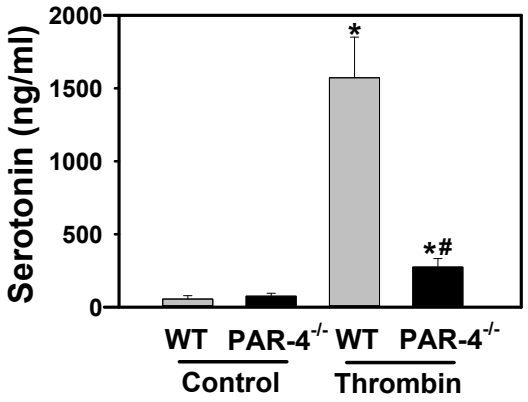
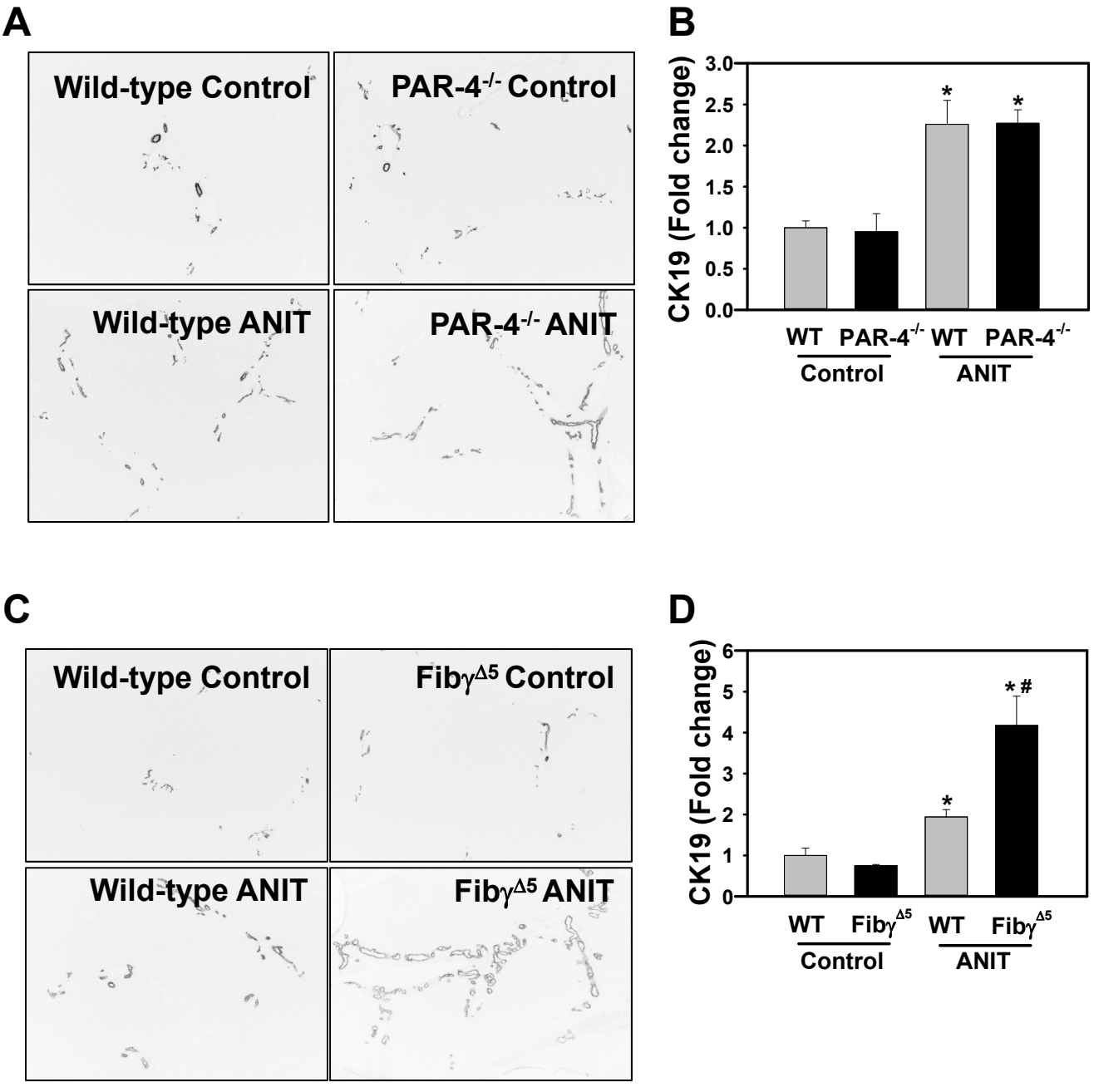
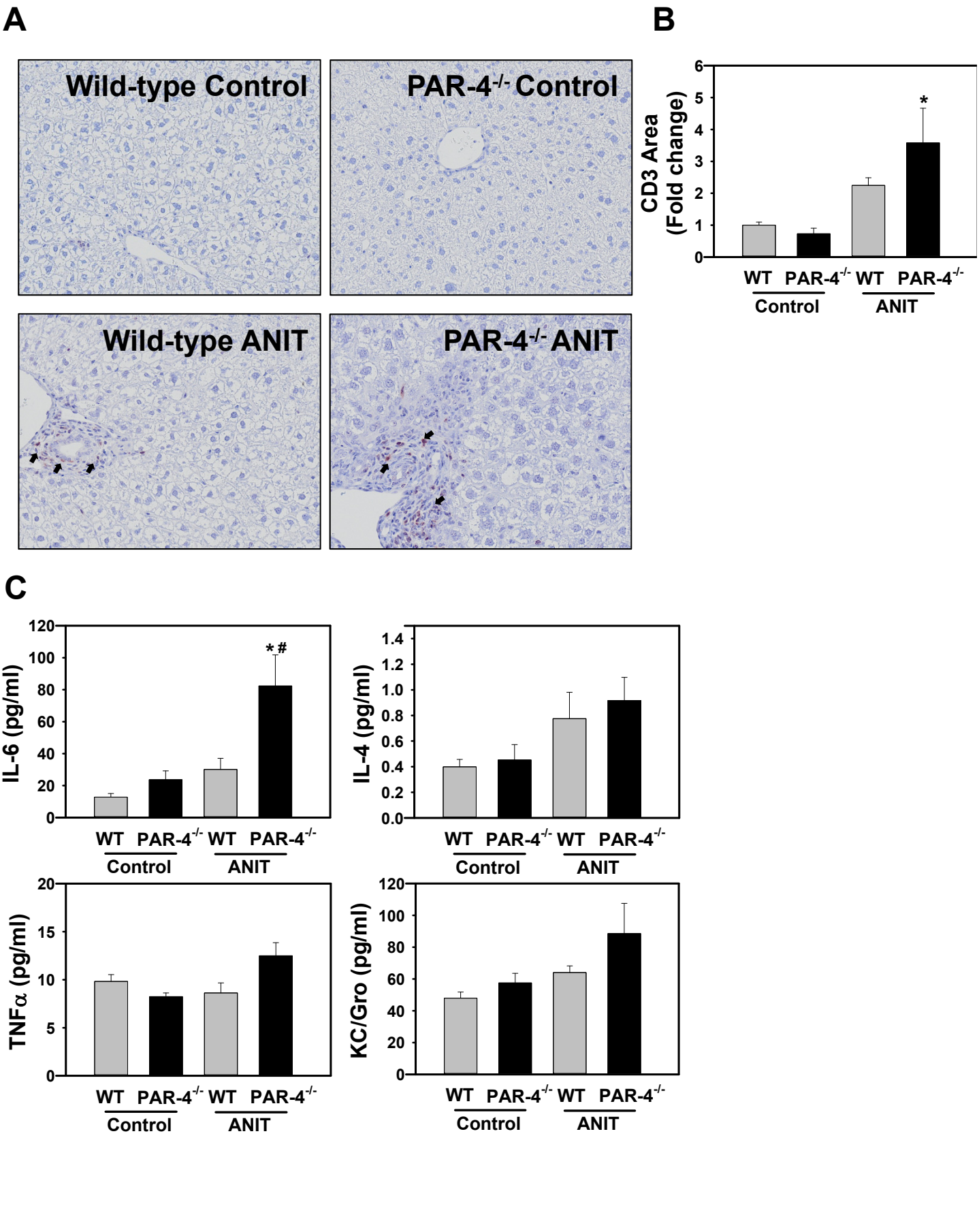
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4

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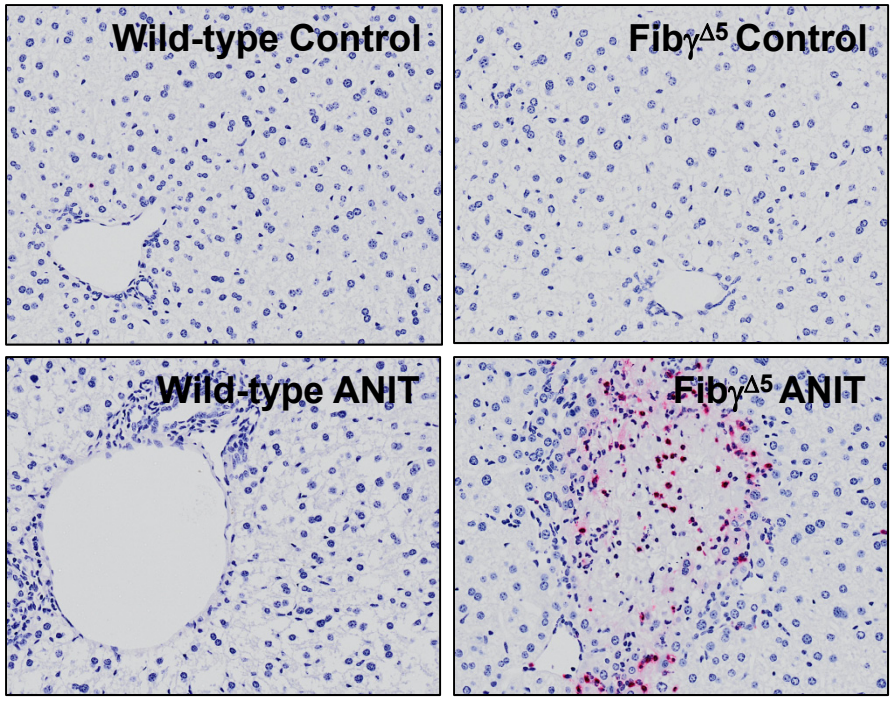

Supplemental Figure 1. Thrombin-mediated serotonin release is PAR-4-dependent in mouse platelets. Approximately 1 x 10^8 platelets from wild-type (WT) mice and PAR-$4^{-/-}$ mice were stimulated with thrombin (10 U/ml) or vehicle (PBS) for 15 minutes. Serotonin levels were analyzed in supernatants by ELISA. Platelets from 3 independent mice were utilized for each treatment group. Data are expressed as mean ± SEM. *$p<0.05$ vs. control treatment within genotype and #$p<0.05$ vs. thrombin-treated WT platelets.

Supplemental Figure 2. Biliary hyperplasia in ANIT-treated PAR-$4^{-/-}$ mice and Fib$\gamma^{\Delta 5}$ mice. Wild-type (WT), PAR-$4^{-/-}$ and Fib$\gamma^{\Delta 5}$mice were fed control diet (AIN-93M) or an identical diet containing 0.025% ANIT for 4 weeks. (A, C) Representative photomicrographs (100X) show liver sections stained for cytokeratin-19 (CK19, bile ducts). Images were converted to grayscale and inverted such that CK19 staining is dark. (B, D) The area of positive staining was quantified as described in Materials and Methods. Data are expressed as mean ± SEM; n = 4-5 mice per group for control diet and 9-11 mice per group for ANIT-treated mice. *$p<0.05$ vs. control diet within genotype and #$p<0.05$ vs. WT mice fed the same diet.

Supplemental Figure 3. Hepatic inflammation in ANIT-treated PAR-$4^{-/-}$ mice. Wild-type (WT) and PAR-$4^{-/-}$ mice were fed control diet (AIN-93M) or an identical diet containing 0.025% ANIT for 4 weeks. (A) Representative photomicrographs (200X) and (B) quantification of CD3 staining. (C) Serum levels of cytokines IL-6, IL-4, TNFα, and KC/Gro were determined as described in Materials and Methods. Arrows denote positive CD3 staining in A-B. Data are expressed as mean ± SEM; n = 5 mice per group for control diet and 10-11 mice per group for

mice fed ANIT diet. *$p<0.05$ vs. control diet within genotype and #$p<0.05$ vs. WT mice fed the same diet.

Supplemental Figure 4. Hepatic neutrophil accumulation in ANIT-treated Fib$\gamma^{\Delta 5}$ mice. Wild-type (WT) and Fib$\gamma^{\Delta 5}$ mice were fed control diet (AIN-93M) or an identical diet containing 0.025% ANIT for 4 weeks. Representative photomicrographs (200X) show neutrophil staining, particularly within areas of necrosis in livers of ANIT-treated Fib$\gamma^{\Delta 5}$ mice.