Meylan et al. Figure S1

(a) Histological sections of various genotypes:
- WT
- TL1A Tg
- Jα18−/− TL1A Tg
- CD1d−/− TL1A Tg
- KitW-sh/W-sh TL1A Tg

(b) Graphs showing:
- Avg Goblet Cell Area (µm²)
- Mucosal Thickness Index

(c) Bar graph showing IL-13 mRNA fold change for:
- WT
- TL1A Tg
- Jα18−/− TL1A Tg
- CD1d−/− TL1A Tg
- KitW-sh/W-sh TL1A Tg
Meylan et al. Figure S2

(a) Flow cytometry plots showing the distribution of ILC1, ILC2, and ILC3 populations based on NK1.1, KLRG1, CD127, RORγt, and DR3 expression.

(c) Histograms illustrating the expression levels of DR3 among ILC1, ILC2, and ILC3 populations in WT and DR3−/− mutant mice.

(d) Scatter plot showing the cell number of ILC1, ILC2, and ILC3 in WT and DR3−/− mice, with error bars indicating the standard deviation.
Meylan et al. Figure S3

**a**
- 4C13R reporter
- 4C13R + IL-25
- 4C13R x CD2-TL1A Tg

**b**
- IL13-dsRed
- IL4-AmCyan
Meylan et al. Figure S4

The figure shows flow cytometry dot plots comparing the expression of Lin and ICOS in WT and DR3−/− mice treated with PBS, IL-25, or IL-33. The dot plots indicate the percentage of cells in each quadrant, with numbers showing the proportion of Lin−ICOS+ cells.

The bar graph in panel b quantifies the expression of Lin−ICOS+ cells across different treatments and genotypes, with error bars indicating the range of values.
Meylan et al. Figure S5

(a) Liver weight as a percentage of body weight for WT, DR3 KO, and DR3-/- groups.

(b) Granuloma size in mm$^3 \times 10^{-3}$ for WT, DR3 KO, and DR3-/- groups.

(c) Liver weight distribution for WT, DR3 KO, and DR3-/- groups.

(d) Total eggs per liver, comparing WT, DR3 KO, and DR3-/- groups.

(e) Relative expression of IL-13, IL-10, and IFN-γ in liver and duodenum for WT, DR3 KO, and DR3-/- groups.

(f) Hydroxyproline levels (µM/worm pair) for WT, DR3 KO, and DR3-/- groups.
Supplemental Figure Legends

Figure S1. TL1A driven small bowel pathology is IL-13 dependent but does not require NKT or mast cells, related to Figure 1
(a) Representative transverse histological ileum sections stained with PAS from 14-18 weeks old mice are shown. Scale bars =100 μm. Histological characteristics quantified as described in the methods sections represent the compilation of 6-18 mice per group. (b) Histological characteristics quantified as described in the methods sections. (c) mRNA expression of IL-13 from ileal tissue normalized to β2m expression and shown relative to expression levels in untreated WT mice. Data represent mean ± SEM analyzed with Mann-Whitney (*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001).

Figure S2. DR3 Expression on ILC subsets and role of DR3 in ILC homeostasis, related to Figure 3
(a) DR3 expression was performed in cell populations discriminated based on expression of NK1.1, KLRG1, CD127 and RORγt. ILC1 (NK1.1+), ILC2 (NK1.1’KLRG1+) and ILC3 (CD127’Rorγt+) populations were gated as shown. (b) DR3 expression levels were evaluated by flow cytometry in WT mice (blue), DR3-deficient mice (green), or with an isotype control (IC) antibody (red). (c) Absolute numbers of ILC1 (NK1.1+), ILC2 (NK1.1’KLRG1+) and ILC3 (CD127’Rorγt+) in the mesenteric lymph nodes are shown. Each dot represents an individual mouse. Mean +/- SEM depicted.

Figure S3. Expression of IL-4 and IL-13 reporters in TL1A transgenic mice crossed to 4C13R reporter mice, related to Figure 4
FACS plots of ICOS vs. reporter expression in Lin’ (CD19’, CD3’) cells are shown. IL-13 (a) and IL-4 (b) reporter expression in mesenteric lymph nodes from IL-4/AmCyan/IL-13/dsRED BAC transgenic mice untreated, given 400 ng of IL-25 for three consecutive days, or crossed to CD2-TL1A transgenic mice. Examples are representative of 3 mice per group.
Figure S4. ILC2 expansion in response to IL-25 and IL-33 is independent of DR3, related to Figure 5
(a) Lineage (CD3, CD4, CD8, CD11b, CD11c, CD19, GR1, NK1.1) vs ICOS expression in mesenteric lymph nodes of WT and DR3-deficient mice treated or not with four consecutive days of i.p. IL-25 (2 ug per day) or IL-33 (0.5 ug per day). (b) Yield of Lin^− ICOS^+ cells gated as in (A) from the mesenteric lymph nodes was calculated for mice from each treatment group with 3 mice per group.

Figure S5. Host defense and type 2 immune response to Schistosoma mansoni infection is independent of DR3, related to Figure 5
Expression of cytokines in the liver (a) and small intestine (b) of mice challenged with Schistosoma mansoni. (c) Liver weight, hepatic granuloma size and percentage of eosinophils in granulomas from WT and DR3-deficient S. mansoni infected mice. (d) Numbers of adult Schistosoma worm pairs in the mesenteric veins and calculated total liver egg burden per mouse. Data represent mean ± SEM analyzed with Mann-Whitney (*p<0.05). (e) Leukocyte yields in the mesenteric lymph nodes from WT and DR3-deficient S. Mansoni infected mice. (f) Hydroxyproline measured and normalized to worm pair in WT and DR3-deficient S. Mansoni infected mice.