Supporting Information

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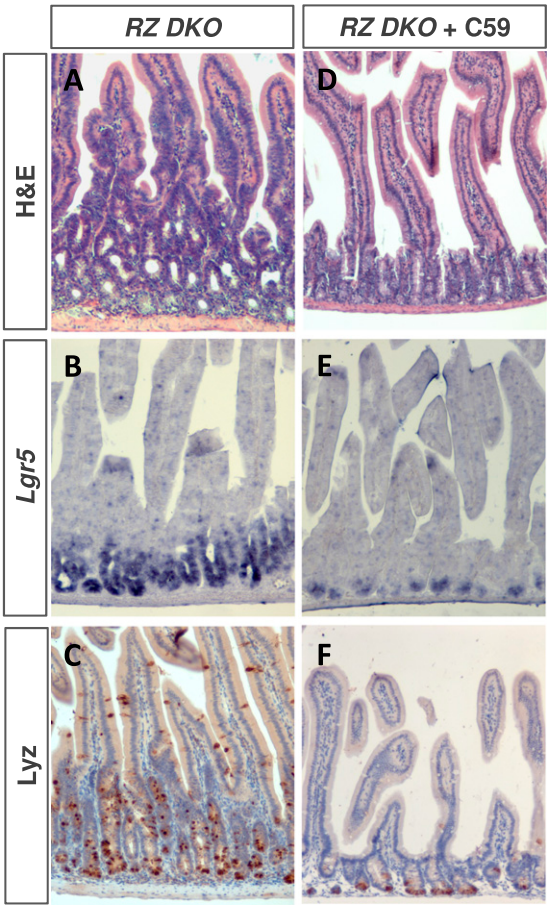

Fig. S1. Porcupine inhibitor C59 prevents tumorigenic outgrowth of *Rnf43* and *Znrf3* mutant epithelia. Mice were treated with C59 porcupine inhibitor for seven consecutive days upon tamoxifen (Tam) administration to *RZ* (*D*–*F*) mutant mice. C59 untreated, but tamoxifen-treated *RZ* mutant mouse was used as tumorigenic positive control (*A*–*C*). Sections were analyzed by *Lgr5*, a marker for intestinal stem cells (*B* and *E*), and Lysozyme (Lyz), a marker for Paneth cells (*C* and *F*).

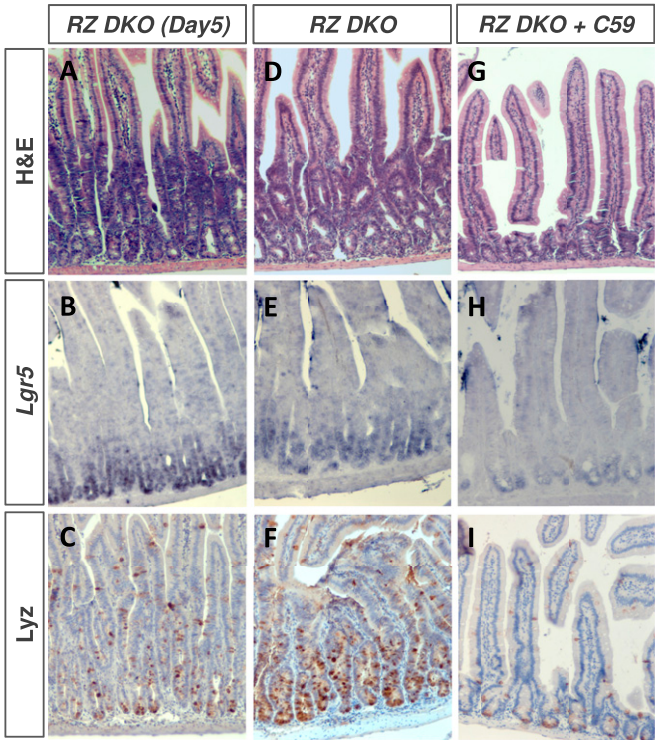

Fig. S2. Porcupine inhibitor C59 eradicates preestablished neoplasia induced by *Rnf43* and *Znrf3* loss. Mice were treated with C59 porcupine inhibitor 5 d after initial tamoxifen (Tam) administration to *RZ* (*G–I*) mutant mice. C59 untreated, but tamoxifen-treated RZ mutant mice were used as control (*D–F*). *RZ* mutant mice were analyzed on day 5 to examine the status of hyperplasia at the time point when C59 treatment was started (*A–C*). Sections were analyzed by *Lgr5*, a marker for intestinal stem cells (*B*, *E*, and *H*) and Lysozyme (Lyz), a marker for Paneth cells (*C*, *F*, and *I*).