Supplementary Figures

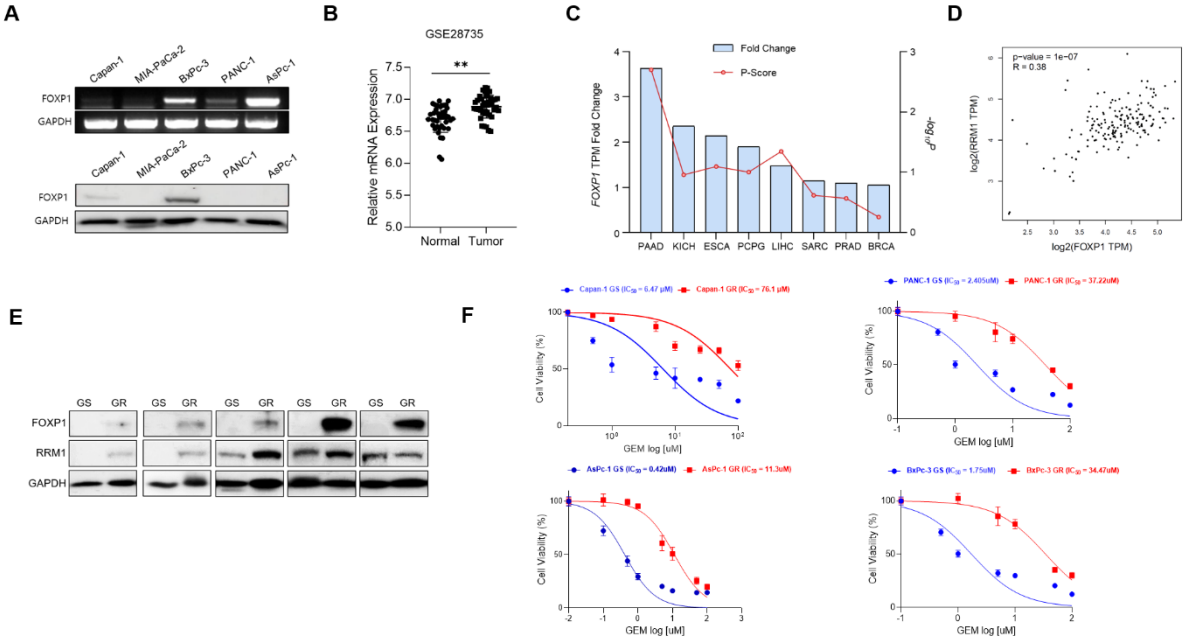

Figure S1. FOXP1 is upregulated in gemcitabine-resistant (GR) PDAC. (A) FOXP1 mRNA and protein expression in PDAC cell lines analyzed via RT-PCR and Western blot. **(B)** Differential gene expression analysis from the GSE28735 dataset reveals higher expression of FOXP1 in tumor samples compared to normal tissues (N=40, T=40) **(C)** Comparative analyses of FOXP1 expression levels across various cancer types (PAAD: Pancreatic Adenocarcinoma; KICH: Kidney Chromophobe; ESCA: Esophageal Carcinoma; PCPG: Pheochromocytoma and Paraganglioma; LIHC: Liver Hepatocellular Carcinoma; SARC: Sarcoma; PRAD: Prostate Adenocarcinoma; BRCA: Breast Cancer) **(D)** Correlation analysis between FOXP1 and RRM1 mRNA levels in the TCGA–PAAD dataset (R = 0.38, p = 1e−07). **(E)** Western blot analysis of FOXP1 and RRM1 protein levels in gemcitabine-sensitive (GS) and gemcitabine-resistant (GR) patient tumor samples. **(F)** Dose-response curves showing the effect of gemcitabine (GEM) treatment on cell viability (%) in GS and GR PDAC cell lines.

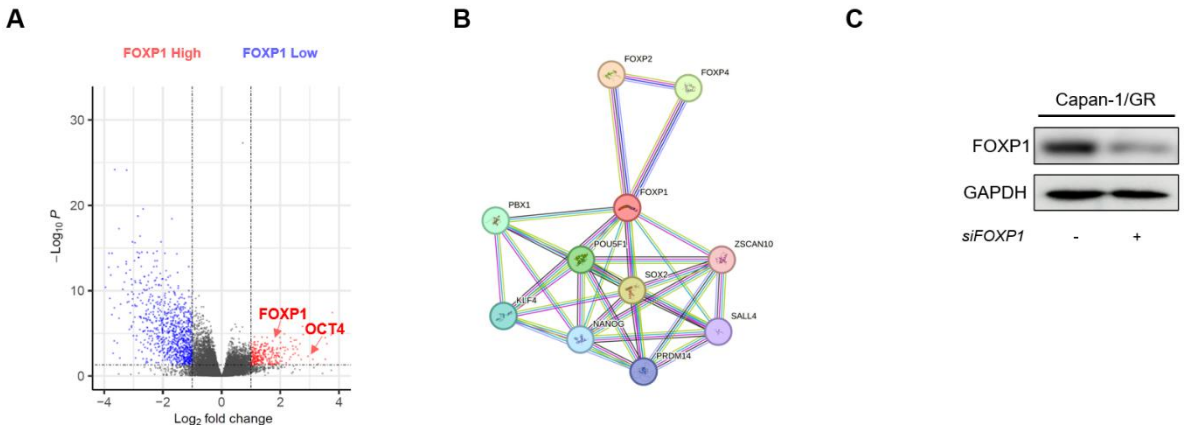

Figure S2. FOXP1 promotes the proliferation of CSCs in GR PDAC. (A) Volcano plot showing differential gene expressions in TCGA-PAAD samples with high versus low FOXP1 expressions. **(B)** STRING protein-protein interaction network analysis of FOXP1. **(C)** The protein expression of FOXP1 after siRNA-mediated knockdown of FOXP1 (siFOXP1).

A

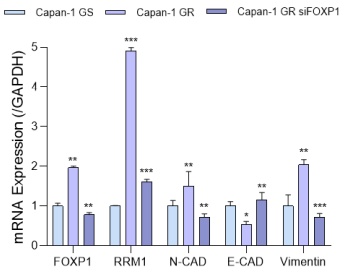

Figure S3. FOXP1 enhances EMT and induces proliferation in GR PDAC. (A) qRT-PCR analysis of mRNA expression levels for FOXP1, RRM1, N-cadherin (N-CAD), E-cadherin (E-CAD), and Vimentin in GS, GR, and KD cells. GAPDH was used as the normalization control. *p < 0.05, **p < 0.01, ***p < 0.001.

A

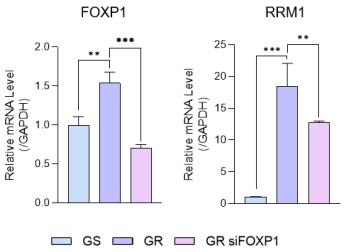

Figure S4. FOXP1 induces metabolic reprogramming by promoting glycolysis. (A) qRT-PCR analysis of mRNA expressions of FOXP1 and RRM1. GAPDH was used as the normalization control. **p < 0.01, ***p < 0.001.

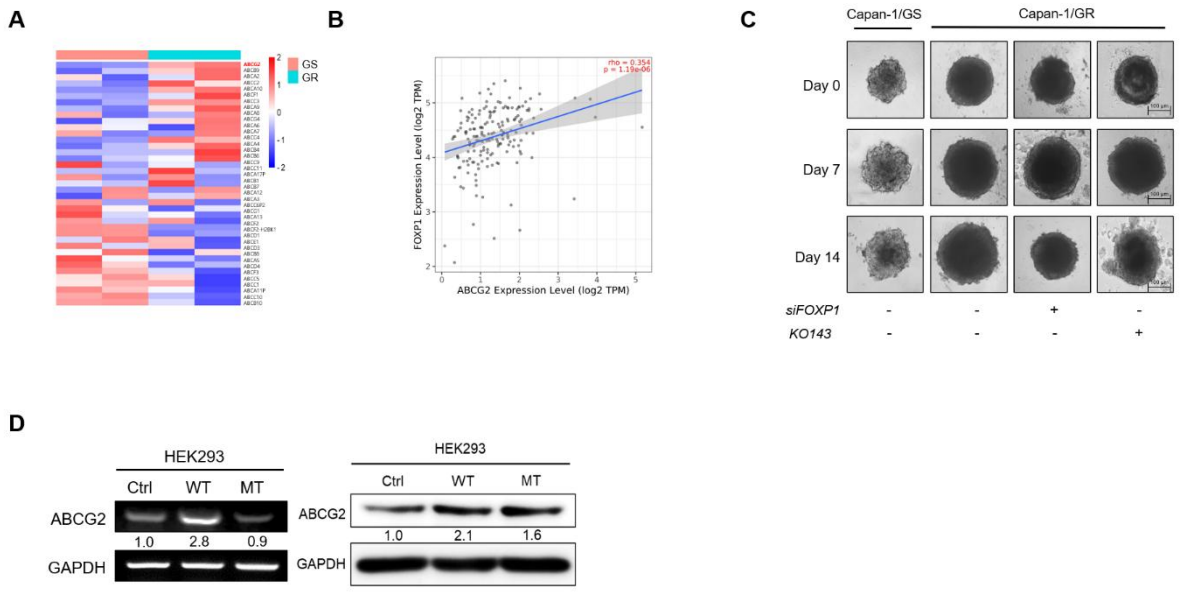

Figure S5. FOXP1 chemosensitizes PDAC to gemcitabine by upregulating ABCG2. (A) Heatmap of ABC transporter gene expression in GS and GR cells. **(B)** Correlation analysis between FOXP1 and ABCG2 mRNA levels in TCGA-PAAD (ρ = 0.354, p = 1.19e−06). **(C)** Relative images of Capan-1 GS and GR spheres treated with siFOXP1 or KO143. **(D)** mRNA and protein expression of ABCG2 in HEK293 cells transfected with wild-type (WT) or mutant (MT) FOXP1.

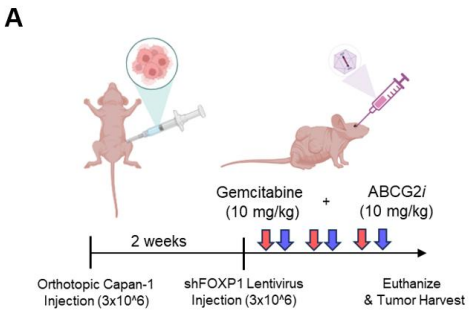

Figure S6. Reduced FOXP1 and ABCG2 expressions lead to reduced tumor growth and increased chemosensitivity in mouse models. (A) Schematic of the orthotopic mouse model. Orthotopic injection of Capan-1 cells was followed by shFOXP1 lentivirus injection after 2 weeks. Gemcitabine (10 mg/kg) and ABCG2 inhibitor (10 mg/kg) treatments were administered prior to tumor harvest.