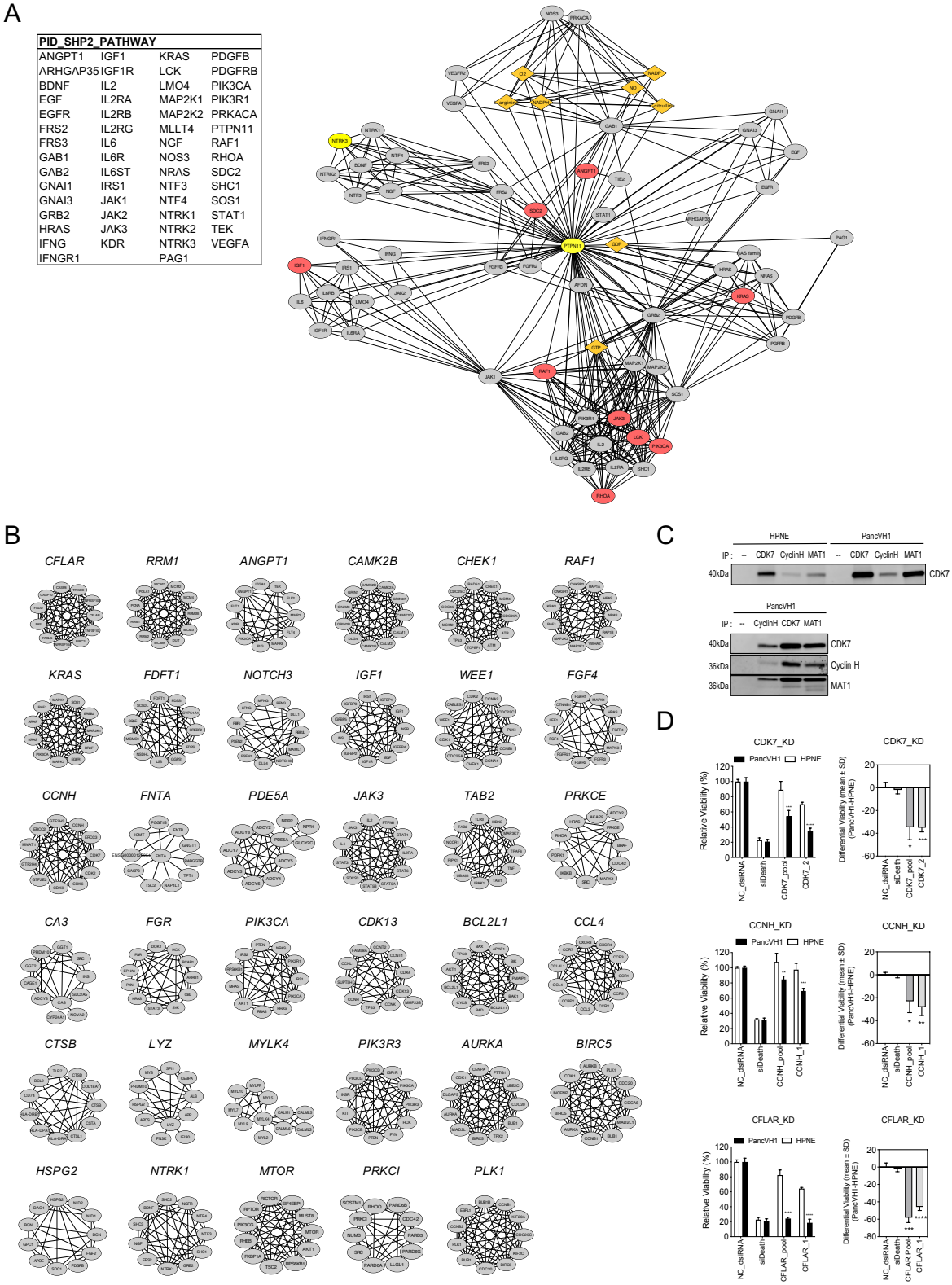

Figure S3. Extended Data. A. Left: Pathway Interaction DataBase (PID) PTPN11/SHP2 Pathway Genes. Right: PTPN11/SHP2 Pathway Network with PancVH1 RNAi hits in red and PancVH1 somatic variants in yellow. KRAS is both a somatic variant (G12V) and RNAi hit (red). **B**. 35 druggable signaling nodes nominated by functional approach on KRAS TP53 mutant PancVH1; compilation of PancVH1 pancreatic pathway control hits (< KRAS median) (Fig.1D), druggable RNAi targets from RNAi secondary screen (SI Dataset S3), PancVH1 rank differentials with HPNE (Fig.1F) annotated by functional data cross reference to KRAS mutant JHU PDAC cell line RNAi extended kinome screens - custom designed pancreatic oncolibrary, DNA damage and response library (DDR), and a human kinome library (Fig.S2D); druggable signaling nodes displayed as STRING: functional protein association networks (https://string-db.org/) with default settings. **C**. CAK complex in PancVH1 and HPNE. Immunoprecipitation of Cyclin H, MAT1, CDK7 and immunoblotting of each subunit of the complex. **D**. Bar graphs of relative viability of dsiRNA pooled and individual knockdowns of CDK7, Cyclin H (CCNH), and CFLAR in PancVH1 and HPNE; negative control dsiRNA (NC_dsiRNA); positive control AllStars siDeath (siDeath);120hr assay, dsiRNA targeted knockdowns were statistically significant versus negative control dsiRNA (left), and differential viabilities statistically significant between PancVH1 and HPNE (right); unpaired t-test; ****P<0.0001, ***P<0.001, **P<0.01, *P<0.05.