**SUPPLEMENTARY FIGURE LEGENDS**

**Supplementary Figure 1.** **PAK1 regulates β-catenin expression throughout the intestine**. (A) Immunohistochemical (IHC) staining of β-catenin in large and small bowel tissue sections in untreated WT and PAK1-/- mice. In comparison to WT, PAK1-/- mice had less β-catenin in the cytoplasm and nucleus throughout the crypt axis. (B) IHC staining of PAK1 in APCmin and APCmin/PAK1-/- adenomas. PAK1 was expressed throughout the tumor in APCmin mice and absent in APCmin/ PAK1-/- mice.

**Supplementary Figure 2. PAK1 regulates β-catenin signaling in APCmin adenomas**. Dot plots are mean IRS’s for β-catenin, p-β-catenin (Ser 675) Cyclin D1 C-Myc, and p-AKT (Thr 308) expression in adenomas of APCmin and APCmin/ PAK1-/- mice. Deletion of PAK1 reduced β-catenin expression in the cytoplasm and nucleus. Cyclin D1 expression was not altered upon PAK1 deletion. C-Myc expression was reduced in APCmin/PAK1-/- adenomas. P-AKT (Thr 308) is reduced upon PAK1 deletion. All data are at least (n=4) mice per group. Independent samples T-test, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001.

**Supplementary Figure 3 (A-E). Effect of PAK1 deletion on tumorigenesis in an AOM/DSS model**. (A) Weight curves of female mice over the course of 12 weeks. (B) Representative H&E images which were evaluated and scored for inflammation. PAK1 deletion did not alter the inflammatory grade in AOM/DSS mice. 5-ASA restored crypt architecture and reduced inflammation in the lamina propria in WT and PAK1-/- mice. (C) The box plot depicts the inflammatory score in male and female mice. 5-ASA reduced inflammatory grade in WT and PAK1-/- mice. Data are (n=8) WT, (n=13) PAK1-/-, (n=16) WT + 5-ASA, and (n=13) PAK1-/- + 5-ASA mice and WT (n=22), PAK1-/- (n=11), WT + 5-ASA (n=6), and PAK1-/- + 5-ASA (n=8) female mice. (D) Boxplots are colonoscopy data of total tumor number, small, medium, and large tumors in female mice. PAK1 deletion does not impede tumorigenesis in female mice. (E) Microscopic analysis of tumor number, dysplastic lesions, and carcinoma in situ. 5-ASA but not PAK1 deletion impeded tumorigenesis. Data are WT (n=22), PAK1-/- (n=11), WT + 5-ASA (n=6), and PAK1-/- + 5-ASA (n=8) female mice. Statistical analysis were performed by ANOVA using LSD post hoc analysis, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001.

**Supplementary Figure 4 (A-E).** **Inhibition of PAK1 impedes AKT/ β-catenin signaling in AOM/DSS mice.** (A) Immunohistochemical staining of PAK1 in WT and PAK1-/- tumors as a positive and negative control. (B) Representative IHC pictures and box plots of p65, PPARγ, and p-ERK, and immunoreactivity scores (IRS) from tumors of AOM/ DSS treated mice. Neither PAK1 deletion nor 5-ASA significantly altered p65, PPARγ, or p-ERK signaling. (C) Mean IRS of cytoplasmic and nuclear β-catenin and p-β-catenin (Ser-675) in AOM/DSS mice. PAK1 deletion and 5-ASA treatment reduced phospho and total β-catenin levels in the cytoplasm and nucleus. (D) Dot plots are mean IRS for c-Myc and p-AKT (Thr 308) in AOM/DSS mice. PAK1 deletion and 5-ASA treatment in WT mice reduce c-Myc and p-AKT (Thr 308). (E) Representative images for IHC staining of p-mTOR and the IRS generated from tumors of AOM/DSS mice. PAK1 deletion and 5-ASA reduced p-mTOR. All IRS data are at least (n=4) mice per group. Statistical significance was calculated using ANOVA with LSD post hoc analysis, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001.