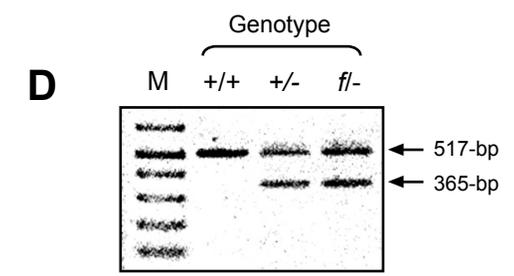
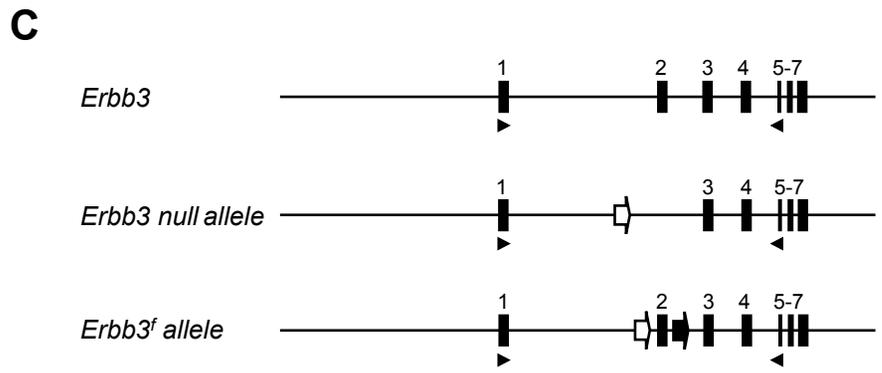
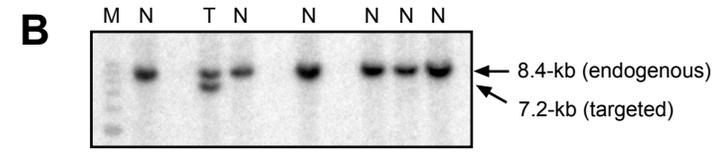
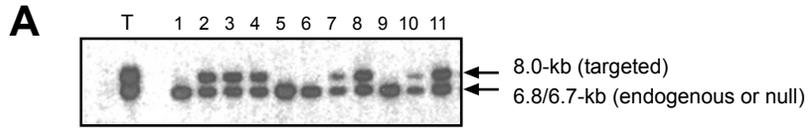


## Supplemental Figure 1

Analysis of *ErbB3* targeting. **(A)** CRE-mediated excision was analyzed by Southern blot from ES cell subclones (1 to 11) derived from the one of the targeted ES cell clone (T) shown in Figure 1A. ES cell subclones 1, 5, 6, and 9 show complete CRE-mediated excision. **(B)** Conditional *ErbB3* targeting was analyzed by Southern blot using probe shown in Figure 1B. T denotes one of the targeted ES cell clone, N shows no targeted clones and M represents DNA size marker, respectively. **(C)** Schematic of *ErbB3*, *ErbB3* null and *ErbB3<sup>f</sup>* alleles. The number (1-7) indicates exons. **(D)** Expression of engineered *ErbB3* alleles. Total RNA from the small intestine was prepared from mice with different *ErbB3* genotypes using Trizol (Invitrogen). One microgram of total RNA was reverse transcribed with Superscript II reverse transcriptase (Invitrogen) with random hexamers. One twentieth of the reverse transcription (RT) product was amplified by PCR with *ErbB3* primers Erbb3-Ex1S, 5'-TTCCGAGATGGGCAACTCTC -3' (sense primer from exon 1) and Erbb3-Ex5AS, 5'-CTTGCAGACTTCGTGACAGG -3' (antisense primer from exon 5). The reverse RT-PCR products were resolved with 1.2% agarose gel electrophoresis and visualized with ethidium bromide staining. The Erbb3-Ex1S and Erbb3-Ex5AS primers produce a 517-bp PCR product for wildtype and 365-bp PCR product without exon 2 for *ErbB3* null allele.



## **Supplemental Figure 2**

Gene expression of *ErbB* family members. Total RNA from the various organs was prepared from wildtype 129/SvEvTAC male and RT-PCR was performed as described in Supplemental Figure 1 with primers specific for *Egfr*, *ErbB2*, *ErbB3* (30 cycles), *ErbB4* (35 cycles), and *Actb* (25 cycles).



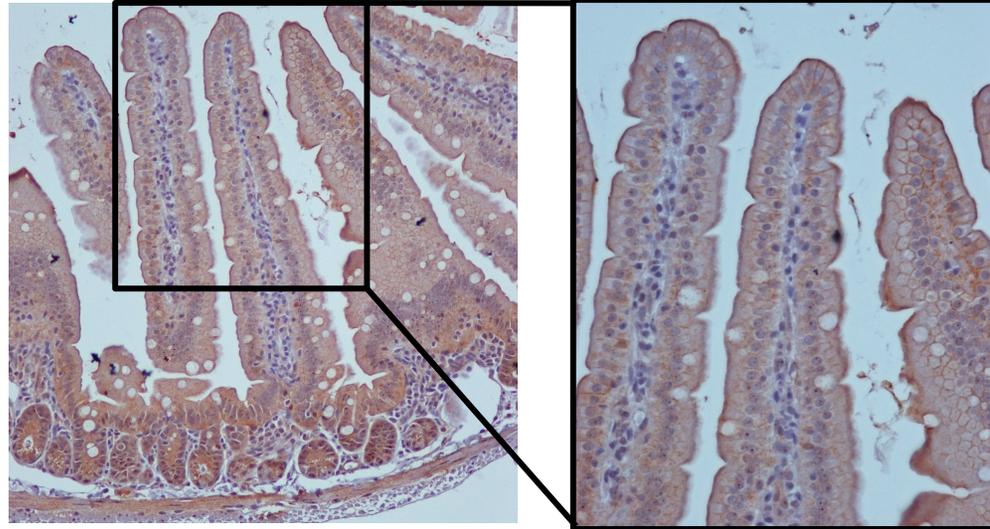
### **Supplemental Figure 3**

Immunostaining of intestinal sections for ERBB3 expression using peroxidase detection.

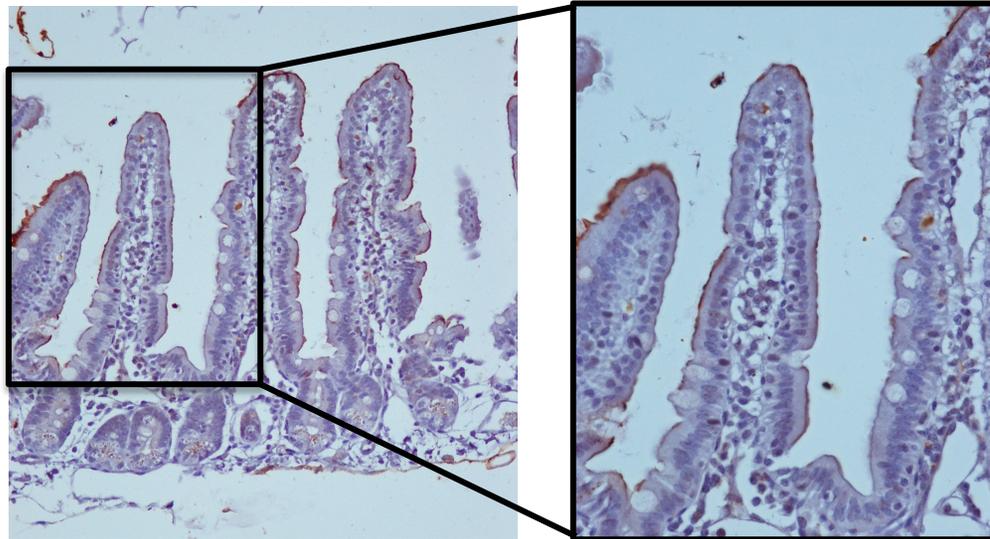
Control (top) shows extensive ERBB3 staining compared to *ErbB3* mutant (bottom).

Magnification, 40X (left) and 200X (right).

Control



*ErbB3* mutant



#### **Supplemental Figure 4**

Distribution of intestinal polyps in *Apc<sup>Min</sup>* mice. Solid bars represent *Apc<sup>Min</sup>* control mice and open bars represent *Apc<sup>Min</sup>, Erbb3* mutant mice. \*\*\*,  $P < 0.0001$ ; \*\*\*\*,  $P < 0.00001$ ; Mann-Whitney U test.

