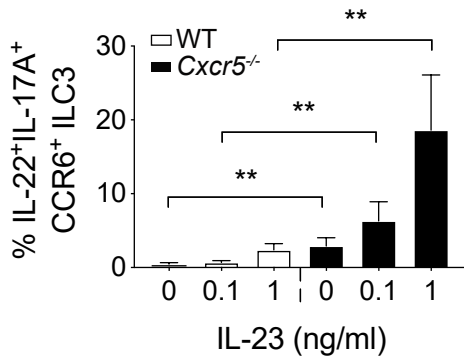
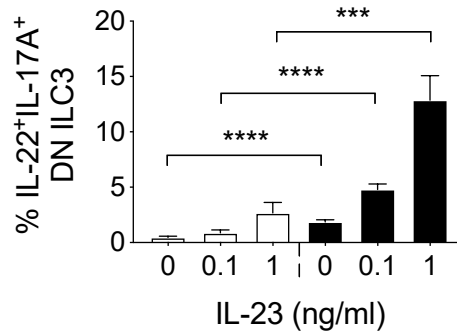
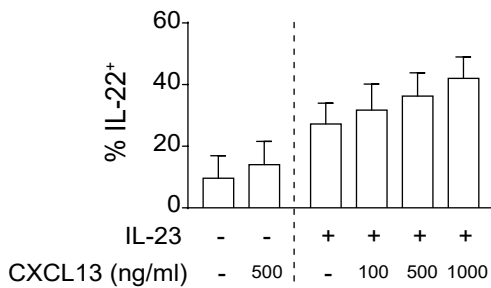
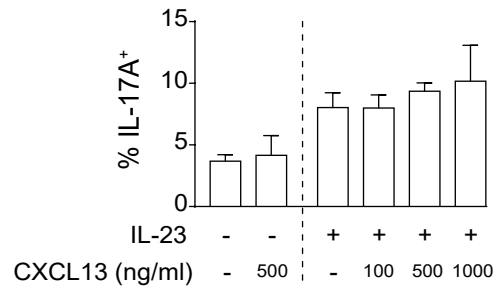
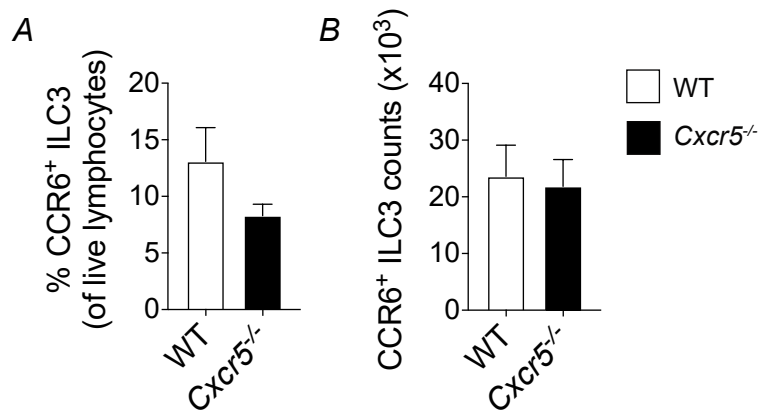


A**B**

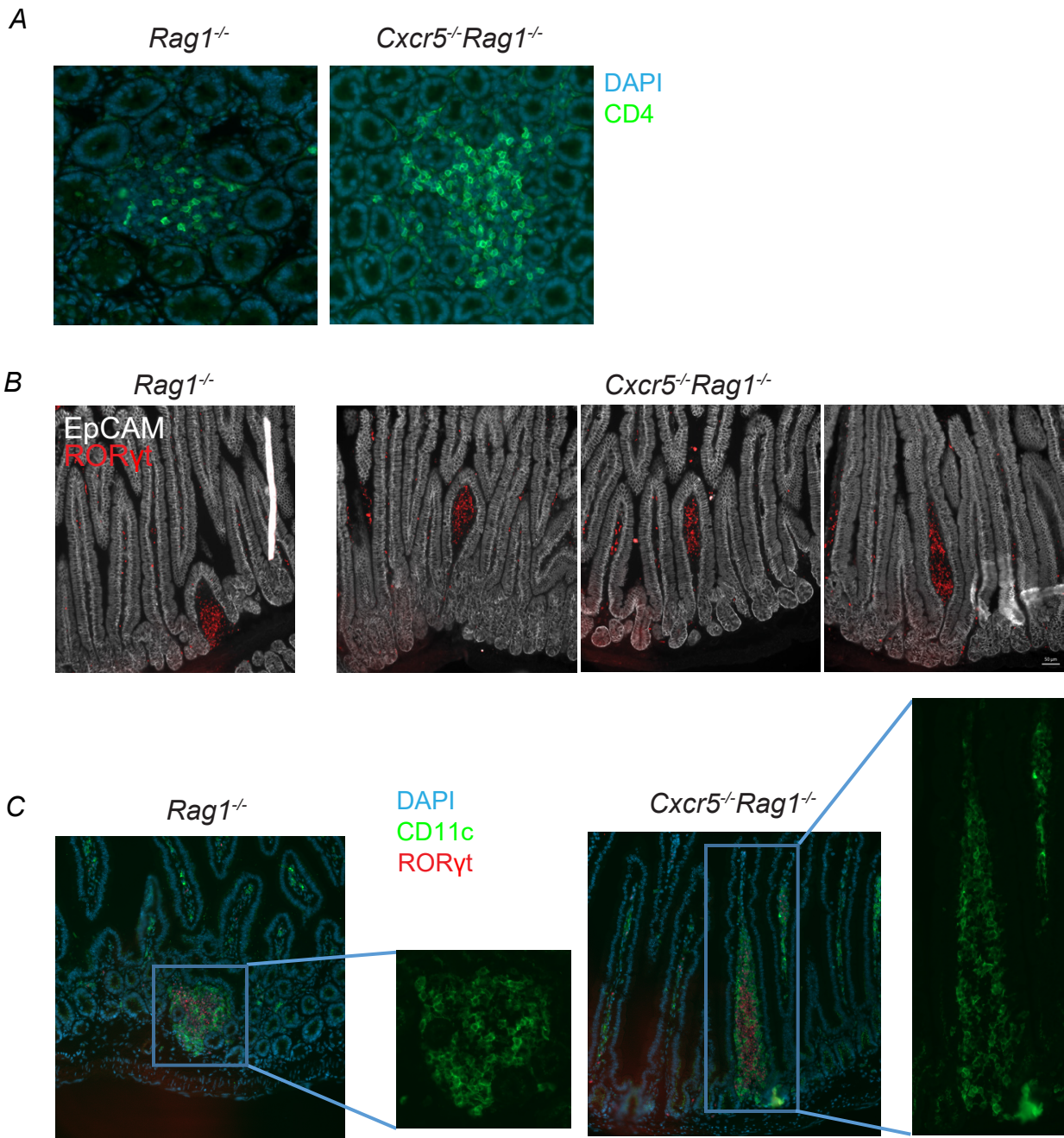
SI Appendix, Fig. S1. Frequencies of *Cxcr5*^{-/-} small intestine ILC3 that simultaneously produce IL-17A and IL-22 upon stimulation. Frequencies of IL-22- and IL-17A-double producing (A) LTi-like cells and (B) DN ILC3 after ex-vivo stimulation for 3 h with the indicated doses of IL-23 (n=4). Bar graphs show mean ± SEM. ** P<0.01, *** P<0.001 and **** P<0.0001 (unpaired Student's t-test). Data shown are representative of 3 independent experiments.

A**B**

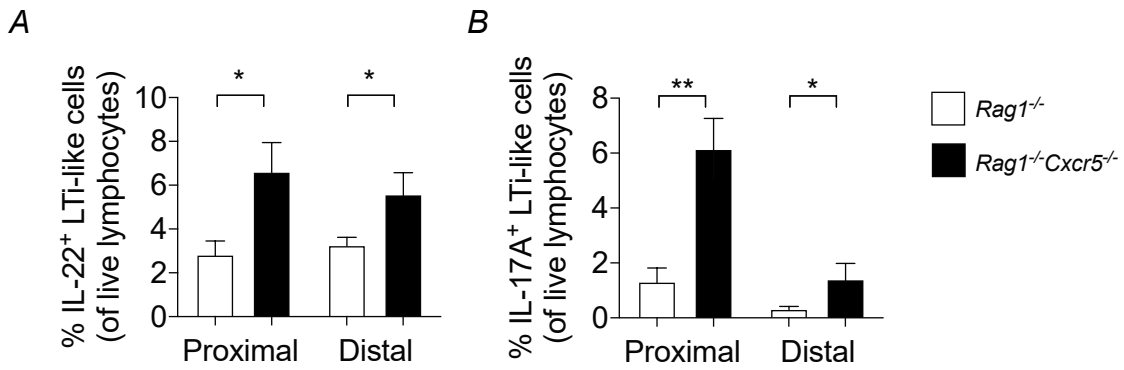
SI Appendix, Fig. S2. CXCL13 does not directly suppress LTi-like cell cytokine production. Frequencies of (A) IL-22- and (B) IL-17A-producing small intestine LTi-like cells after ex-vivo stimulation with 1 ng/ml IL-23 in the presence of varying amounts of CXCL13, as indicated (n=3). Stimulations were carried out for 3 h. Bar graphs show mean ± SEM. Data shown are representative of 2 independent experiments.



SI Appendix, Fig. S3. Abundance of CCR6⁺ ILC3 in small intestines of *Cxcr5*^{-/-} and WT neonates. (A) Frequencies and (B) absolute numbers of CCR6⁺ ILC3 in small intestines of *Cxcr5*^{-/-} and WT control mice at postnatal day 0 (n=4). Bar graphs show mean \pm SEM.

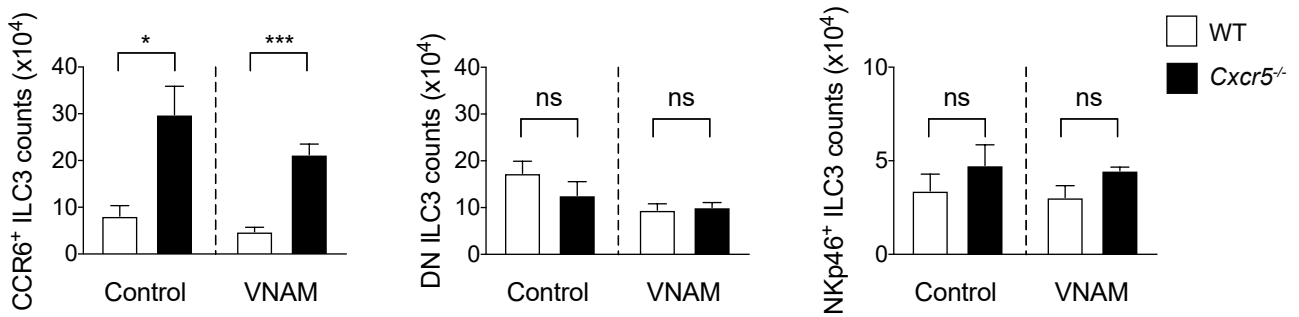


SI Appendix, Fig. S4. Characterization of ileal SILT in *Cxcr5*^{-/-}*Rag1*^{-/-} small intestines. (A) Representative images of crypt-level CD4⁺ LTi-like cell aggregates in the distal small intestines of *Cxcr5*^{-/-}*Rag1*^{-/-} and *Rag1*^{-/-} control mice. (B) Representative images of villus RORγt⁺ ILC3 aggregates in the proximal intestines of *Cxcr5*^{-/-}*Rag1*^{-/-} and *Rag1*^{-/-} control mice. (C) Representative images of CD11c⁺ DCs in the proximal small intestines of *Cxcr5*^{-/-}*Rag1*^{-/-} and *Rag1*^{-/-} control mice. Insets from boxed areas show CD11c staining only. Tissue sections were stained with DAPI for nuclei labeling or EpCAM for epithelial cells visualization as indicated.

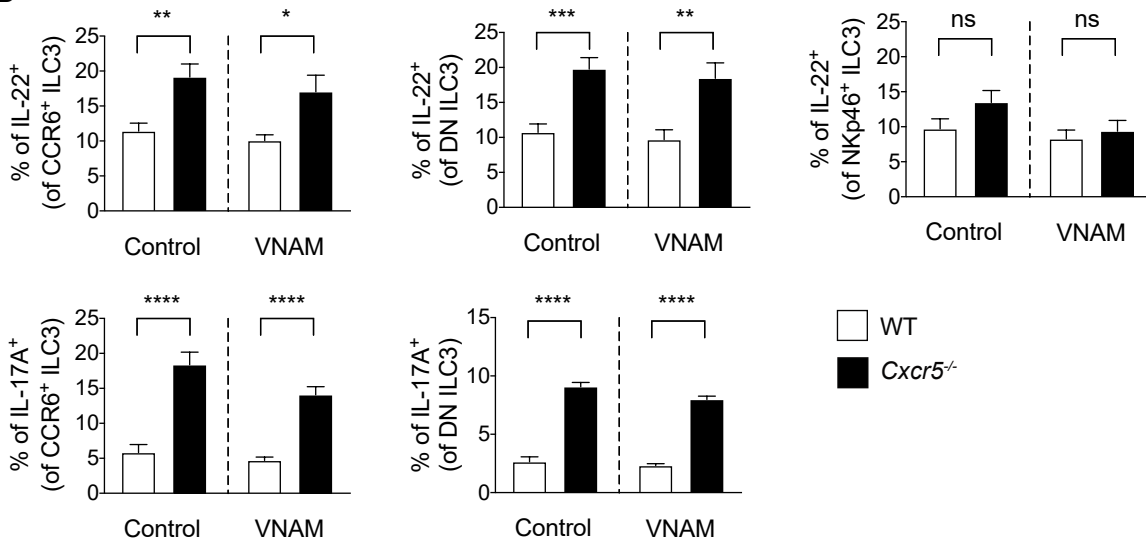


SI Appendix, Fig. S5. Abundance of cytokine-producing LTI-like cells as a percentage of all live lymphocytes in proximal and distal areas of *Cxcr5*^{-/-}*Rag1*^{-/-} and *Rag1*^{-/-} small intestines. (A) IL-22- and (B) IL-17A-producing LTI-like cells expressed as a frequency of all small intestine live lymphocytes. Bar graphs show mean ± SD. * P<0.05 and ** P<0.01. Data shown are representative of 2 independent experiments.

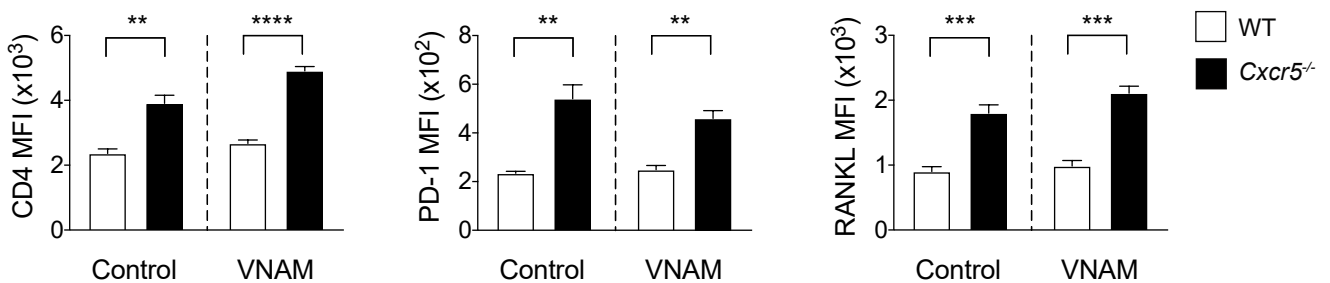
A



B



C



SI Appendix, Fig. S6. Heightened LTi-like cell activity in *Cxcr5*^{-/-} mice does not require microbio-ta-derived signals. (A) Total cell counts of small intestine LTi-like, DN and NKp46⁺ ILC3 in *Cxcr5*^{-/-} and WT mice that were administered VNAM or control drinking water for 4 weeks. (B) Frequencies of IL-22- and IL-17A-producing LTi-like, DN and NKp46⁺ ILC3 from VNAM-treated or control mice after *ex vivo* stimulation with 1 ng/mL of IL-23. Stimulations were carried out for 3 h. (C) CD4, PD-1 and RANKL cell surface expression by LTi-like cells isolated from control or VNAM-treated *Cxcr5*^{-/-} and WT mice. Bar graphs show mean \pm SEM. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ and **** $P < 0.0001$. Data from A and C are representative of 2 independent experiments (n=3-4). Data in B were pooled from 2 independent experiments (n=7-8).