**Supplemental Figure Legends.**

**Supplemental Figure 1. KRAS Mutations in PDAC tumors.** Table summarizing the KRAS mutations detected in each tumor following Sanger sequencing of PCR amplicons derived from genomic DNA yielded from each case at the G12 and G13 position (A). Snap shots of Sanger sequencing traces at the KRAS G12/G13 codons for each PDAC tumor (B).

**Supplemental Figure 2. Frequency copy number plots at the *SMAD4* *locus* (A), chromosome 18 (B), *FHIT* (C), *ZNF521* (D) loci in the primary PDAC tumors and for *SMAD4*, *FHIT* and *ZNF521* in the PDX tumors (E).** (A,C,D,E) The upper black and central grey lines in each example indicates the expected 2 and 1 gene copy levels from normalized levels across the whole genome of that sample. The lower black base line indicates the hg38 chromosomal coordinates (Mb). The frequency of coverage across each region is marked by the black dots within 30kb windows. Gene positions are presented as horizontal double black lines. (B) Copy number across chromosome 18 for each case. Black indicates the expected two allelic copy level. Red and green indicate significant loss or gain of sequence, respectively.

**Supplemental Figure 3. Expression level changes of commonly hit genes.** Fold expression change levels of each gene compared to normalized normal duct expression levels are presented for each gene commonly mutated by rearrangements in this study. The Average Tumor/Normal (T/N) expression level values are presented on larger (upper graph) and more focused (lower graph) y-axis ranges. The 1.25-fold increased and decreased expression levels are indicated on the lower graph as two horizontal blue lines.

**Supplemental Figure 4. TGFbeta responsive genes.** Average mRNA expression levels for specific genes from the RNAseq data represented as Log2 of median tumor levels divided by median dN levels. The twenty-seven genes were selected according to the presence of SMAD binding elements in their promoter regions and the regulated expression by TGFbeta-SMAD-dependent signaling reported in Qin H. et al BMC Syst Biol. (2009) and Gomis RR et al Proc Natl Acad Sci U S A. (2006).

**Supplemental Figure 5. FHIT pathway genes and signaling networks.** (A) Somatically mutated genes with binding or pathway related functions with FHIT presented per case. (B) A network of the listed genes visualizing predicted protein-protein interactions (PPI) using the STRING database v9.1 (Franceschini et al 2013).