

Figure S1. Screening of monomeric compounds with anti-ICC activity. (A) Viability of HCCC9810 and RBE cells after treatment with 2,538 monomeric compounds at 10  $\mu$ M for 72 h. (B) Viability of HCCC9810 and RBE cells after treatment with 83 monomeric compounds at 10  $\mu$ M for 72 h. (C) Viability of HiBEpicCs after treatment with 83 monomeric compounds at 10  $\mu$ M for 72 h. (D) Viability of ICC cells and HiBEpicCs after treatment with 15 monomeric compounds at 10  $\mu$ M for 72 h. Error bars represent the mean  $\pm$  SD obtained from three separate experiments. \*\*\*\*P<0.0001. ICC, intrahepatic cholangiocarcinoma; HiBEpicCs, intrahepatic bile duct epithelial cells.

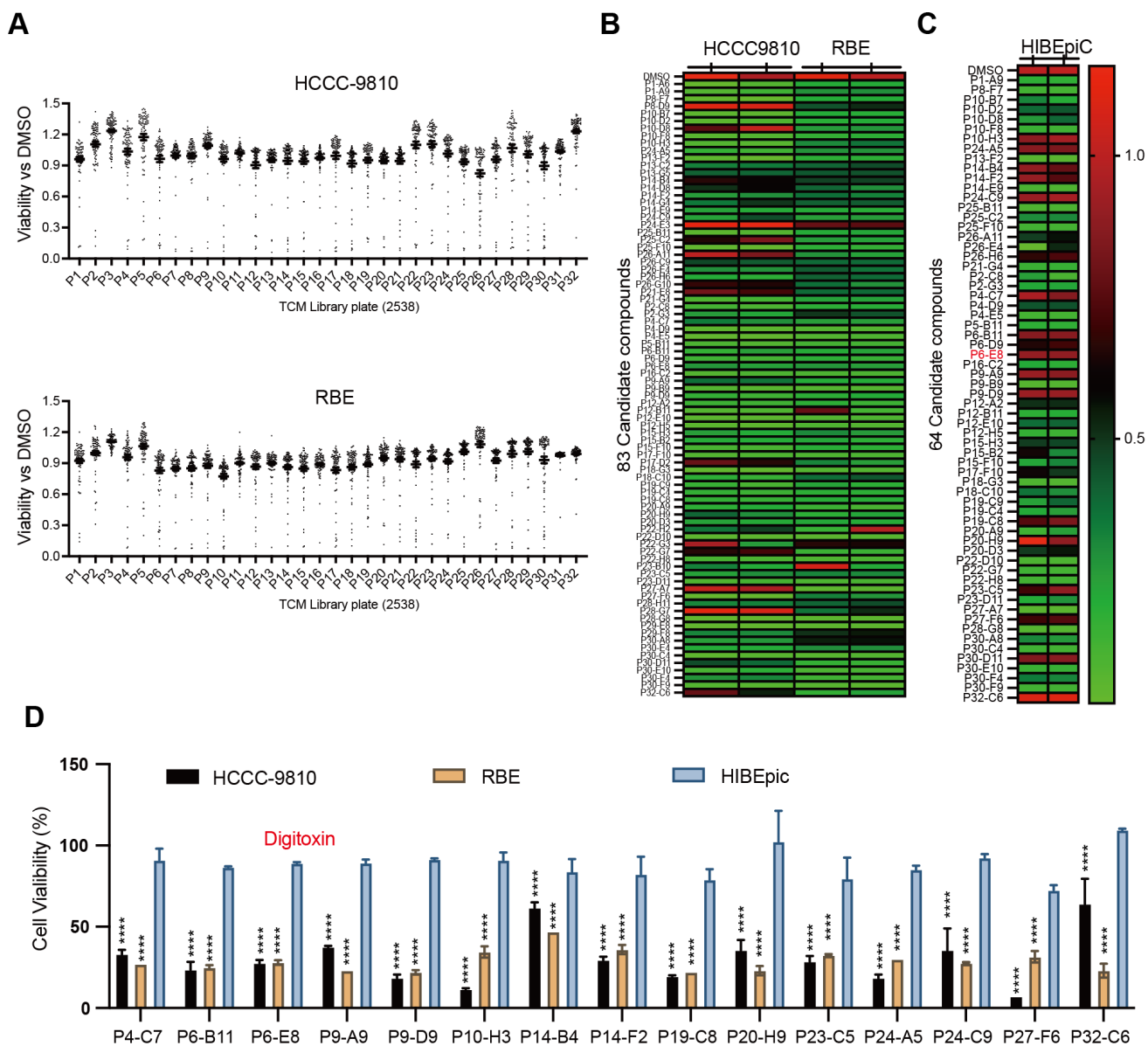


Figure S2. Relative western blot grayscale statistical chart for protein expression following DT treatment in intrahepatic cholangiocarcinoma cell lines. Western blotting was used to assess the expression levels of apoptosis-related proteins, p-NF- $\kappa$ B/NF- $\kappa$ B, p-P38/P38, p-STAT3/STAT3, and ST6GAL1 following DT treatment. The statistical charts for Fig. 3 include: (A) HuCCT1 cell lines and (B) HCCC9810 cell lines. Error bars represent the mean  $\pm$  SD of three separate experiments. \*P<0.05, \*\*P<0.01 and \*\*\*P<0.001. DT, digitoxin; ns, no significance.

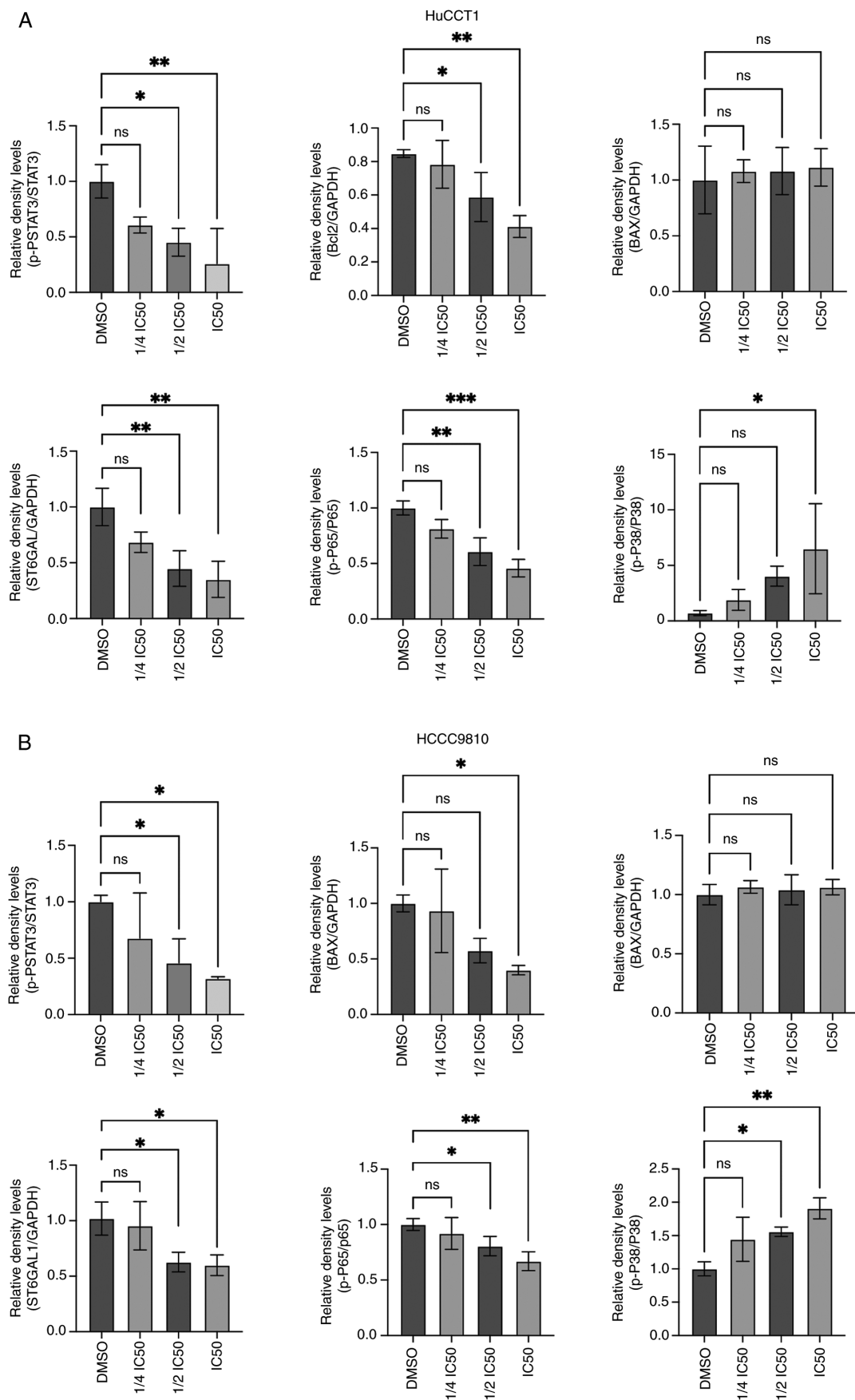


Figure S3. P65/NF- $\kappa$ B overexpression upregulates the expression of ST6GAL1 in 293T cells. (A and B) Reverse transcription-quantitative PCR and western blotting were used to assess the mRNA and protein expression of ST6GAL1 in 293T cells. Error bars represent the mean  $\pm$  SD of three separate experiments. \* $P$ <0.05, \*\* $P$ <0.01, \*\*\* $P$ <0.001 and \*\*\*\* $P$ <0.0001. ST6GAL1, ST6  $\beta$ -galactoside  $\alpha$ -2,6-sialyltransferase 1; DT, digitoxin.

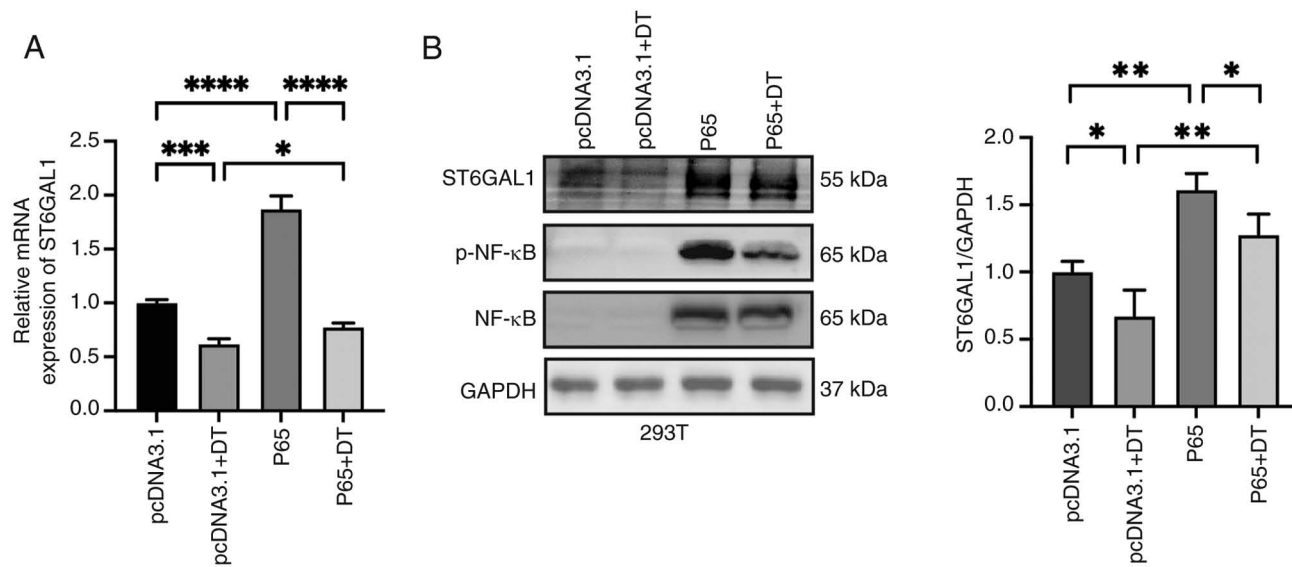


Figure S4. Verification of ST6GAL1 overexpression in intrahepatic cholangiocarcinoma cells. (A and B) Reverse transcription-quantitative PCR and western blotting were used to assess the mRNA and protein expression of ST6GAL1 in HCCC9810 and HuCCT1 cells. Error bars represent the mean  $\pm$  SD obtained from three separate experiments. ST6GAL1, ST6  $\beta$ -galactoside  $\alpha$ -2,6-sialyltransferase 1.

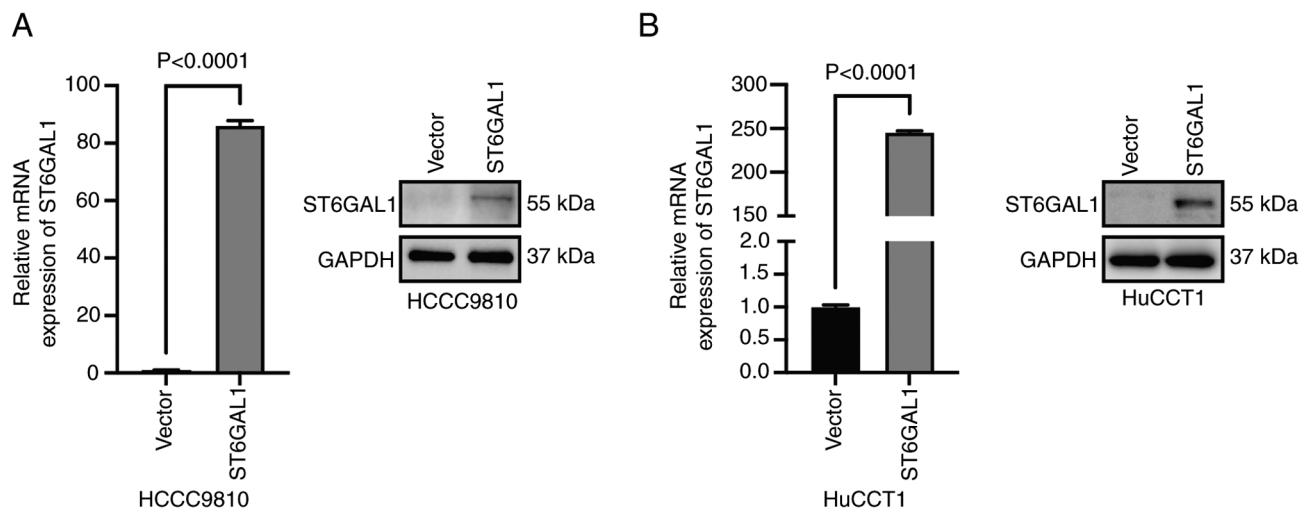


Figure S5. Western blot grayscale statistical chart for protein expression in ST6GAL1-overexpressing intrahepatic cholangiocarcinoma cell lines following DT treatment. Statistical charts depicted the band intensity for various proteins in whole cells and nuclear extracts. (A and B) Expression levels of Bcl-2, ST6GAL1, p-STAT3/STAT3, p-P38/P38 and p-NF- $\kappa$ B/NF- $\kappa$ B in HCCC9810 and HuCCT1 whole cells. (C and D) Expression levels of p-STAT3/STAT3, p-P38/P38 and p-NF- $\kappa$ B/NF- $\kappa$ B in HCCC9810 and HuCCT1 nuclear fractions. Error bars represent the mean  $\pm$  SD obtained from three separate experiments. \* $P$ <0.05 compared with the Vector group; # $P$ <0.05 compared with the Vector + DT group; and  $\Delta P$ <0.05 compared with the ST6GAL1 group. ST6GAL1, ST6  $\beta$ -galactoside  $\alpha$ -2,6-sialyltransferase 1; DT, digitoxin; p-, phosphorylated.

