Supplementary Figure Legends

Figure S1. Differential expression of FABP5 and CRABP2 in PDAC cells is associated with distinct alterations in morphology and cell cycle upon ATRA treatment

(A) SAGE analysis of *FABP5* and *CRABP2* tags in a panel of PDAC cell lines. Bar represents the mean of tags, normalized to normal human pancreatic ductal epithelial (HPDE) cells.

(B) Morphological changes upon ATRA treatment. Cells were treated for 48hr with 5μM ATRA or DMSO and images taken at 20X objective using an inverted phase contrast light microscope. Inset shows magnified view of a section to highlight the changes in morphology. The $FABP5^{null}CRABP2^{high}$ Pa01C cells (*left*) develop long dendrite-like processes upon ATRA exposure, while the endogenous processes observed in DMSO-treated $FABP5^{high}CRABP2^{null}$ Pa04C cells are reduced upon ATRA exposure (*right*).

(C) Cell cycle analysis using Propidium Iodide (PI) staining and flow cytometry. Pa01C and Pa04C cell lines were treated with ATRA at indicated dose for 72 hrs, before fixation with cold 70% ethanol and staining with PI.Samples were run on FACSCalibur (BD Biosciences) instrument. The $FABP5^{null}CRABP2^{high}$ Pa01C cells (*left*) demonstrate an increase in the sub-G_0 and G_1, with a concomitant decrease in both S and G_2 stages of cell cycle; no significant cell cycle alterations are observed in the $FABP5^{high}CRABP2^{null}$ Pa04C cells. Histogram denotes mean and error bars represent ± SEM.

Figure S2. *In vivo* therapeutic response to ATRA in PDAC xenografts with differential expression of FABP5 and CRABP2.

Xenografts derived from either **(A)** $FABP5^{null}CRABP2^{high}$ Pa03C or **(B)** $FABP5^{high}CRABP2^{null}$ Pa14C were treated with either ATRA (Red line) or oil as control (Black line). Comparable to data with Pa01C and Pa04C (*Figure 2*), only the $FABP5^{null}CRABP2^{high}$ Pa03C xenografts demonstrate significant tumor growth inhibition ($P<0.01$), while $FABP5^{high}CRABP2^{null}$ Pa14C xenografts are completely resistant. Mean of tumor volumes measured at indicated time intervals plotted with error bar denoting ± SEM.

Figure S3. CRABP2 overexpression in $FABP5^{high}CRABP2^{null}$ Pa20C cell line.

(A) Immunofluorescence assay for FABP5 in Pa20C line. Cells were grown in chamber glass slides (BD Falcon) overnight, and treated with ATRA for 4 hours, before paraformaldehyde fixation. Robust nuclear translocation of FABP5 is observed in the vector transfected cells, while FABP5 undergoes cytoplasmic sequestration in the Pa20C-*CRABP2* cell line. Images taken at 20X objective lens magnification.

(B) Cell cycle analysis using Propidium iodide staining and flow cytometry; **(C)** Bar represents mean of three independent experiments and error bars represent ± SEM.

(D) Invasion assay using modified Boyden Chamber. The enhanced invasion observed with ATRA exposure is mitigated upon ectopic expression of CRABP2. Representative images shown at 20X objective lens magnification.

Figure S4. Epigenetic silencing of *CRABP2* in PDAC.

(A) Graphical view of the putative CRABP2 promoter (image taken from UCSC Genome Browser) with a 1.79Kb genomic region designated as CpG island, calculated using Methyl Primer Express software (V 1.0, Applied Biosystems).

(B) Quantitative RT-PCR for *CRABP2* in FABP5^{high}CRABP2^{null} cell lines (Pa04C, Pa20C and Pa08C) following DAC (1μM) and TSA (100nM) treatment. Re-expression of *CRABP2* transcripts is observed with DAC in all three cell lines, with further accentuation upon combination with TSA in Pa20C and Pa08C. Bars represents mean from 3 independent experiments, for fold change in mRNA levels, normalized to β-actin.

(C) Methylation-specific PCR (MSP) of bisulfate-modified DNA from FABP5^{high}CRABP2^{null} cell lines (Pa04C and Pa20C). The lanes M and U represent the PCR product amplified by primer sets specific for methylated and unmethylated DNA, respectively. *In vitro* methylated DNA (IVM) was used as the positive control for methylation.