SUPPLEMENTAL DATA

Divergence of IL-1, IL-18 and cell death in NLRP3 inflammasomopathies

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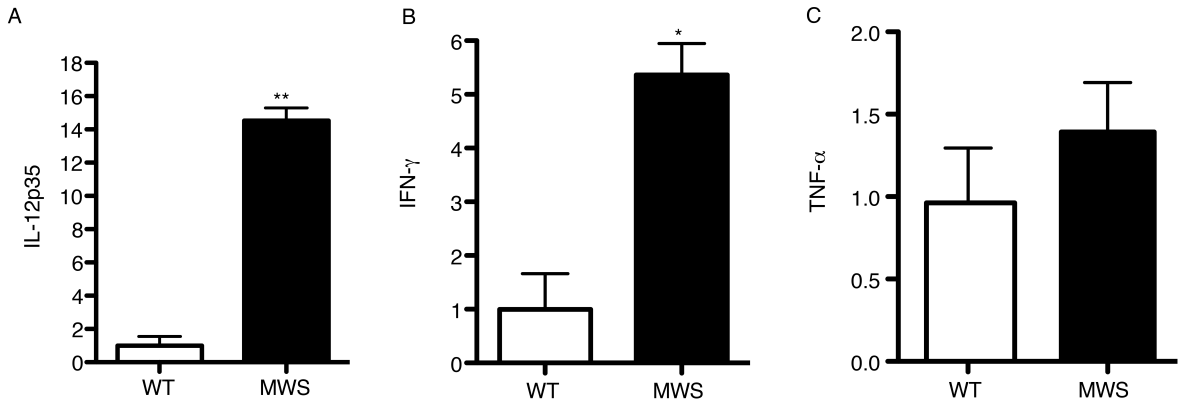

Figure S1. IL-18 present in the skin is biologically active and leads to upregulation of IL-18-targeted cytokines. mRNA expression levels of IL-12p35 (A), IFN-γ (B), and TNF-α (C) in skin biopsies from *MWS* (n=9) and WT (n=7) mice, expressed as fold-change compared to GAPDH, shown as mean ± SEM. *, $p<0.05$; **, $p<0.005$.

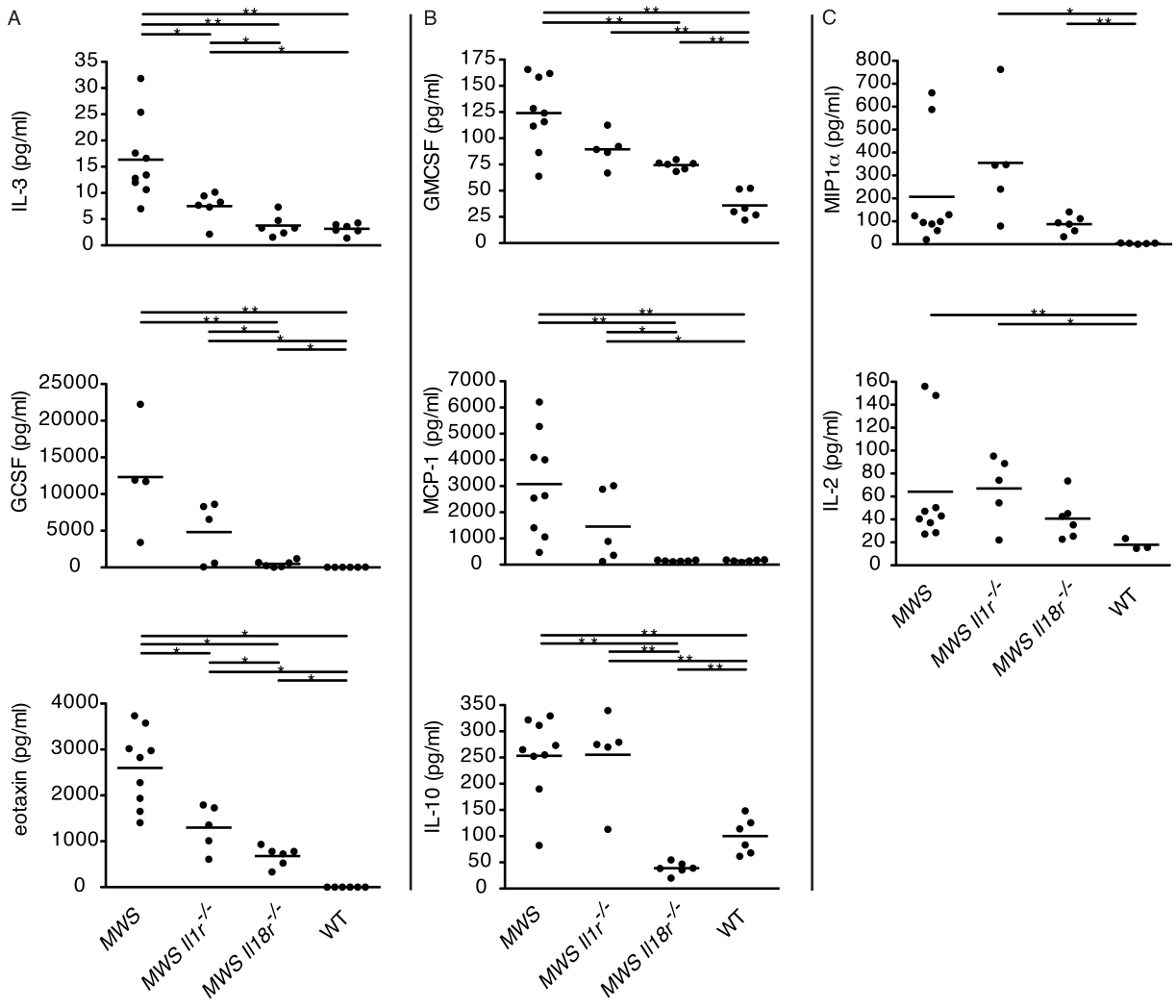

Figure S2. Disruption of IL-18R signaling normalizes key CAPS serum cytokine levels to a greater extent than the absence of IL-1R signaling. Multiplex cytokine analysis of serum obtained at days 6–8 from WT, *MWS, MWS Il1r*$^{-/-}$ and *MWS Il18r*$^{-/-}$ pups, n≥5 mice, each graph point represents 1 mouse, with mean identified. Panels A, B and C indicate the varying degrees of normalization. P values calculated by Student's t test. *, p<0.05; **, p<0.005.

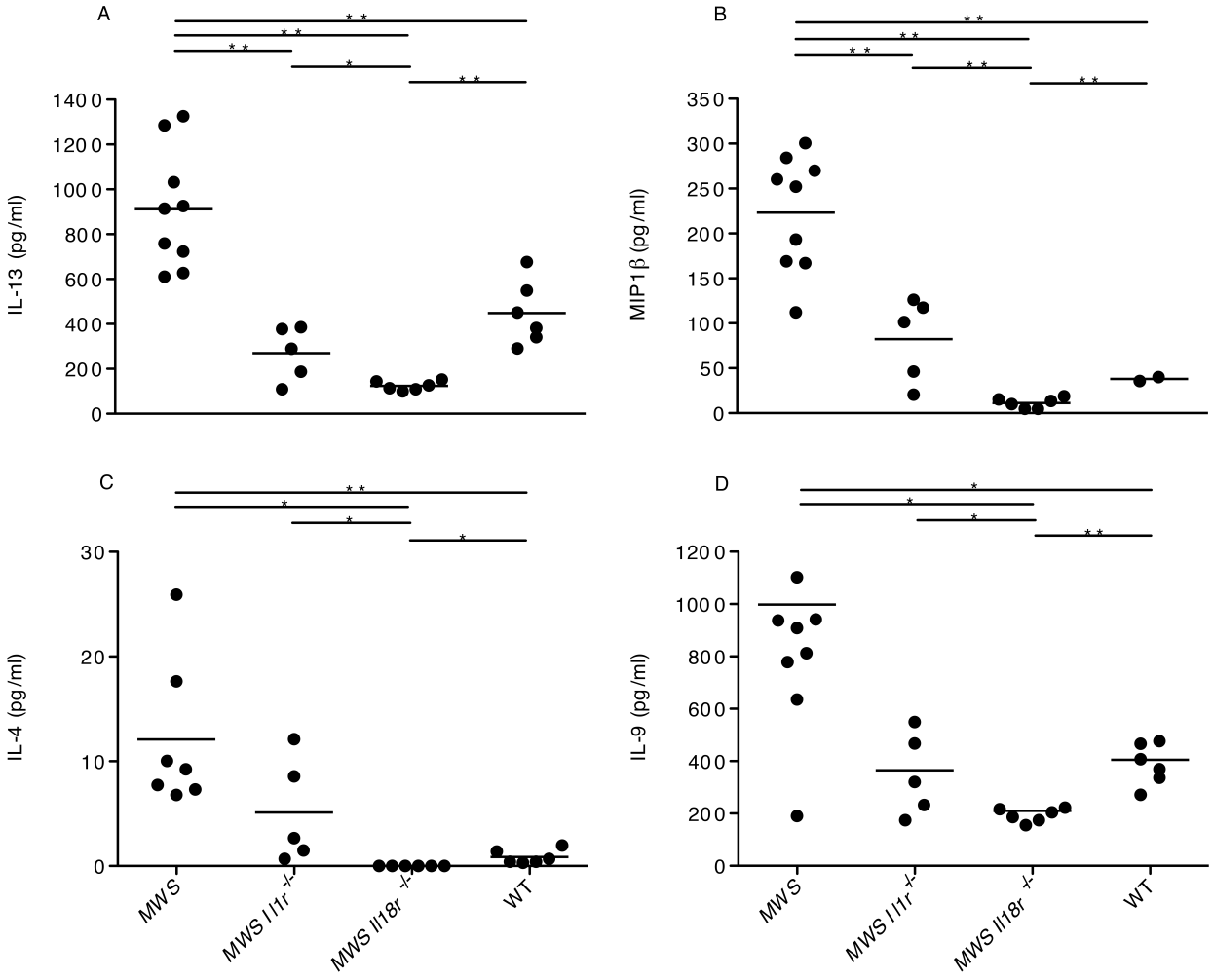

Figure S3. Disruption of IL-18 signaling normalizes additional serum Th2 and chemokine levels in CAPS. Multiplex cytokine analysis of serum obtained at days 6–8 from WT, *MWS, MWS Il1r*$^{-/-}$ and *MWS Il18r*$^{-/-}$ pups, n≥5 mice, each graph point represents 1 mouse, with mean identified. P values calculated by Student's t test. *, p<0.05; **, p<0.005.

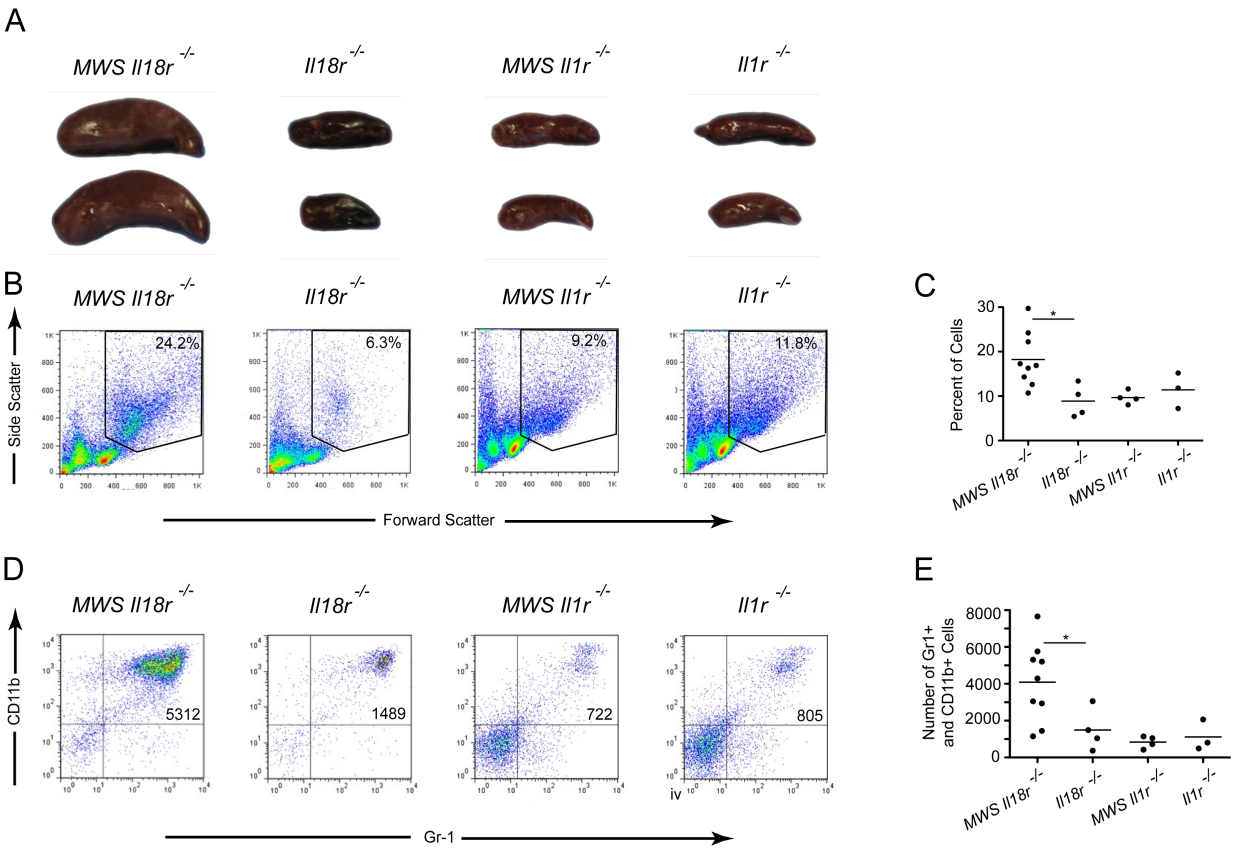

Figure S4. *MWS Il18r*$^{-/-}$ mice display significant splenic inflammation. (A) Whole spleens from *MWS Il18r*$^{-/-}$, *Il18r*$^{-/-}$, *MWS Il1r*$^{-/-}$, and *Il1r*$^{-/-}$ mice. Two representative spleens are shown for each strain. (B) Flow cytometry of splenic cells from adult *MWS Il18r*$^{-/-}$ mice demonstrate increased percentages of large granulocytes compared to age-matched *Il18r*$^{-/-}$, *MWS Il1r*$^{-/-}$, and *Il1r*$^{-/-}$ mice. Panels are representative of 3-9 mice per strain. Results are summarized in (C). *, $p<0.05$. (D) Two-color immunofluorescent staining identifies these cells as Gr-1^{+} CD11b^{+} neutrophils with increased absolute numbers in MWS *Il18r*$^{-/-}$ mice compared to *Il18r*$^{-/-}$, MWS *Il1r*$^{-/-}$, and *Il1r*$^{-/-}$ mice. Flow cytometry panels are representative of 3-9 mice per strain. Results are summarized in (E). *, $p<0.05$.