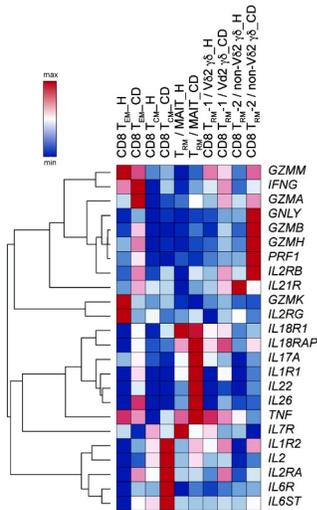


# Supplementary Material

## Supplementary Figures

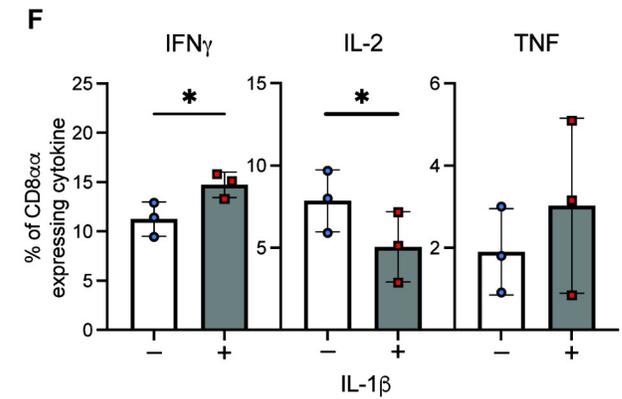
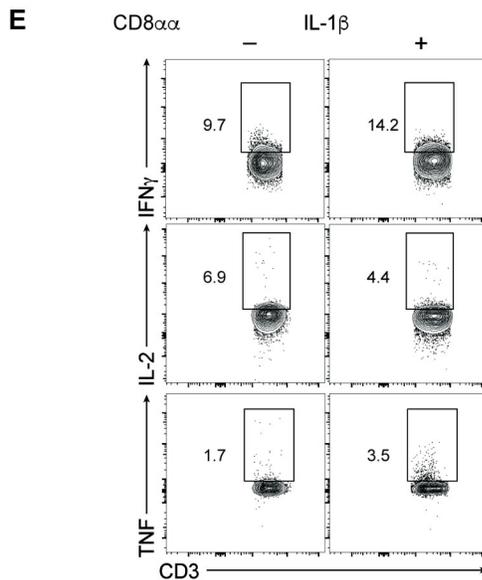
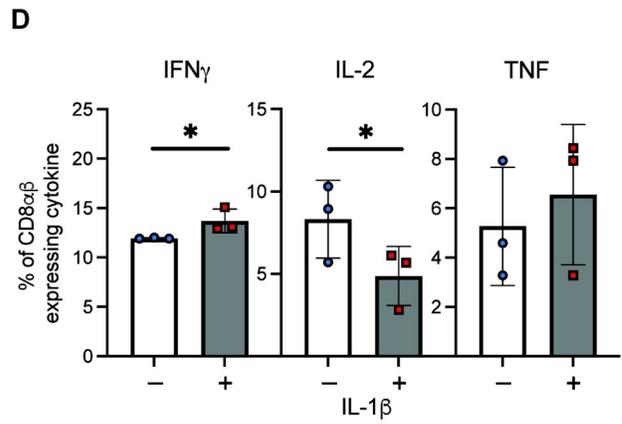
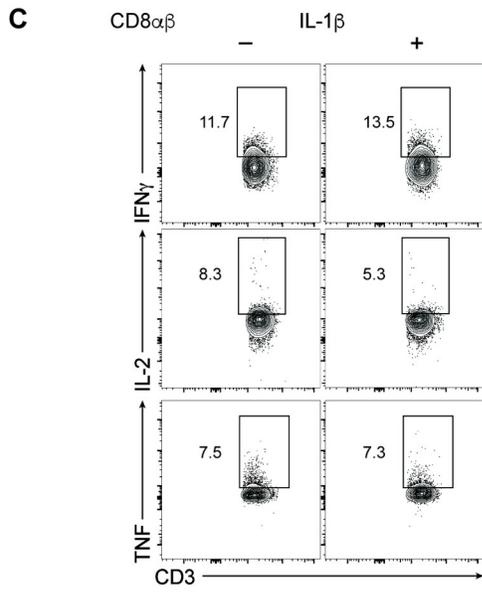
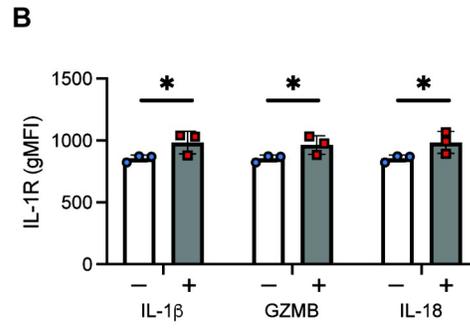
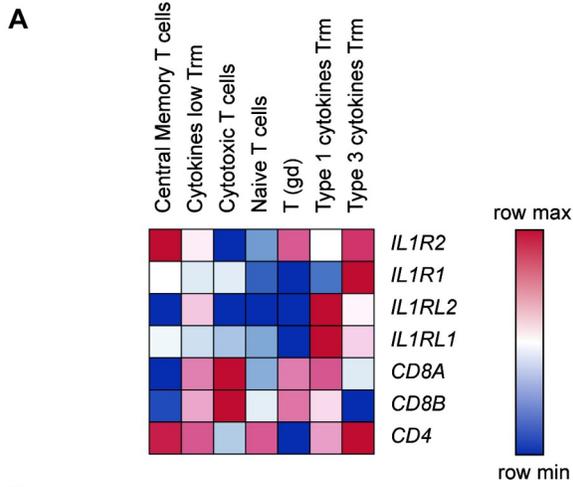
### Supplementary Figure 1



**Supplementary Figure 1. Expression of selected genes among CD8<sup>+</sup> T cell subsets from healthy subjects vs. CD patients.** Relative expression of selected genes in CD8<sup>+</sup> T cell subsets from healthy (H) subjects vs. CD patients (CD), represented as hierarchically clustered summary heatmaps, with rows representing selected genes and columns representing CD8<sup>+</sup> T cell subsets.

Supplementary Material

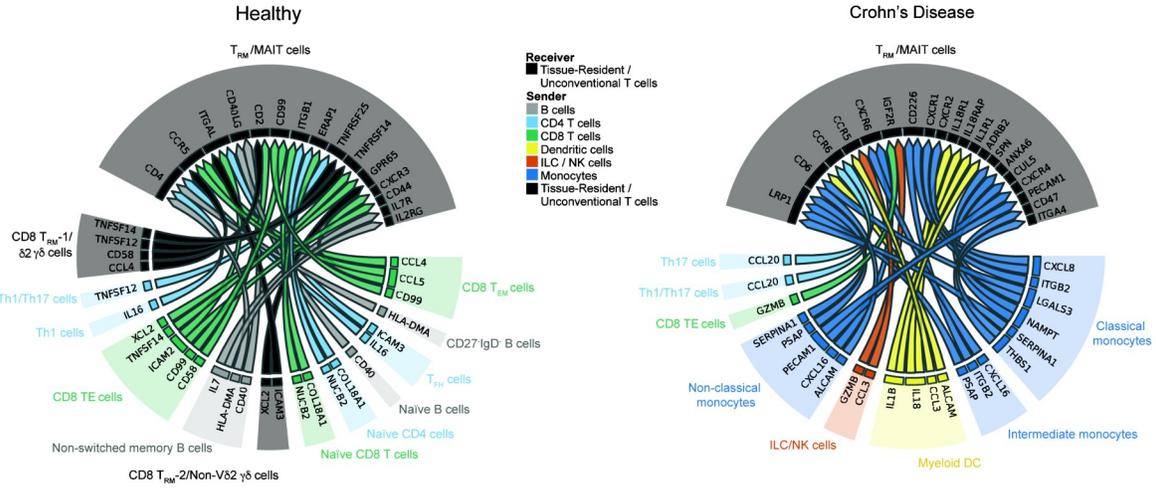
Supplementary Figure 2



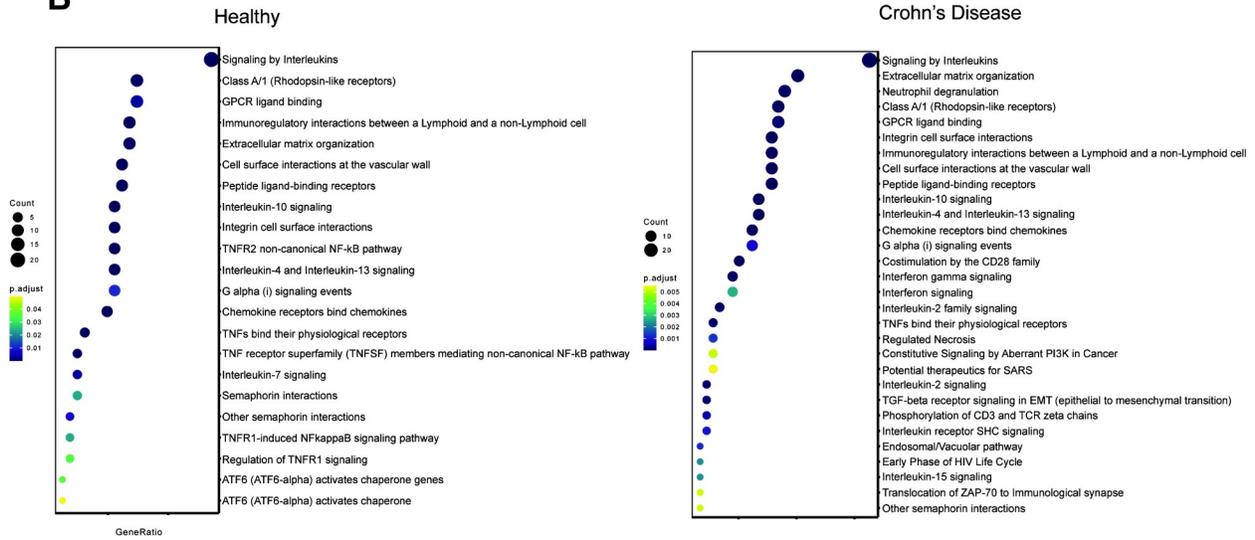
**Supplementary Figure 2. Cytokine production in CD8 T cells modulated by interleukin-1 $\beta$  (IL-1 $\beta$ ).** (A) Gene expression of IL-1 family members in T cell subsets derived from Martin et al., *Cell* 2019, represented as a summary heatmap. Small intestine cells isolated from 3 individual mice were treated with 1 ng/mL of IL-1 $\beta$ , granzyme B (GZMB), interleukin-18 (IL-18), or vehicle control in the presence of phorbol myristate acetate, ionomycin, brefeldin A, and monensin for 4 hours. (B) Geometric mean fluorescence intensity (gMFI) of IL-1R among small intestine CD8 lymphocytes (n = 3, \*  $p < 0.05$ , 2-way ANOVA). (C) Representative flow plots showing interferon- $\gamma$  (IFN $\gamma$ ), interleukin-2 (IL-2), or tumor necrosis factor (TNF) production by CD3<sup>+</sup>CD8 $\alpha\alpha$ <sup>+</sup> T lymphocytes. (D) Quantification of the percentage of live CD3<sup>+</sup>CD8 $\alpha\alpha$ <sup>+</sup> T lymphocytes expressing cytokines, represented as a bar plot (n = 3, \*  $p < 0.05$ , 2-way ANOVA). (E) Representative flow plots showing IFN $\gamma$ , IL-2, and TNF production by CD3<sup>+</sup>CD8 $\alpha\beta$ <sup>+</sup> T lymphocytes. (F) Quantification of the percentage of live CD3<sup>+</sup>CD8 $\alpha\beta$ <sup>+</sup> T lymphocytes expressing cytokines, represented as a bar plot (n = 3, \*  $p < 0.05$ , 2-way ANOVA).

Supplementary Figure 3

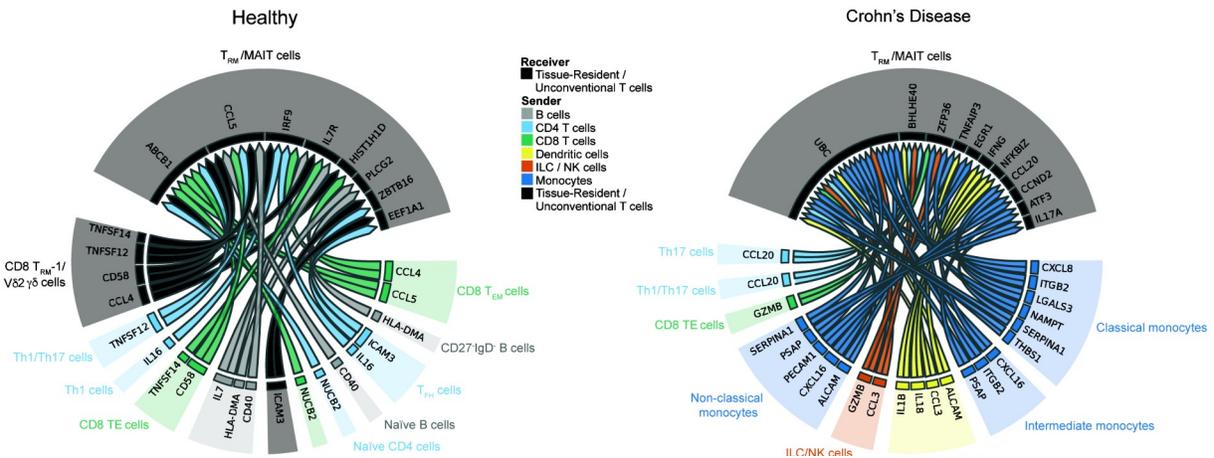
A



B



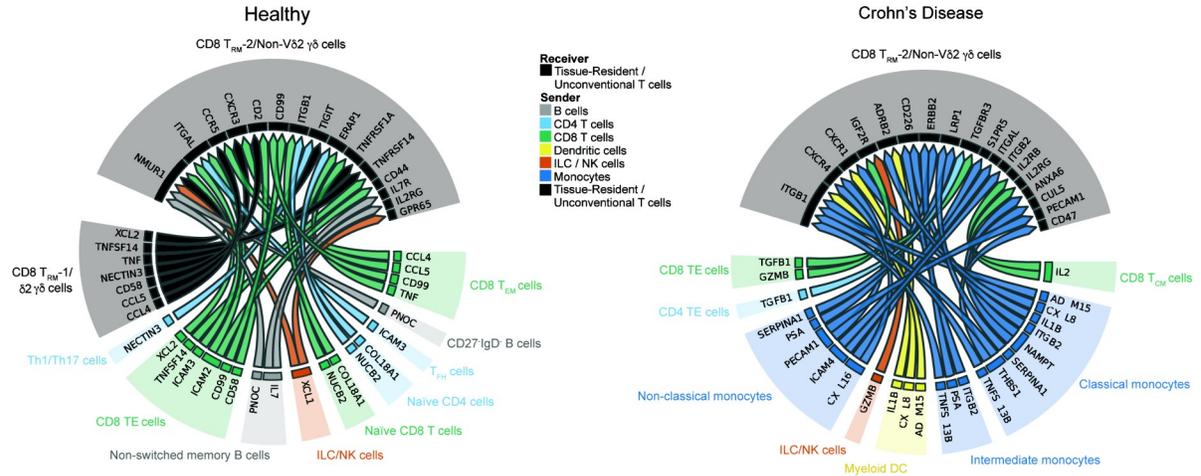
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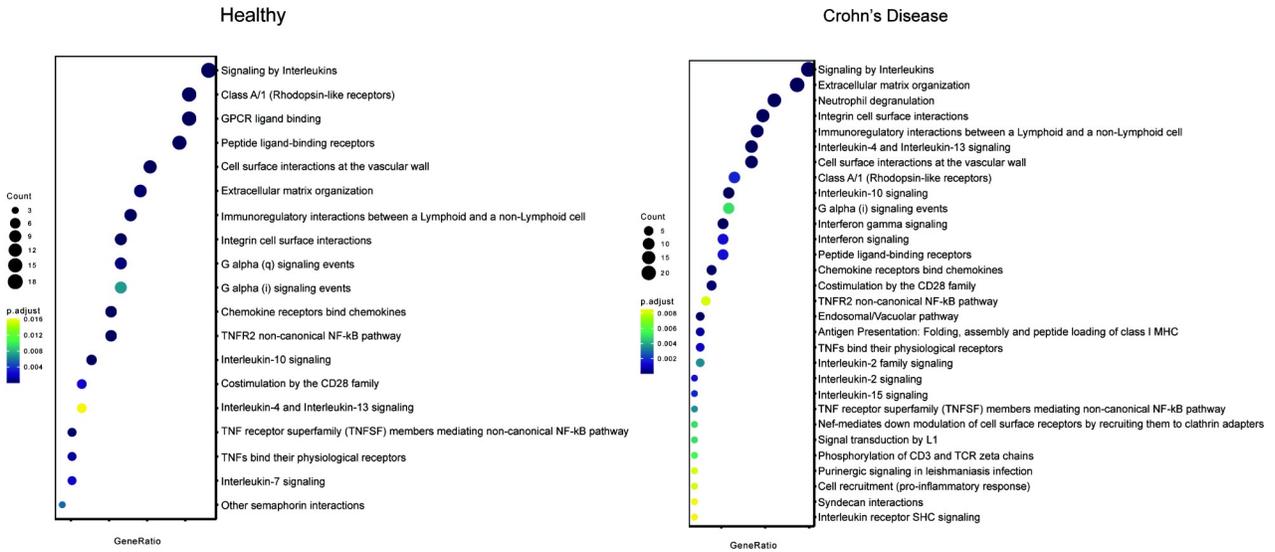
**supplementary Figure 3. NicheNet analyses of real TRM/MAIT cell interactions with other immune cells in health vs. Crohn's disease.** (a) Putative ligand: receptor pairs on 'sender' immune cells and 'receiver' cells (TRM/MAIT cells), represented as Circos plots, in healthy subjects (left) or CD patients (right). Colors indicate major immune cell type; each major cell type is also indicated in the caption between the two Circos plots. Specific immune cell subsets are labeled around the Circos plot. (b) Pathway analyses of enriched genes downstream of predicted ligand:receptor pairs, represented as reactome plots, in healthy subjects (left) or CD patients (right). (c) Genes predicted to be induced in TRM/MAIT cells by predicted ligand:receptor interactions.

Supplementary Figure 4

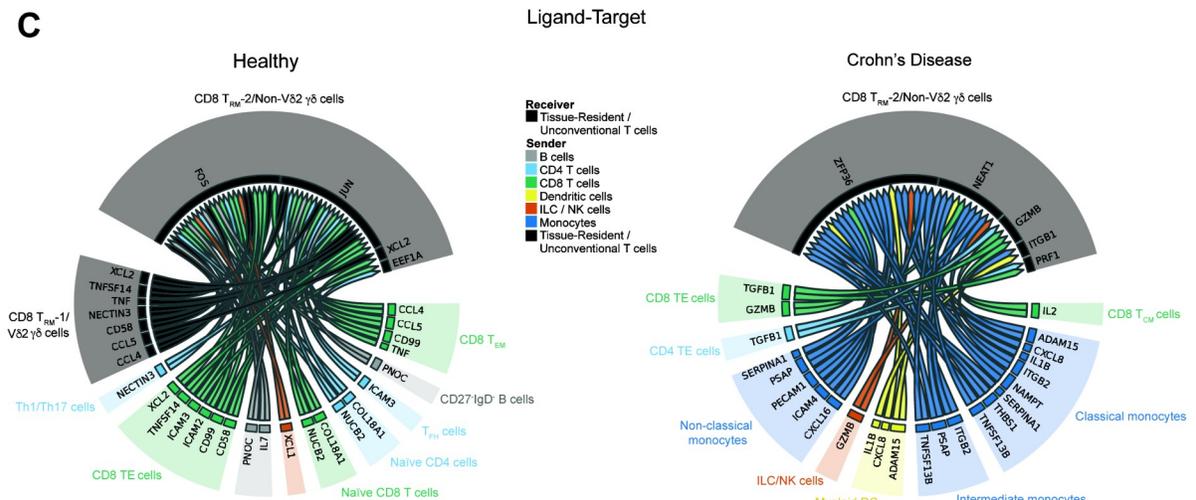
A



B



C



**supplementary Figure 4. NicheNet analyses of ileal CD8<sup>TRM-1</sup>/non-Vd2 gd T cell interactions with other immune cells in health vs. Crohn's disease** (a) Putative ligand: receptor pairs on 'sender' immune cells and 'receiver' cells (CD8<sup>TRM-1</sup>/non-Vd2 gd T cells), represented as Circos plots, in healthy subjects (left) or CD patients (right). Colors indicate major immune cell type; each major cell type is also indicated in the caption between the two Circos plots. Specific immune cell subsets are labeled around the Circos plot. (b) Pathway analyses of enriched genes downstream of predicted ligand:receptor pairs, represented as reactome plots, in healthy subjects (left) or CD patients (right). (c) Genes predicted to be induced in CD8<sup>TRM-1</sup>/non-Vd2 gd T cells by prioritized ligand:receptor in