

SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1: Genetic recombination in *Kras.Smad4*^{-/-} mouse tumors. DNA was isolated from tumor and grossly normal lung from two *K5CrePR^{*}.LSL-Kras^{G12D}.Smad4^{fl/fl}* animals. Genotyping from lung and tumor DNA was identical; however the recombinant *Smad4* and *Kras* alleles were detected only in tumor.

Supplemental Figure 2: Confirmation of reduced *Smad4* expression in cell lines. (A-C) Reduced *Smad4* mRNA expression in Beas2B airway epithelial cells and H1299 cells with a stable *Smad4* knockdown and A549 lung adenocarcinoma cells with a Zn finger engineered *Smad4* deletion. (D) Reduced *Smad4* protein levels in each cell line.

Supplemental Figure 3: *pH2AX* and apoptosis in chemotherapy treated A549 cells.

Increased *pH2AX* staining in Annexin V positive cells after treatment with 10 μ M camptothecin or 100 μ M etoposide. Cells were simultaneously stained for apoptosis (Annexin V) and *pH2AX* then assayed by flow cytometry as described in the Methods.