



Fig. S2 Ablation of Lepr⁺ cells led to disrupted colonic homeostasis. **a** PAS staining in the jejunum from *Lepr-Cre* and *Lepr-Cre;iDTR* mice. The mice were injected intraperitoneally with DT for 10 consecutive days. Quantification of the percentage of goblet cells from *Lepr-Cre* and *Lepr-Cre;iDTR* mice (n=3). Scale bar: 200 μ m. **b, c** Immunohistochemistry for ChgA (**b**) and Dclk1 (**c**) in the jejunum from *Lepr-Cre* and *Lepr-Cre;iDTR* mice. The mice were injected intraperitoneally with DT for 10 consecutive days. The percentage of EECs and Tuft cells in intestine was quantified (n=3). Scale bar: 200 μ m. **d** Immunofluorescence for Lysozyme in the jejunum from *Lepr-Cre* and *Lepr-Cre;iDTR* mice. The mice were injected intraperitoneally with DT for 10 consecutive days. Quantification of Paneth cells per crypt (n=3). Scale bar: 10 μ m. **e** Histology of colons from *Lepr-Cre* and *Lepr-Cre;iDTR* mice treated for 10 consecutive days with DT. Crypt depth was quantified (n=3). Scale bar: 50 μ m. **f** Immunohistochemistry for Ki67 in colons from *Lepr-Cre* and *Lepr-Cre;iDTR* mice treated with DT for 10 consecutive days. Ki67⁺ cells per crypt were quantified (n=3). Scale bar: 50 μ m. **g** Immunofluorescence for BrdU in colons from *Lepr-Cre* and *Lepr-Cre;iDTR* mice at indicated timepoints post BrdU pulse chase. Dashed lines demarcate the top, middle and base of crypts, respectively. n=3 biological replicates at each timepoints. Scale bar: 50 μ m. Values in the graphs represent means \pm SD. Unpaired student's t-test was used for calculating P values in **a - f**, * $P < 0.05$; *** $P < 0.001$; n.s., not significant.