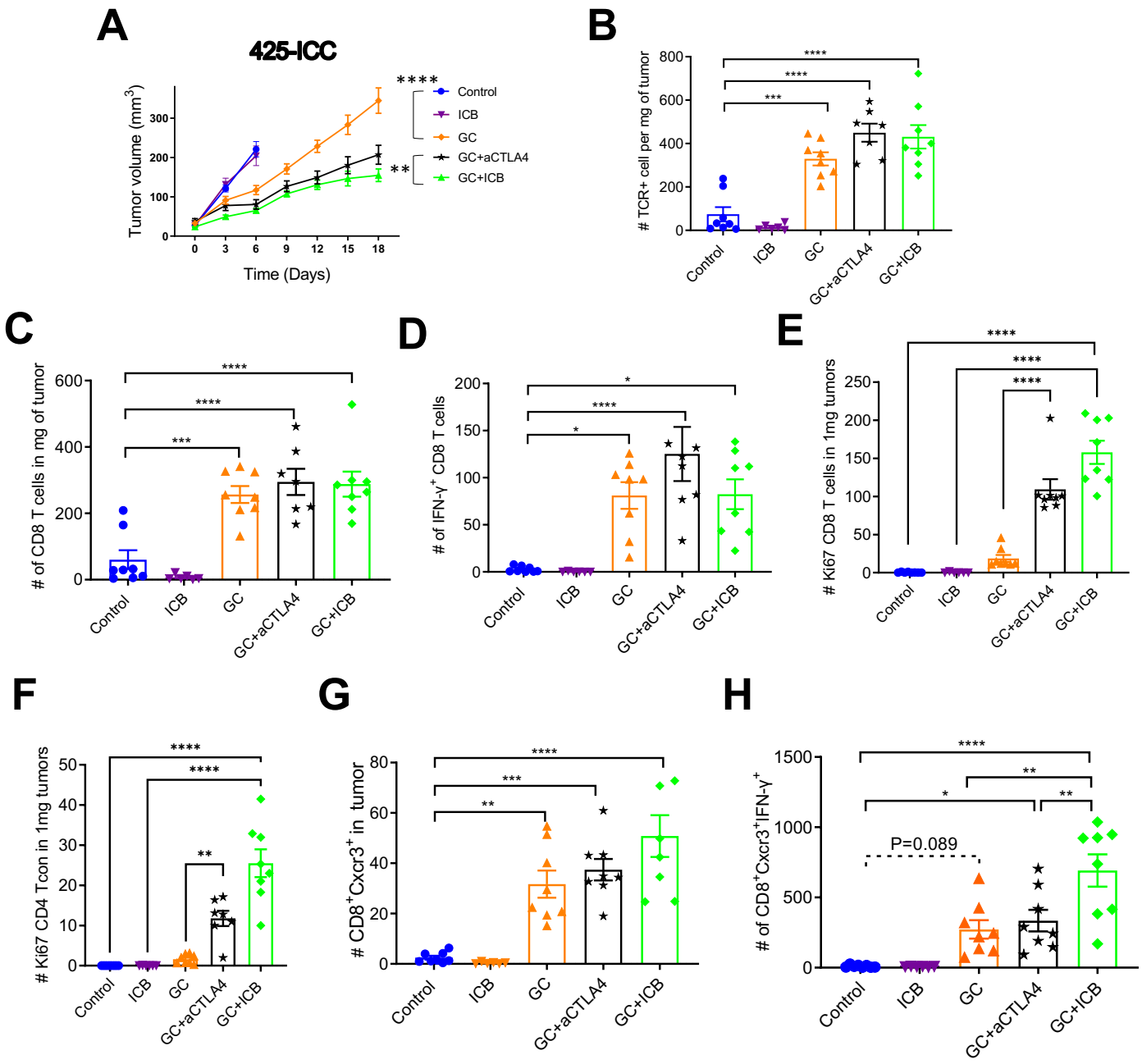


**Supplementary Fig. S6: CTLA-4 blockade mediates the efficacy of GC/ICB therapy in ICC and increases CD8⁺CTL frequency in murine ICC.** (**A**) Tumor growth kinetics after treatment in orthotopic murine 425-ICC model: GC/anti-CTLA4 Ab combination is significantly superior to GC alone and in delaying tumor growth; addition of anti-PD1 Ab to GC/anti-CTLA4 Ab (GC/ICB) induces a greater delay in tumor growth. (**B-F**) Immunophenotyping of treated ICC tissues at days 10 (control and ICB groups) and 20 (GC-containing groups). TCR⁺ TIL numbers were higher in all GC-treated groups (**B**). CD8⁺ T cells numbers (**C**) and CD8⁺IFN-γ⁺ T cell numbers (**D**) were increased in all GC-treated groups. The numbers of Ki67⁺CD8⁺ (**E**) and Ki67⁺CD4⁺ (**F**) were increased in GC/anti-CTLA4 and GC/dual ICB groups. (**G**) The numbers of CD8⁺Cxcr3⁺ T cells were increased in all GC-treated groups. (**H**) CD8⁺Cxcr3⁺IFN-γ⁺ T cell numbers were significantly increased in the GC/ICB group.
*p < 0.05; **p < 0.01; ***p < 0.001 ; ****p < 0.0001 from Dunnett's multiple comparisons test (**A**) and from Tukey's multiple comparisons test (**B-H**). GC: gemcitabine plus cisplatin; ICB: anti-PD-1 antibody plus anti-CTLA-4 antibody; ICC, intrahepatic cholangiocarcinoma; CTL, cytotoxic T lymphocyte; TCR, T cell receptor.