Supplementary Figure Legends:

Figure S1. Epithelial deletion of Cdc42 abrogates $APC^{Min/+}$ tumorigenesis.

(A) Dysplastic crypts in 7 week old $APC^{Min/+}$ mice contained Lysozyme-expressing cells (green).

(B) No dysplastic crypt but cystic formation was detected in $APC^{Min/+}$;$Cdc42^{\Delta IEC}$ intestines.

Figure S2. Improved body weight in $Catnb^{(ex3)/+}$;$Cdc42^{fl/+}$;Vil-Cre mice.

Figure S3. Epithelial Cdc42 deletion alleviated formation of crypt-like foci.

$Catnb^{(ex3)/+}$;$Cdc42^{fl/fl}$;Vil-Cre mouse intestines contained no crypt-like foci in villus epithelia.

Figure S4. Cdc42 deletion reduced Paneth-like cells in microadenoma foci.

Lysozyme immunohistochemistry was done on tissue sections of indicated genotypes.

Figure S5. CASIN treatment arrested LIM1863 tumor organoids.

(A) Flow cytometry analysis of cell cycle distributions of individual CRC cell lines. Cells were harvested at 70-80% confluence for analysis.

(B) CASIN treatment reduced Cdc42-GTP level in LIM1863 (top left panel) and induced drastic membrane protrusions in LIM1863 tumor organoids (top right panel). All LIM1863 organoids were arrested by CASIN within 48 hrs in culture.