

Figure S1. In vitro CD4+ T cell responses to NX-13. Effect of NX-13 on cell viability after 24 h of treatment by Annexin V assay (A). Differentiation of naïve CD4+ T cells into Th17 cells (B). NX-13 reduces differentiation of Th17 cells, measured by flow cytometry. Differentiation of naïve CD4+ T cells into Th1 (C) and Th17 (D) cells in control and Nlr1-deficient cells. Data presented as mean \pm SEM (n = 5). Asterisks mark significance ($P \leq 0.05$).

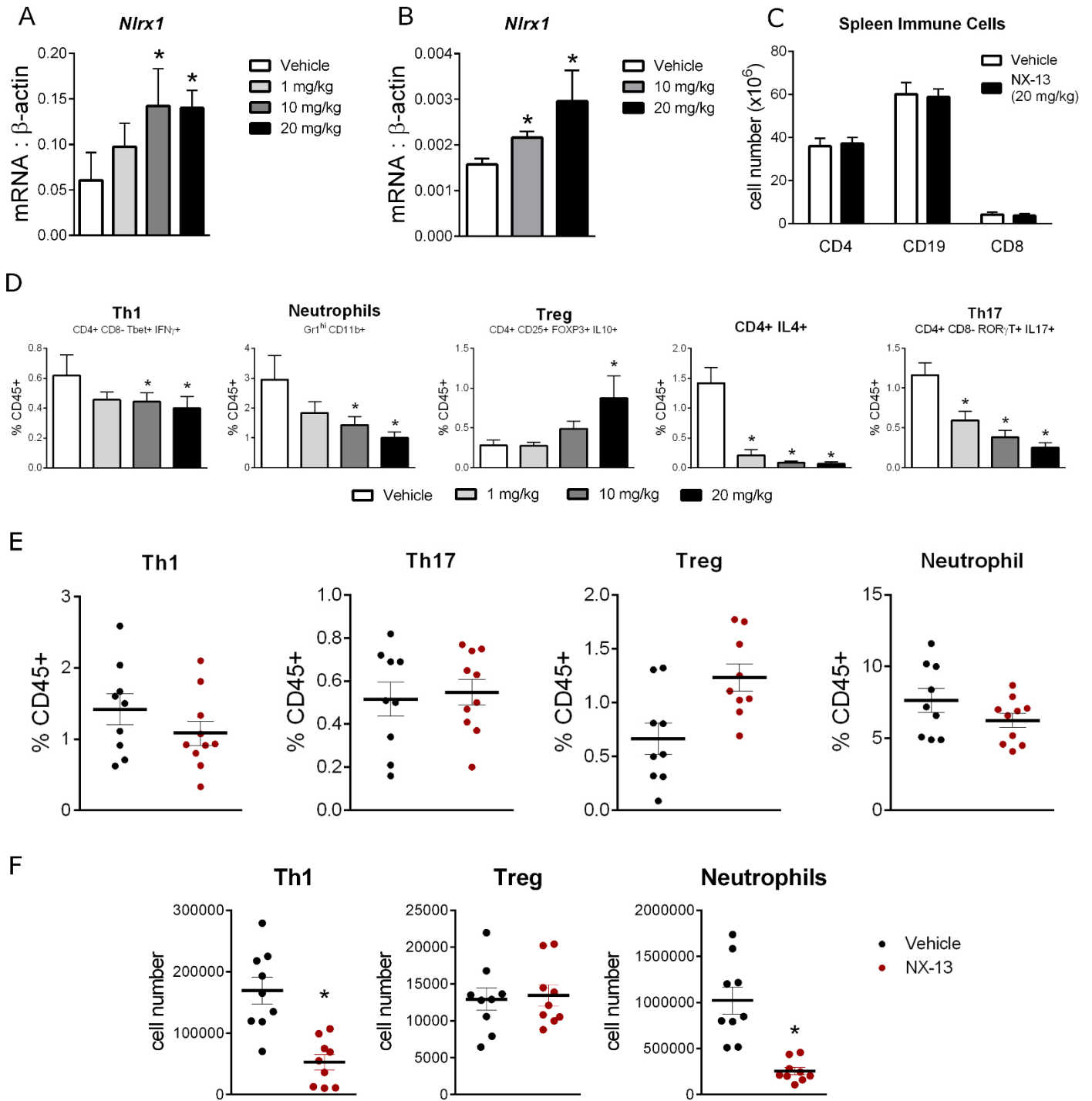


Figure S2. Colonic expression of NLRX1. mRNA expression of NLRX1 in DSS (A) and *Mdr1a*^{-/-} (B) models of colitis after treatment with NX-13 by qRT-PCR. Expression measured at day 7 of DSS challenge and at 10 weeks of age in *Mdr1a*^{-/-}, respectively. Splenic immune cells by flow cytometry after 1 week of treatment with vehicle or NX-13 (20 mg/kg) by oral gavage (C). Data presented as mean \pm SEM (n = 5). Percentage of CD45+ cells after DSS challenge (D, n = 9) after 7 days NX-13 and adoptive transfer (E, n = 10) after 8 weeks NX-13. Total cell number of lamina propria immune cells in *Mdr1a*^{-/-} colitis (F, n = 9) after six weeks of NX-13. Th1 (CD4+ CD8- Tbet+ IFN γ +), neutrophils (Gr1^{hi} CD11b+), Treg (CD4+ CD25+ FOXP3+ IL10+), and Th17 (CD4+ CD8- ROR γ T+ IL17+) cells were quantified by flow cytometry. Asterisks mark significance ($P \leq 0.05$).

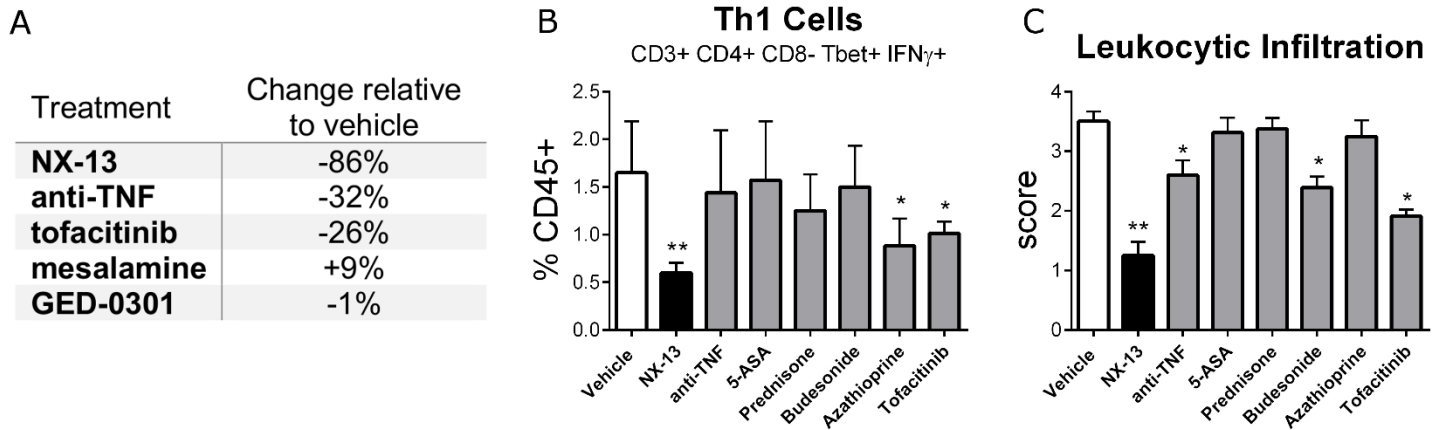


Figure S3. Comparative efficacy of NX-13 to current UC therapeutics. Mean change in day 7 fecal calprotectin concentration relative to vehicle treated mice after DSS challenge (A). Lamina propria Th1 cells by flow cytometry (B) and colonic leukocytic infiltration score by H&E (C) after four weeks of treatment in *Mdr1a*^{-/-} mice. NX-13 was evaluated at a once daily oral dose of 10 mg/kg. Mesalamine was administered at 25 mg/kg once daily by oral gavage. Anti-TNF was administered at 2 mg/kg twice weekly by intravenous injection. Tofacitinib was administered at 0.75 mg doses twice daily by oral gavage. Prednisone (0.625 mg/kg), budesonide (0.125 mg/kg), and azathioprine (2.5 mg/kg) were delivered by oral gavage once daily. Data presented as mean \pm SEM (n = 5). Asterisks mark significance (*, $P \leq 0.05$; **, $P \leq 0.01$).