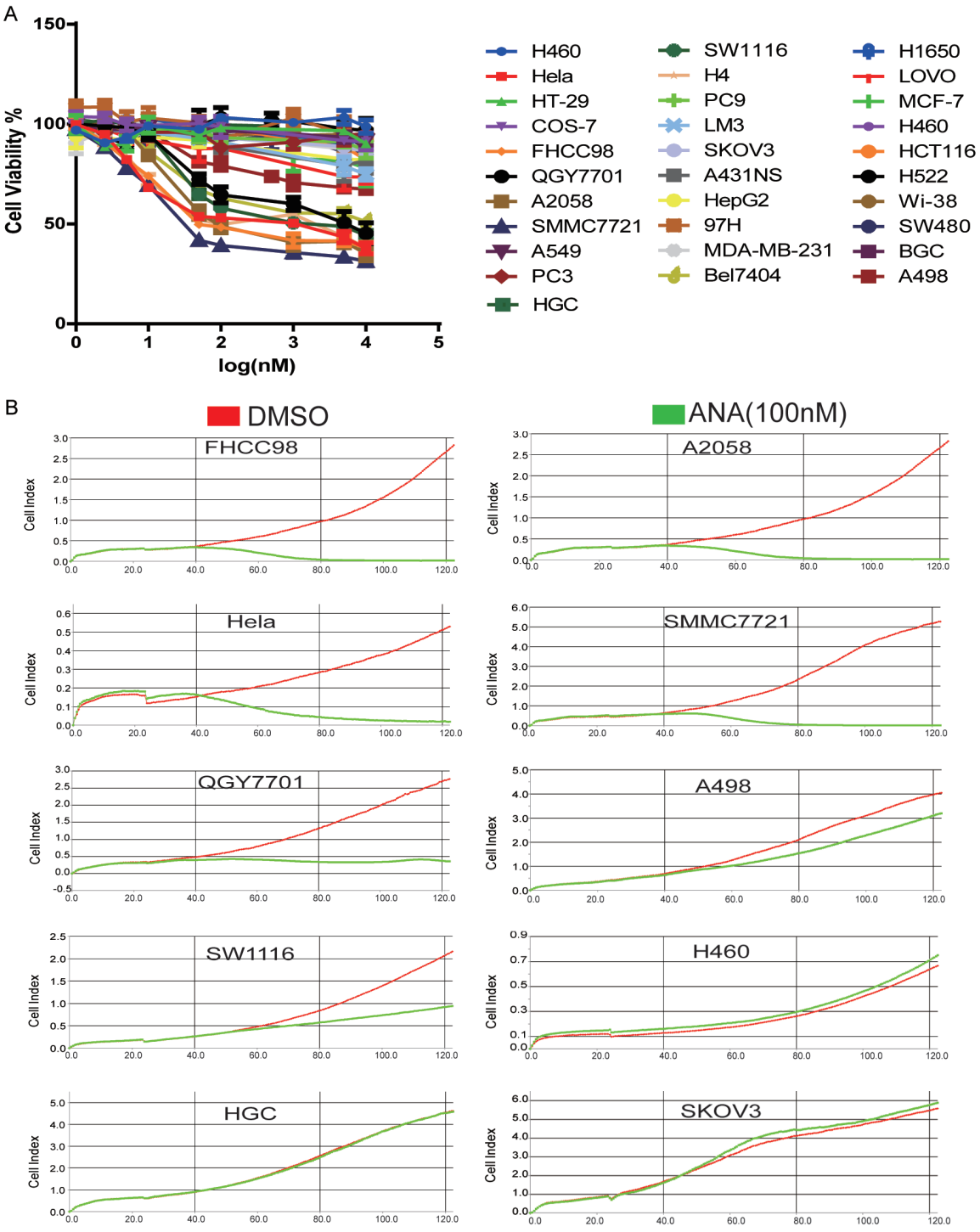
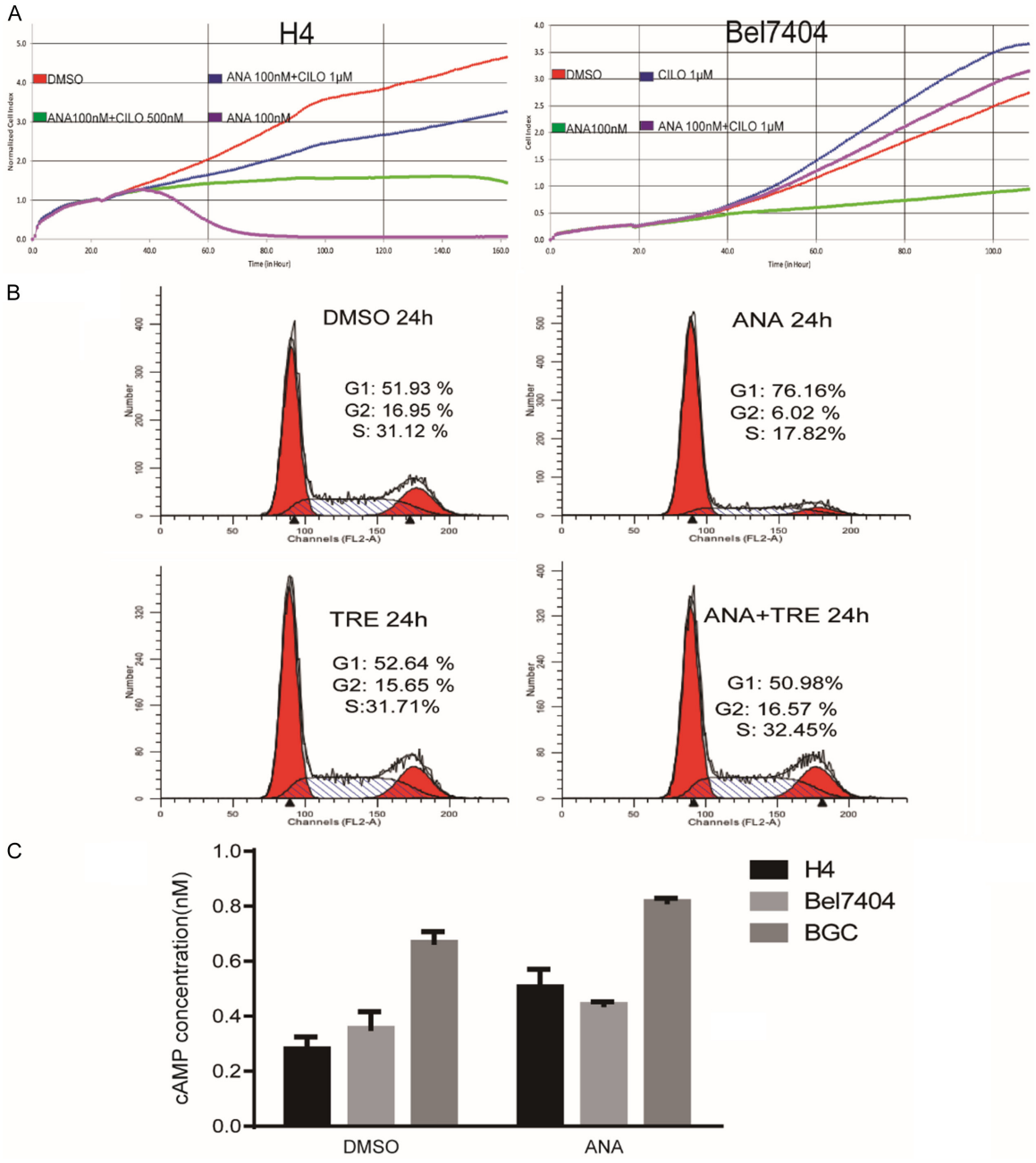
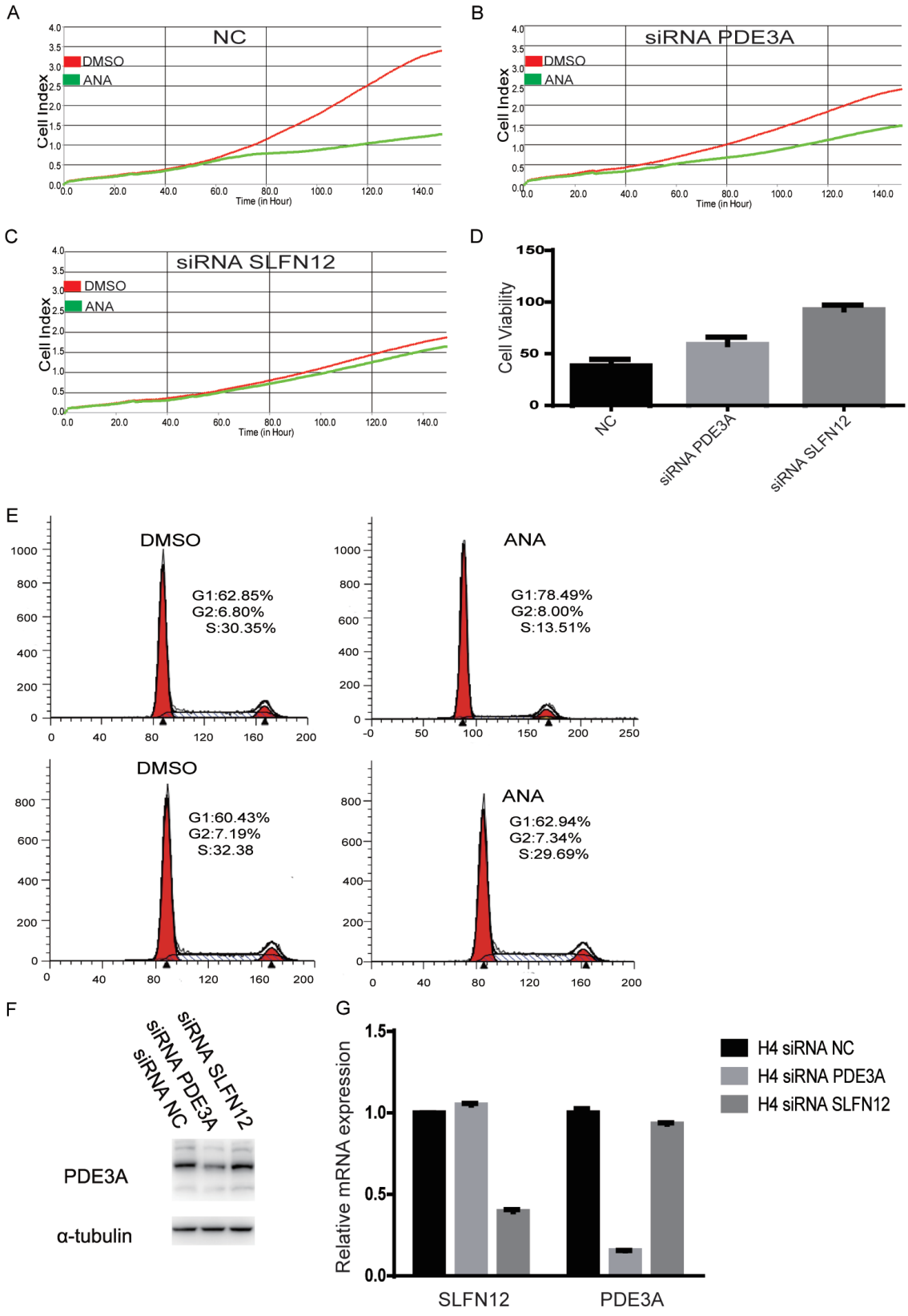


Supplementary Figure 1. Effects of ANA on the growths of different cancer cells. A. MTT analyses of the effects of ANA on the viabilities of different cancer cells. The indicated cells (3000/well) were exposed to indicated concentrations of ANA for 72 h and cell viabilities were measured by the MTT assay. B. RTCA analyses of the effects of ANA on the growths of different cancer cells. The indicated cells were treated with 100 nM ANA (green) or DMSO (red) and the Cell Index were monitored continuously by the RTCA analyzer.

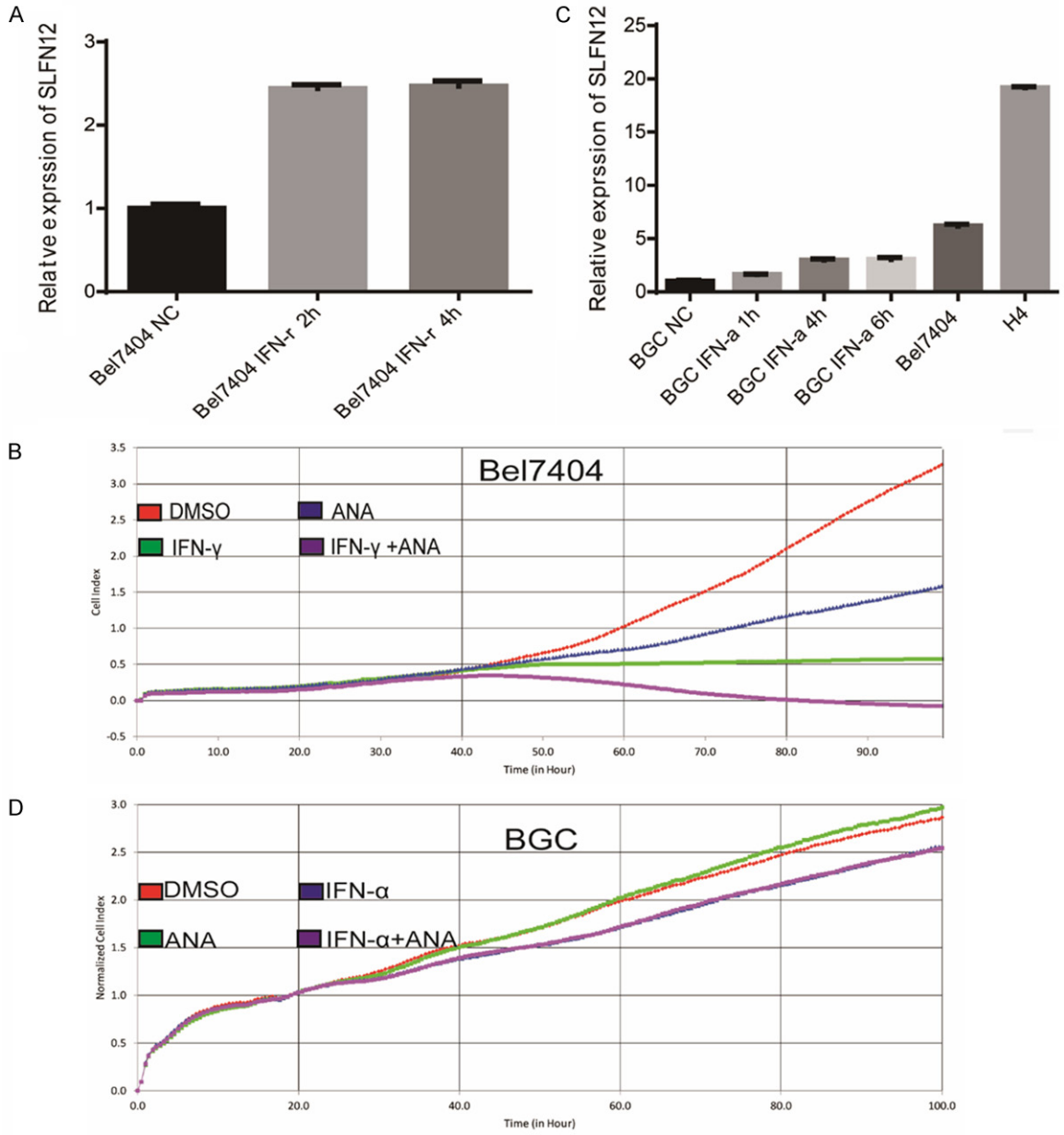


Supplementary Figure 2. Effects of additional PDE3 inhibitors on the ANA-induced cell growth inhibition. A. RTCA analyses of the effects of CILO on the ANA-induced cell growth inhibition. The ANA cell death-sensitive cell line H4 and the ANA cell cycle arrest-sensitive cell line Bel7404 were treated with DMSO, ANA, CILO, or combination of ANA with CILO at the indicated concentrations, followed by RTCA analyses of cell growth. B. Flow cytometry analyses of the effects of TRE on the ANA-induced cell cycle arrest. The cells were exposed to ANA (100 nM), TRE (100 nM), or a combination of ANA and TRE for 24 h. The cell cycle distribution was then measured by flow cytometry. C. cAMP was measured 1 hour after treatment with ANA (100 nM) in indicated cancer cells.



Supplementary Figure 3. SLFN12 was required for the ANA-induced growth inhibition of cancer cells. A-C. RTCA analyses of the effects of knocking down SLFN12 expression on the ANA-induced growth inhibition in the ANA cell cycle arrest-sensitive cell line Bel7404. The siRNA-transfected Bel7404 cells were cultured with ANA 100 nM

(green) or DMSO (red), and the growth of the cells were monitored by the RTCA analyzer. D. The quantitation of the RTCA analyses results. E. Flow cytometry analyses of the effects of knocking down SLFN12 expression on the ANA-induced cell cycle arrest. F. Effects of siRNA knockdown on the protein expressions of PDE3A. H4 cells were transiently transfected with a PDE3A-specific siRNA, a SLFN12-specific siRNA, or a non-specific scrambled control siRNA. Cells were harvested 24 h later and the cell lysates were processed for immunoblotting using an anti-PDE3A antibody, or anti-α-tubulin antibody. G. Effects of siRNA knockdown on the expressions of SLFN12 and PDE3A mRNA. siRNA transfections were performed the same as above. mRNAs were extracted 24 h after siRNA transfection and analyzed by real-time PCR.



Supplementary Figure 4. Effects of the IFNs on the mRNA expression of SLFN12 and the ANA-induced cell growth inhibition. (A and C) Bel7404 and BGC cells were exposed to IFN-γ (10 ng/mL) or IFN-α (3000 IU) for indicated times. SLFN12 mRNA expression was analyzed by Quantitative Real-Time PCR. (B and D) Bel7404 cells and BGC cells were treat with IFN-γ (10 ng/mL), ANA (100 nM), or a combination of IFN-γ and ANA. The cell growths were monitored by the RTCA analyses.