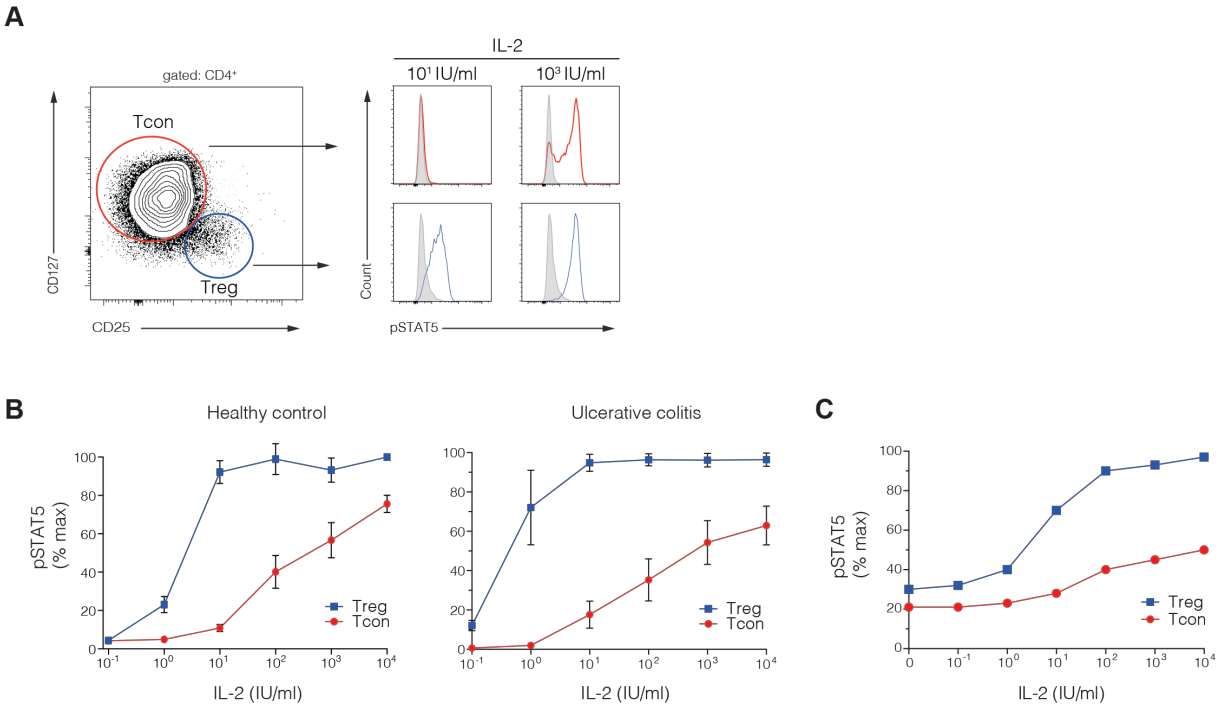
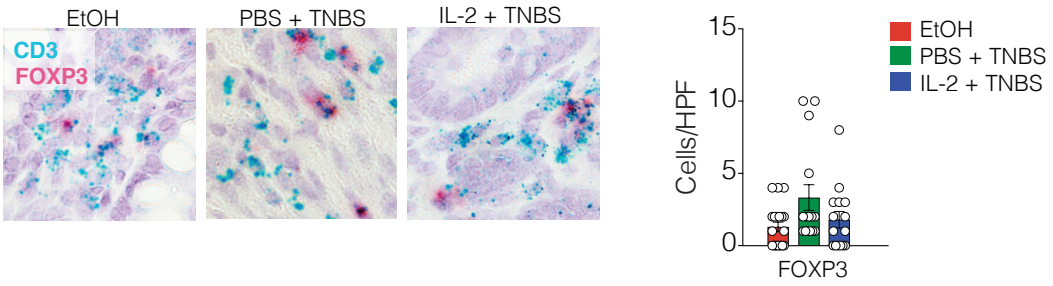
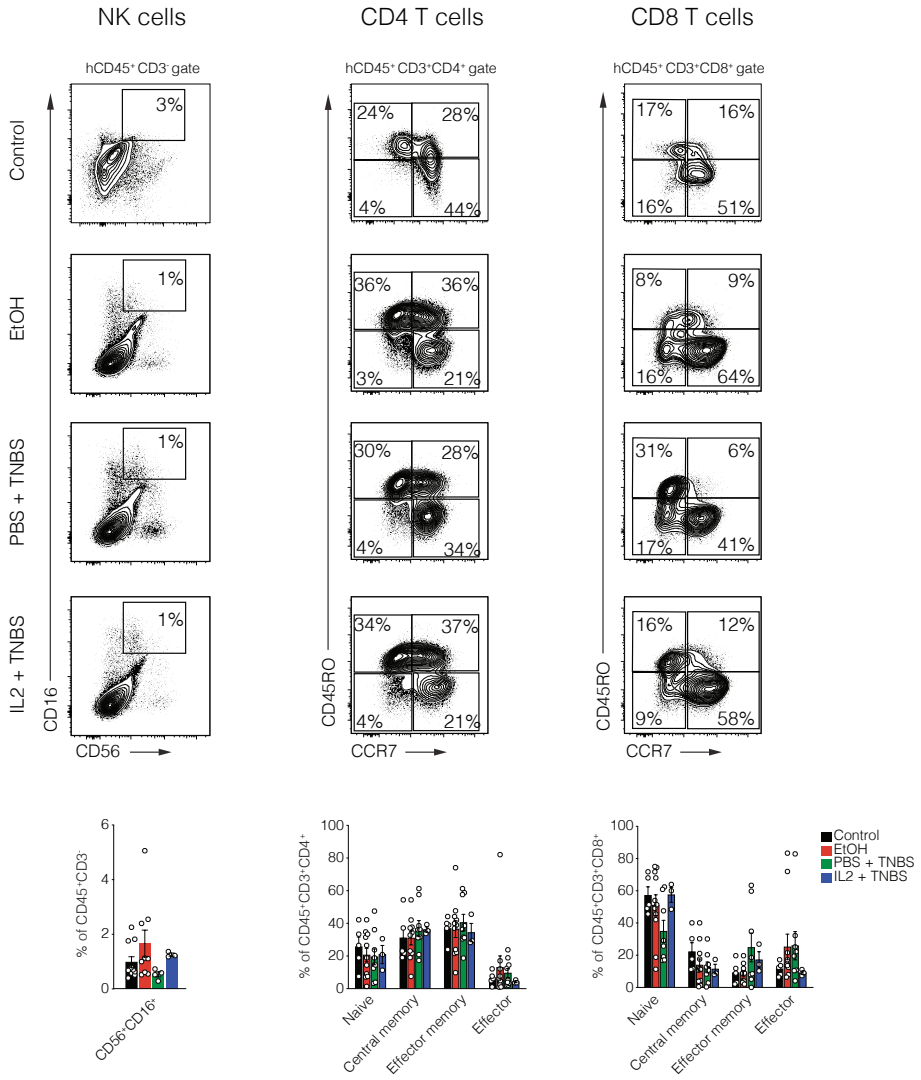


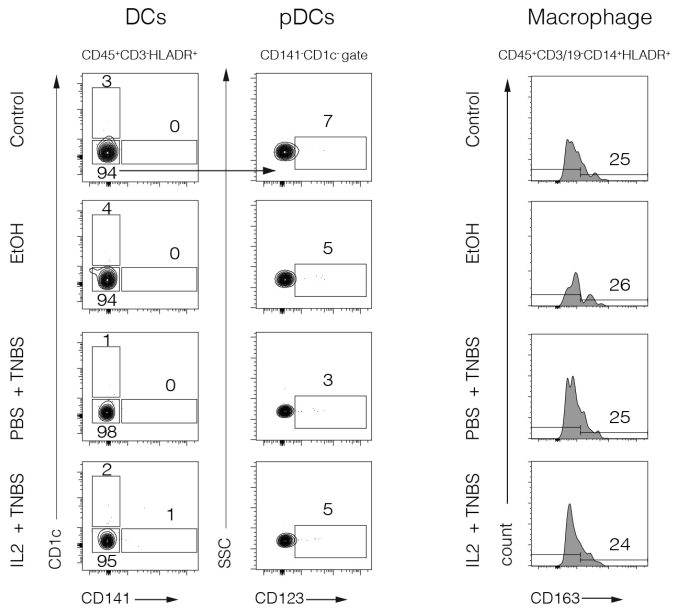
Supplementary Figure 1. Low-dose IL-2 selectively activates human Tregs in healthy donors and UC patients. (*A*) Representative flow cytometry plots of human PBMC treated with 10^1 IUml^{-1} or 10^3 IUml^{-1} IL-2 for 20 min. Treg cells were gated based on CD127^{lo}CD25$^+$ staining (red), whereas conventional T cells (Tcon) were gated based on CD127$^+$CD25$^-$ staining (blue; left). Phosphorylation of STAT5 (pSTAT5, Tyr-694) in Tcon (red) and Treg (blue) is shown in histograms upon stimulation with indicated IL-2 concentrations (right). (*B*) Graphical representation of pSTAT5 in Tcon (red) and Treg (blue) from PBMCs following IL-2 dose escalation ranging from 10^{-1} IUml^{-1} to 10^4 IUml^{-1} for 20 min in healthy control subjects or patients with UC. Error bars represent the SEM of experimental replicates across 2 donors. (*C*) Dose-response curve showing pSTAT5 expression in lamina propria Tregs (blue) and Tcons (red) from a patient with UC. Statistical analysis were performed using an unpaired t-test. Error bars are represent the SEM.



Supplementary Figure 2. Human Tregs were not expanded in colons of humanized mice treated with LD IL-2. RNAscope on formalin-fixed paraffin-embedded colonic sections from humanized NSGIIDQ8 mice treated with PBS or LD IL-2 3 days post enema with TNBS or EtOH as a vehicle control. 5 areas per slide were quantified. Images are 40X Statistical analysis was performed using one-way ANOVA with Tukey's multiple comparisons test. Error bars are represent the SEM.



Supplementary Figure 3. Low dose IL-2 treatment does not alter NK cell and T cell subsets in humanized mice. FACS analysis of reconstituted NSGIIDQ8 mice that were untreated (control, n ≥ 3) or administered a single rectal edema of 50% EtOH (n ≥ 3) or TNBS followed by PBS (n ≥ 3) or LD IL-2 treatment (n ≥ 3). Prior gating is shown on top of each column. Concatenated flow cytometry plots and graphical representation of activated ($CD56^+CD16^+$) NK cells as well as naïve ($CCR7^+CD45RO^-$), central memory ($CCR7^+CD45RO^+$), effector memory ($CCR7^-CD45RO^+$), and effector ($CCR7^-CD45RO^-$) $CD4^+$ and $CD8^+$ T cells. Error bars represent the SEM. Statistical analysis performed using one-way ANOVA with Tukey's multiple comparisons test. Error bars are represent the SEM.



Supplementary Figure 4. Treatment with LD IL-2 was not associated with altered frequencies of dendritic cells or macrophages. FACS analysis of concatenated colonic lamina propria cells from reconstituted NSGIIDQ8 mice that were untreated (control, n ≥ 3) or administered a single rectal edema of 50% EtOH (n ≥ 3) or TNBS followed by PBS (n ≥ 3) or LD IL-2 treatment (n ≥ 3). Gating strategy is shown on top.