Supplemental Table S1. Full Results of Primary Gemcitabine Sensitivity Screen

Supplemental Table S2. Known DNA Damage Response Genes Identified as Hits in Gemcitabine Sensitivity Screen

Supplemental Table S3. Dysregulation, Differential Expression, and Literature RNAi Cross-Reference for Known DDR Genes and Select Hits

Supplemental Table S4. Selected Top 15% of Gemcitabine Sensitivity Genes Tested on Secondary Screen

Supplemental Fig S1. Representative Immunohistochemistry for CHD7 Expression in Primary Tumor Tissue. CHD7 exhibits a nuclear staining pattern and is differentially expressed, as demonstrated by these two samples from our clinical cohort. The staining pattern on the left exhibits low intensity of staining, while the staining pattern on the right exhibits high intensity

Supplemental Fig S2. Network Analysis via MetaCore ExPlain Process Network Analysis for genes involved in CHK1, CDC25A, AURKB, PLK1, HUS1 pathway. Hits from primary gemcitabine sensitivity screen are labeled in blue.

Supplemental Fig S3. CHD7 Knockdown Causes Gemcitabine Sensitization. (A) MIA PaCa-2 cells were transfected with siRNA against NT, ATR, or CHD7, and treated with or without gemcitabine at IC5, IC25, and IC50 concentrations for 72 hours prior to assaying for cell proliferation using WST-1 reagent. Treated versus untreated percent viability was calculated and the mean and standard deviation from three replicas is

shown. * indicates $p < 0.05$. (B) BxPC-3 cells were transfected with siRNA against NT, ATR, or CHD7, and treated with or without gemcitabine at IC5, IC25, and IC50 for 72 hours prior to assaying for cell proliferation using WST-1 reagent. Treated versus untreated percent viability was calculated and the mean and standard deviation from three replicas is shown. * indicates $p < 0.05$. (C) HPAC cells were transfected with siRNA against NT, ATR, or CHD7, and treated with or without gemcitabine at IC25 for 72 hours prior to assaying for cell proliferation using WST-1 reagent. Treated versus untreated percent viability was calculated and the mean and standard deviation from three replicas is shown. * indicates $p < 0.05$. (D) Percent survival of MIA PaCa-2 cells following transfection with NT or CHD7 siRNA for 120 hours.

Supplemental Fig S4. Mice with Xenograft Tumors Showed No Significant Difference in Body Weight. Athymic nude mice with shCHD7-2 and shControl MIA PaCa-2 tumor xenografts were treated with or without gemcitabine (100 mg/kg) on days 0, 7, and 14, and body weight was measured every 4 days. Mean and standard error of mean from 6 tumors are shown.

Supplemental Fig S5. CHD7 Knockdown Effect on Cell Cycle. MIA PaCa-2 cells were transfected with NT, CHD7, or ATR siRNA, treated without (A) or with 13 nM gemcitabine for 24 hours (B) and analyzed for DNA content by flow cytometry. Mean and standard deviation of gated cells from three replicas is shown.

Supplemental Fig S6. Gemcitabine Does Not Significantly Change CHD7 Protein Levels in Cells. Western blot analysis of lysate from MIA PaCa-2 cells treated with or without the indicated concentrations of gemcitabine for 6 hours and probed with anti-

CHD7 and anti-GAPDH antibodies shows no significant difference in CHD7 protein levels following gemcitabine treatment.