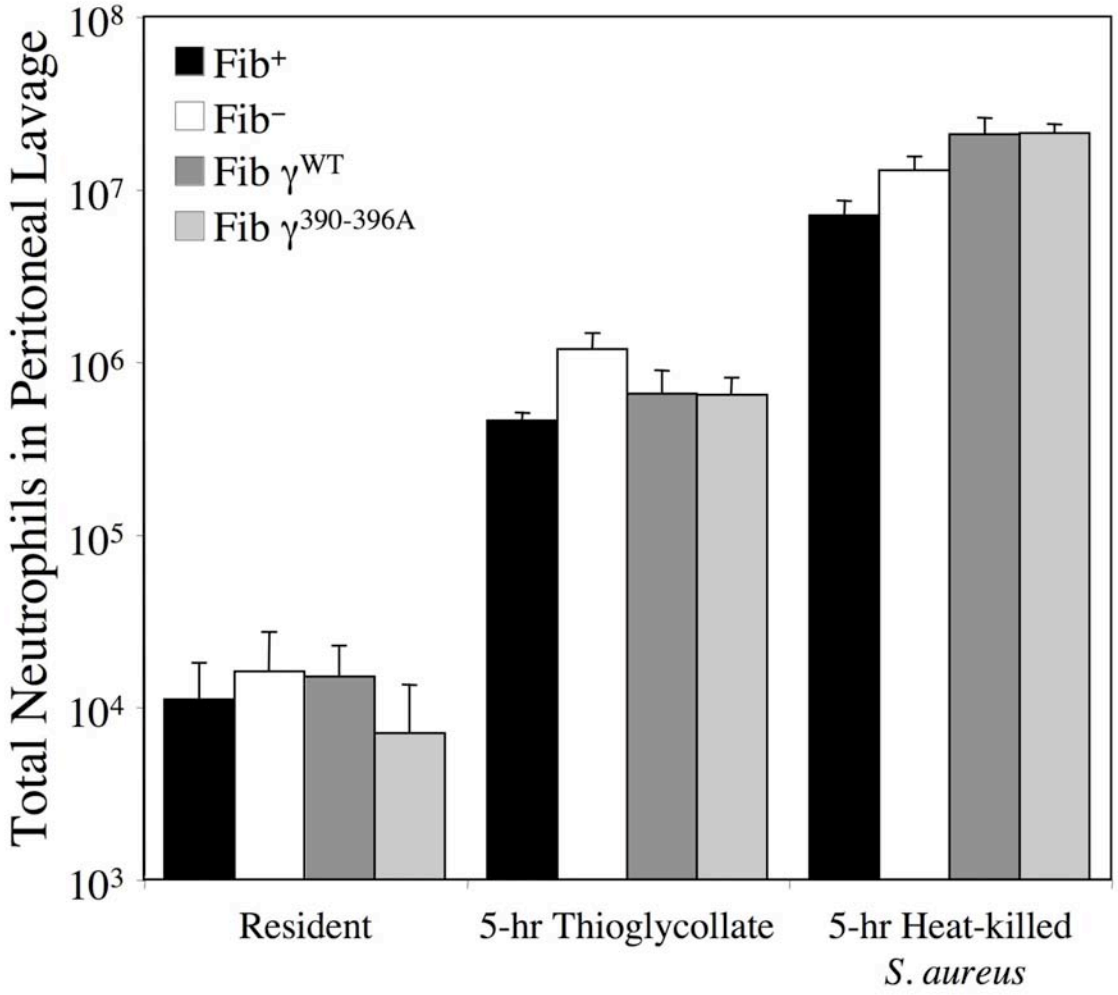


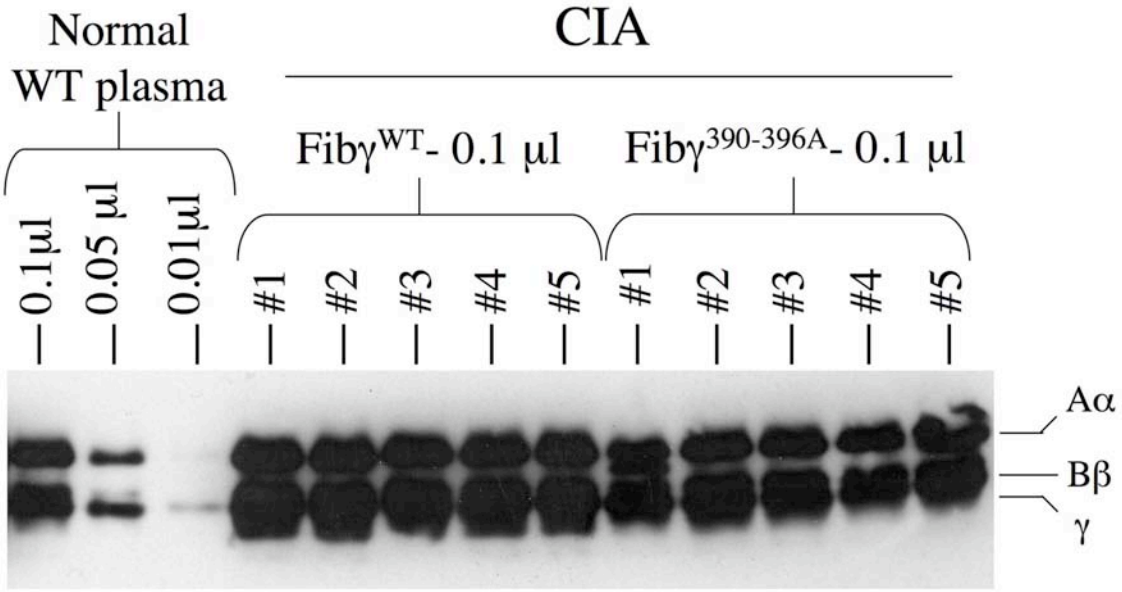
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4

Supplemental Figure 1 Fibrinogen deficiency results in diminished macroscopic CIA in female mice. Representative experiment with cohorts of female Fib^+ and Fib^- mice (n=13 pairs) immunized with CII. Median Arthritic Index (**A**) and Median Arthritic Severity of paws (**B**) * $p<0.05$ by Mann-Whitney *U* test.

Supplemental Figure 2 Microscopic analyses of knee joint pathology in male Fib^+ and Fib^- mice following CIA. Representative examples of H&E stained knee joint sections taken from Fib^+ (**A**, **B**, **E**, and **F**) and Fib^- (**C**, **D**, **G**, and **H**) mice at day 28 following CII-immunization. Note that at this early time point some individuals from both the Fib^+ (**A**, **E**) and Fib^- (**C**, **G**) cohorts were found to be free of histological signs of inflammatory joint disease. Other individual Fib^+ (**B**, **F**) and Fib^- (**D**, **H**) mice at day 28 exhibited early evidence of arthritis within knee joints, include inflammatory cell infiltrates (*arrowhead*) and synovial hyperplasia (*arrows*). (**I**-**T**) A more comprehensive gallery of views of knee joint microscopy at day 40 following CII-immunization (also see Figure 3 in the main text). Note that knees from Fib^+ mice (**I**, **J**, **M**, **N**, **Q**, **R**) typically display severe joint pathology with robust inflammatory cell infiltrates, synovial hyperplasia, pannus formation, and cartilage and bone degeneration. In some cases granulation tissue penetrated to the bone growth plate (*arrows*; **J**, **N**, **R**). In contrast, knees from Fib^- mice (**K**, **L**, **O**, **P**, **S**, **T**) typically exhibited milder disease pathology characterized by only inflammatory cell infiltrates (*arrowheads*) and modest synovial hyperplasia (*arrows*). Scale bar is equal to 100 μm.

Supplemental Figure 3 Leukocyte trafficking in Fib^{-} and $Fib\gamma^{390-396A}$ mice is identical to that observed in wildtype mice. Peritonitis was induced in Fib^{+}, Fib^{-}, $Fib\gamma^{WT}$ and $Fib\gamma^{390-396A}$ mice by intraperitoneal injection of either 1 ml of thioglycollate medium or $1x10^{9}$ heat-killed *S. aureus*. Peritoneal lavage was performed using 5 ml of PBS 5 hours after induction of peritonitis. Total cell counts were calculated using a hemocytometer and cell differentials were determined from cytospin preparations of lavage fluid. Total mean neutrophil number ± SEM in lavage fluid is presented for unchallenged and challenged mice. Note that mice of each genotype had similar resident neutrophil numbers and that similar numbers of neutrophils are able to traffic to the peritoneal cavity following introduction of pro-inflammatory stimuli regardless of genotype.

Supplemental Figure 4 Western blot analysis of citrate-anticoagulated plasma collected from either unchallenged wildtype mice or from CII-immunized wildtype and $Fib\gamma^{390-396A}$ mice at day 42 following CII-immunization. Consistent with prior findings (14) showing that $Fib\gamma^{390-396A}$ knock-in mutants carry plasma fibrinogen levels that are similar to wildtype mice, plasma fibrinogen levels are comparable in $Fib\gamma^{390-396A}$ and wildtype mice following the induction of CIA. Detection of mouse fibrinogen was done using a rabbit polyclonal anti-mouse fibrinogen antibody that reacts with all three fibrinogen chains albeit most strongly with the $A\alpha$ and $B\beta$ chains (14).