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Supplemental information

SMAD4 represses FOSL1 expression and pancreatic cancer metastatic colonization

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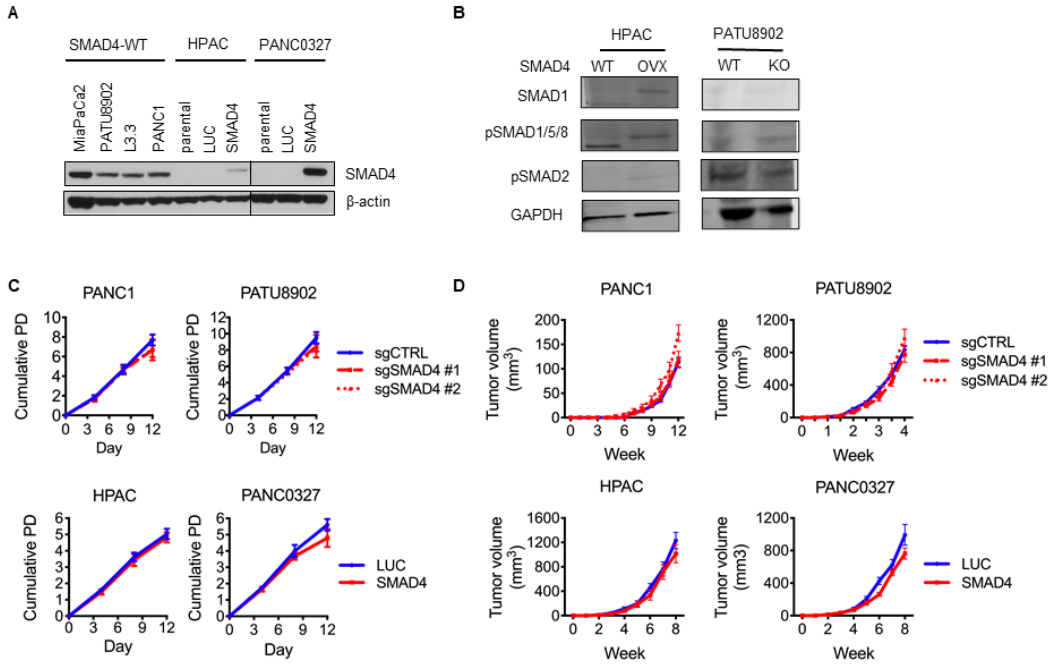
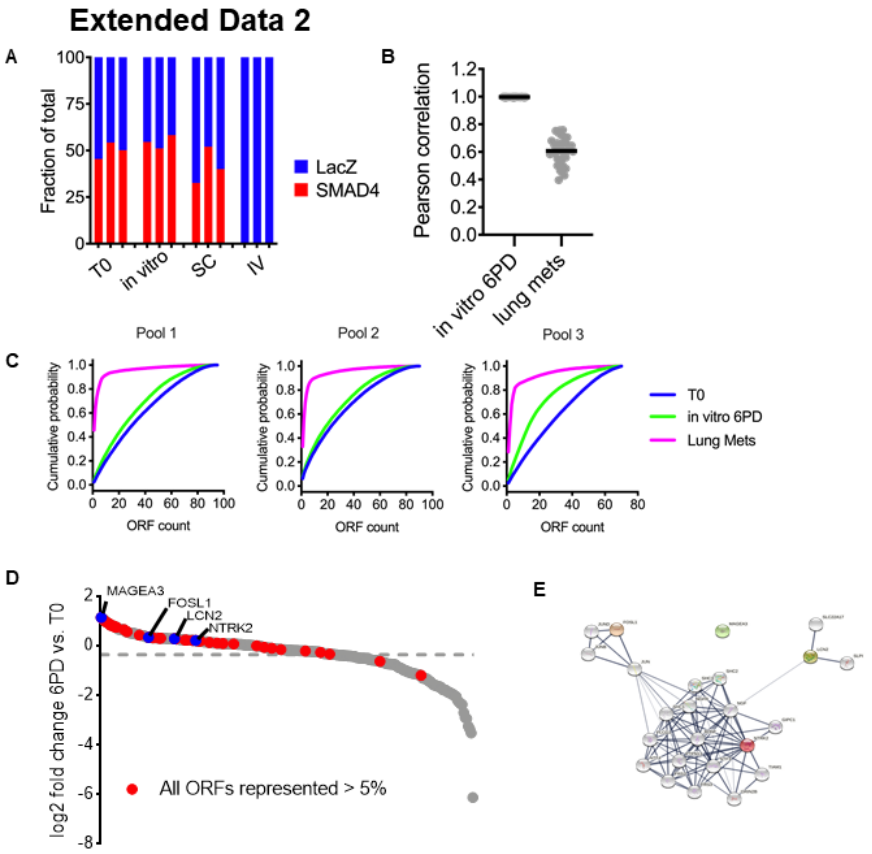
Extended Data 1



Extended Data 1: SMAD4 manipulation alters molecular signaling but not growth rate of cell lines

Related to Figure 1

A) Immunoblot of exogenous expression of SMAD4 in *SMAD4*-null PDA cell lines (HPAC and PANC0327) compared to SMAD4 expression levels in *SMAD4*-WT PDAC cell lines.
B) Immunblots of SMAD family members in SMAD4 overexpression line (left) and KO line (right)
C) *In vitro* growth rate of SMAD4 loss (top) or overexpression (bottom) (n=3, standard deviation is reported in error bars)
D) Subcutaneous tumor growth rate for SMAD4 loss (top) or overexpression (bottom) (n=5, standard deviation is reported in error bars)



Extended Data 2: Bias is not reported in guide abundance

Related to Figure 2

A) Competition of LacZ- and SMAD4-expressing HPAC cells *in vitro* and *in vivo*. LacZ- and SMAD4- expressing HPAC cells are barcoded and mixed 1:1 and co-cultured in vitro, or the mixture was implanted subcutaneously or injected IV in NCr nude mice for *in vitro* and *in vivo* competition. Relative abundance of barcodes was quantified 4 weeks following competition. Three biological replicates are shown for each condition.

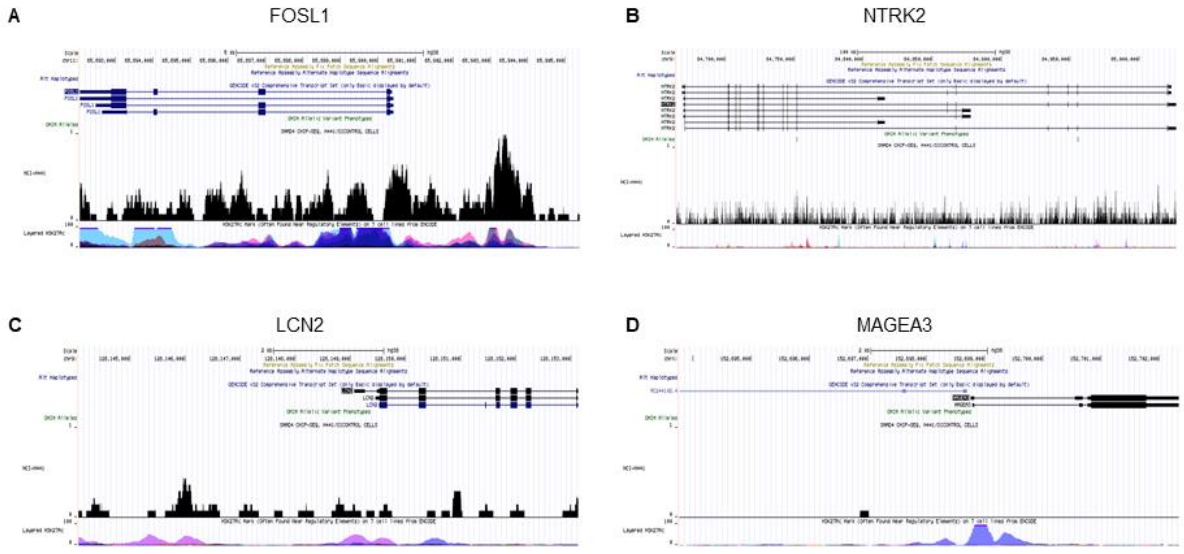
B) NxN Pearson correlation of ORF representation in in vitro proliferation sample and in lung metastases.

C) Cumulative distribution of ORFs in each sub-pool for pre-injection cell pellet, in vitro proliferation sample, and lung metastases.

D) Log_2 fold change of ORF representation in in vitro proliferation sample vs. pre-injection cell pellet.

E) STRING-Db network of target genes (colored nodes) and 20 closest neighbor nodes (grey)

Extended Data 3

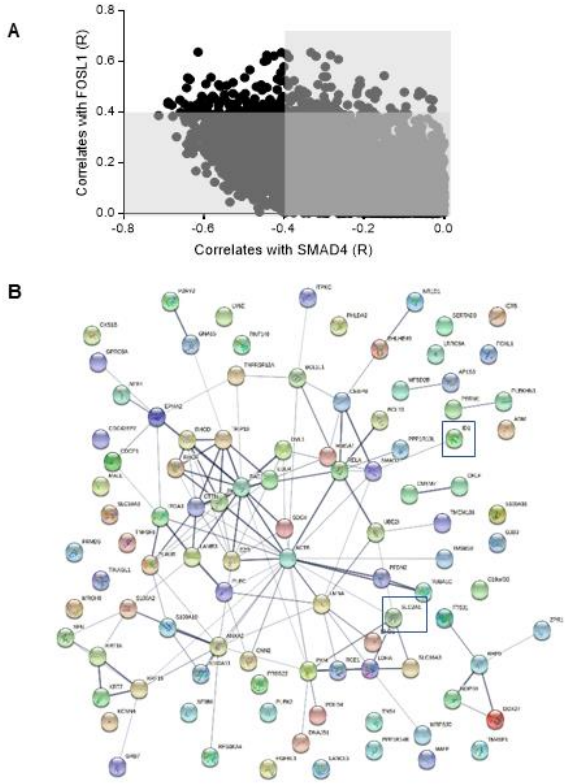


Extended Data 3: SMAD4 binds the FOSL1 gene locus

Related to Figure 3

SMAD4 ChIP-seq signal for each target gene

Extended Data 4



Extended Data 4: Rho/Rac centric network of genes is correlated with FOSL1 and SMAD4 expression

Related to Figure 4

A) Values of gene-gene correlations of each gene with FOSL1 (y) or SMAD4 (x) across TCGA Pancreatic cancer cohort. Genes significantly correlated with FOSL1 and inversely correlated with SMAD4 are in the unshaded quadrant
B) String-db network of significant genes from S3B. Genes that scored in the colonization screen are boxed