SUPPLEMENTAL MATERIAL

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Figure S1. Broad expression of Notch signaling components. In situ hybridization of mouse stomachs at E14 with Notch1, ligands Jagged 2 and Delta3, and Hes1. Lu, gastric lumen. Bar, 50 μm. Experiments were repeated twice, with similar results.

Figure S2. Effects of pharmacologic inhibition of the Notch pathway in adult mouse gut. (A and B) Reproducible replication arrest and goblet cell metaplasia in intestinal epithelium after treatment with 20 μmol/kg DBZ, revealed by staining with Ki67 Ab (A) or Alcian blue dye (B). (C) DBZ abolished Hes1 expression in intestine (Int) and stomach (St). (D) Chromogranin A+ EE cells were mildly increased in DBZ-treated mice. Bars, 50 μm. Quantification in D was made using three mice per group, and all other experiments were repeated twice, with similar results. Error bars represent standard deviations.
Figure S3. Characterization of Atp4b-Cre and dedifferentiation by Notch activation. (A) Co-labeling of YFP and Atp4b in 8-d-old Atp4b-Cre;Rosa26+/YFP mice. (B) Nonoverlapping expression of chief (GIF) and parietal (Atp4b) cell differentiation markers. (C) Lack of proliferation (EdU uptake) in fully differentiated, Atp4b-expressing parietal cells. (D and E) YFP+ cells in Atp4b-Cre;Rosa26+/YFP mouse stomach never express the EE marker chromogranin A (D), nor are they ever present in the pit-cell zone bordering the stomach lumen (E). DAPI nuclear staining of full glands is shown to the right. (F) YFP+ cells in 6-wk-old Atp4b-Cre;Rosa26NICD/YFP mouse stomach form mature, Atp4b+ parietal cells. (G) Occasionally, glands that were fully YFP+ were found in the Atp4b-Cre;Rosa26NICD/YFP stomach antrum. (H) As with the YFP reporter, Atp4b-Cre;Rosa26NICD/LacZ mice also show fully β-gal+ gastric glands, mixed with occasional glands showing persistent parietal cell–restricted β-gal expression. Dashed lines (A, C, and E) demarcate the luminal edge of stomach glands. Bars, 50 μm. All experiments used at least four mice per group, and stains were done in duplicate, with similar results.

Figure S4. Delayed formation of sessile adenomas upon constitutive Notch activation. Low-magnification view of H&E-stained 18-wk-old Atp4b-Cre;Rosa26NICD/YFP stomach. Bar, 50 μm. Experiments were repeated twice using five mice, with similar results.