



**Fig. S6 Diet modulates ISCs and precursors.** **a, b** Immunofluorescence for Ki67/ $\beta$ -Catenin (**a**) and Sox9/ $\beta$ -Catenin (**b**) in the jejunum from *ad libitum*-fed and fasted mice at 48 hours. Number of Ki67<sup>+</sup> cells per crypt and Sox9<sup>+</sup> cells per crypt were quantified (n=3). Scale bar: 25  $\mu$ m. **c** Immunocytochemistry for cleaved Caspase 3 in the jejunum from *ad libitum*-fed and fasted mice at indicated time (n=3). Caspase3<sup>+</sup> cells at the top of villi were used as positive control. Scale bar: 50  $\mu$ m. **d** *In situ* hybridization for *LEPR* in intestinal crypts from lean (n=3, BMI  $\leq$  21.1 kg/m<sup>2</sup>) and obese (n=3, BMI  $\geq$  25.8 kg/m<sup>2</sup>) human individuals. Scale bar: 25  $\mu$ m. **e, f** Immunofluorescence for Ki67/ $\beta$ -Catenin (**e**) and Sox9/ $\beta$ -Catenin (**f**) in the jejunum from mice placed under ND or HFD regimes. Number of Ki67<sup>+</sup> cells per crypt and Sox9<sup>+</sup> cells per crypt were quantified (n=3). Scale bar: 25  $\mu$ m. **g, h** Immunofluorescence for Ki67/ $\beta$ -Catenin (**g**) and Sox9/ $\beta$ -Catenin (**h**) in the jejunum of mice treated with recombinant mouse Leptin protein. Number of Ki67<sup>+</sup> cells per crypt and Sox9<sup>+</sup> cells per crypt were quantified (n=3). Scale bar: 25  $\mu$ m. **i** qRT-PCR analysis for *Igf1* in primary intestinal mesenchymal cells treated with recombinant mouse Leptin protein at 100 and 200 ng/mL of concentration for 24 hours (n=3). **j** Western blotting for Igf1 and p-STAT3 in primary intestinal mesenchymal cells treated with recombinant mouse Leptin protein at 200 ng/mL of concentration for 24 hours.  $\beta$ -Actin was used as a loading control. **k** qRT-PCR analysis for *Igf1* in intestine from *ad libitum* and fasted mice at 48 hours (n=3). **l** qRT-PCR analysis for *Igf1* in the intestines of mice placed under ND and HFD regimes (n=3). **m** qRT-PCR analysis for *Igf1* in the intestines treated with recombinant mouse Leptin protein (n=3). **n** The growth curve of primary MCs treat with recombinant Igf1 protein; n=3 at each timepoint. Values in the graphs represent means  $\pm$  SD. Unpaired student's t-test was used for calculating P values in **a, b, e - i** and **k - n**, \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .