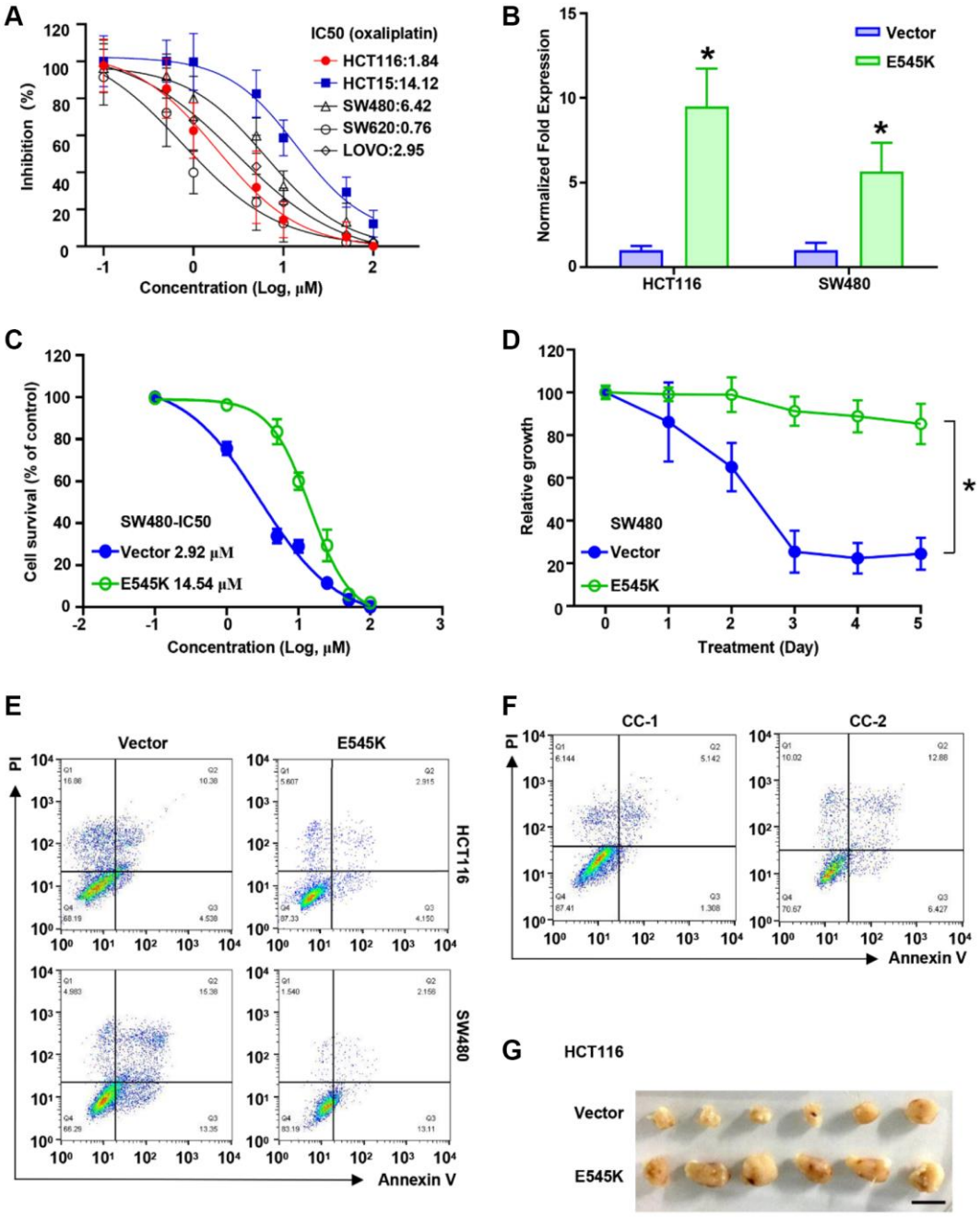
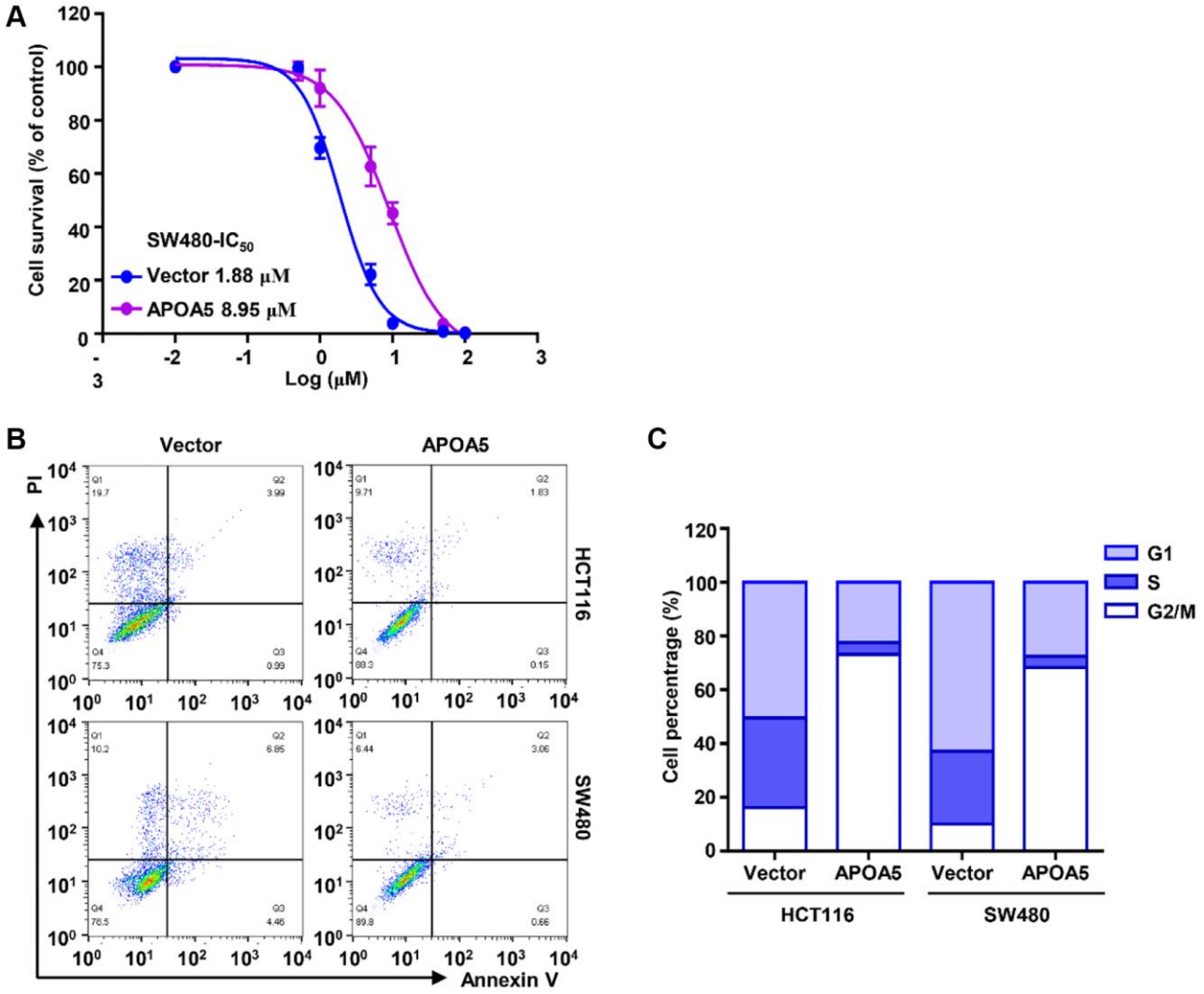
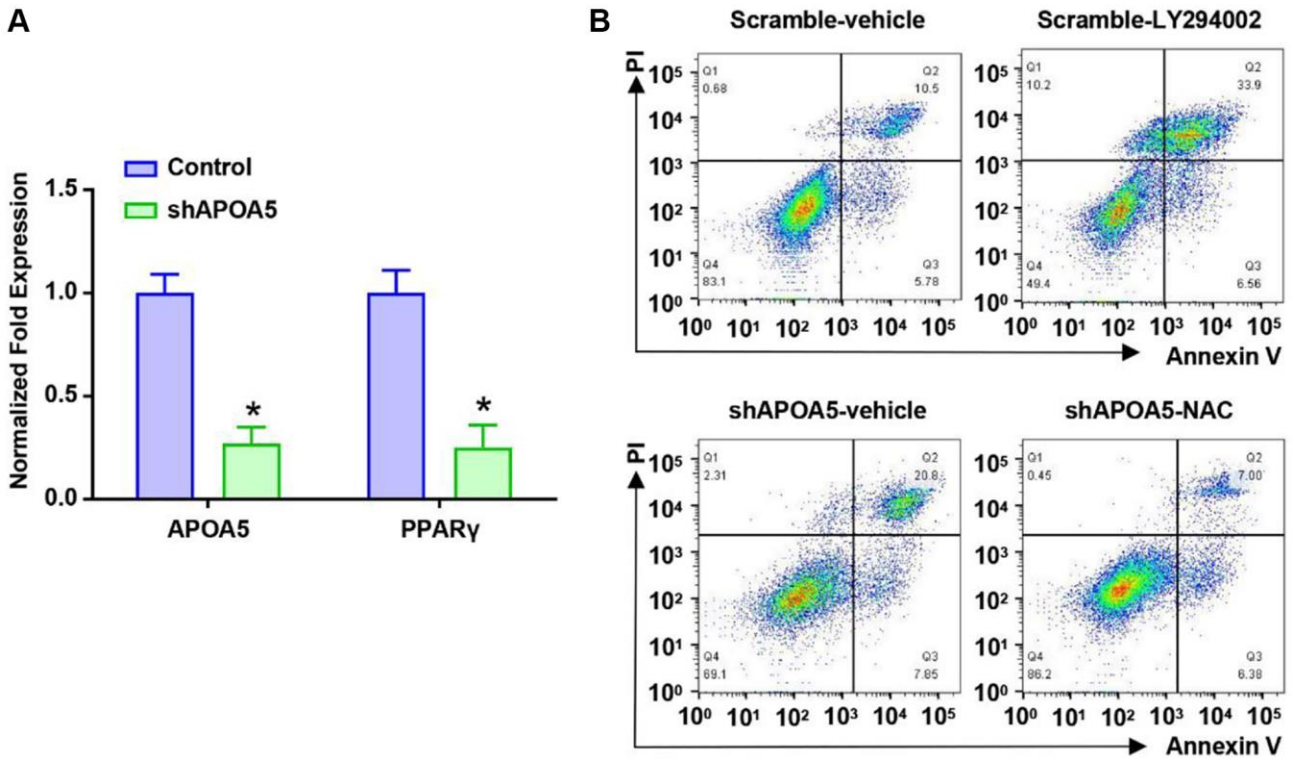
SUPPLEMENTARY FIGURES



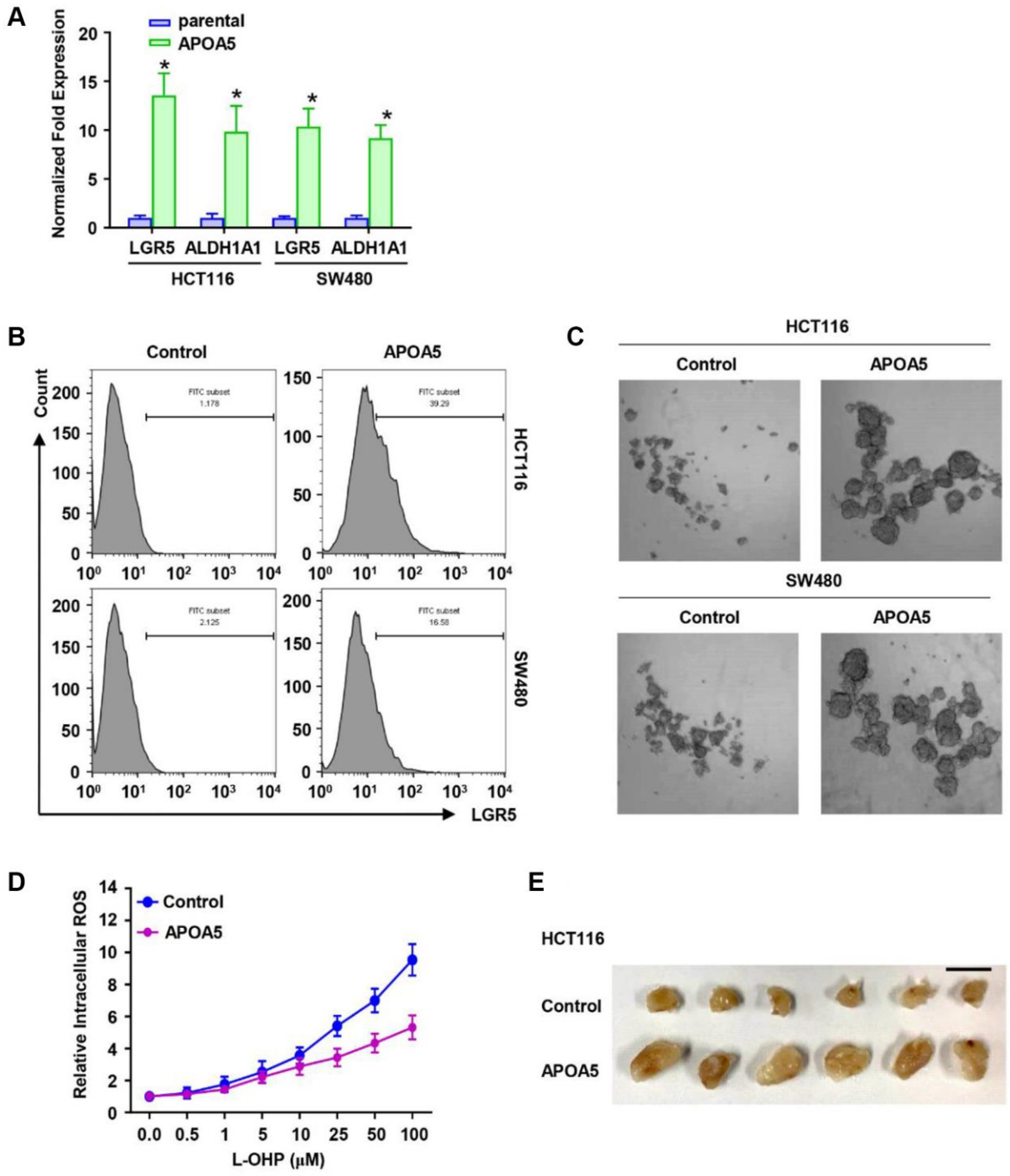
Supplementary Figure 1. PIK3CA-E545K mutation promotes L-OHP resistance in CRC cells. (**A**) IC_{50} of CRC cells was determined by treating L-OHP in a dose dependent manner, including HCT15 (PIK3CA-E545K mutation), HCT116 (PIK3CA-H1047R mutation), SW480, SW620, LOVO cells (PIK3CA wild type). (**B**) Relative PIK3CA mRNA expression was analyzed in PIK3CA-E454K or vector plasmids infected HCT116 and SW480 cells by qRT-PCR. β-actin was used as control. (**C**) IC_{50} of L-OHP was determined by treating PIK3CA-E454K or empty vector infected SW480 cells in a dose dependent manner. (**D**) Infected SW480/E454K cells were challenged with 2 μM L-OHP treatment, which showed increased resistance to L-OHP than the control according to cell viability analysis. (**E**) The percentage of cell apoptosis activation after 48 hours of 2 μM L-OHP exposure was measured by FITC-Annexin V/PI double staining. (**F**) The percentage of cell apoptosis of primary cells (CC-1/2) of 1 μM L-OHP exposure for 48 hours was measured by FITC-Annexin V/PI double staining. (**G**) Effect of PIK3CA-E454K on xenograft tumor growth was analyzed with subcutaneously injected HCT116 cells with L-OHP treatment (10 mg/kg). Total of 27 days after L-OHP treatment, the xenograft tumors were dissected and presented. Bar = 1 cm.



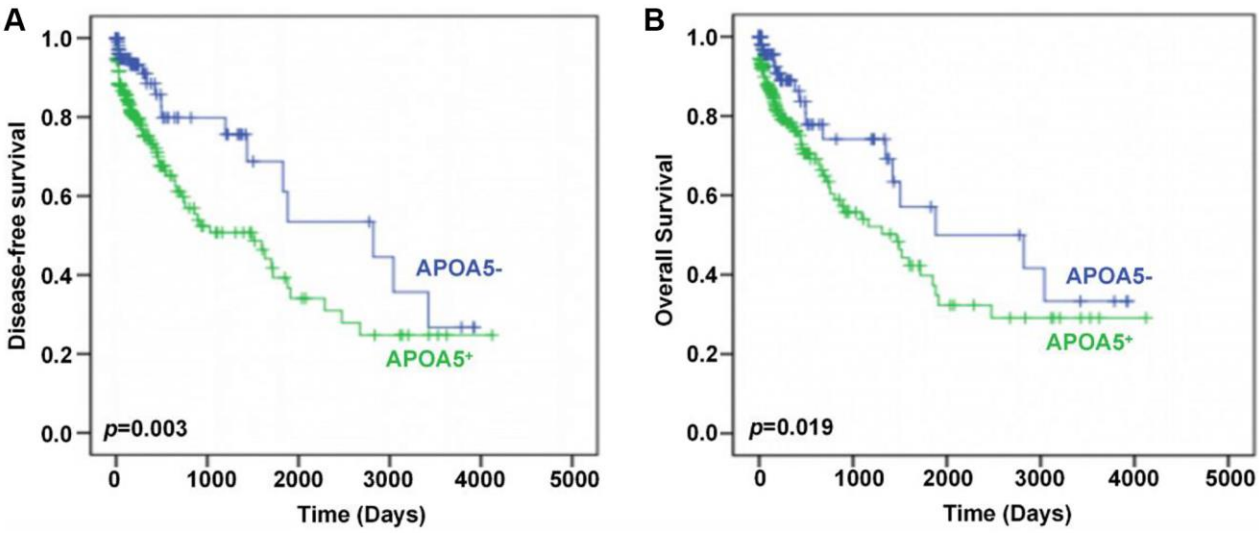
Supplementary Figure 2. APOA5 contributes to PIK3CA-E545K related L-OHP resistance of CRC cells. (**A**) The IC_{50} of SW480/APOA5 and control cells was analyzed with cell viability with gradient L-OHP treatment. The IC_{50} were 8.95 μM and 1.88 μM, respectively. (**B**) Flow cytometry was performed to determine cell apoptosis of APOA5 overexpressed HCT116 and SW480 cells which were treated with L-OHP (2 μM). (**C**) Cell cycle distribution in APOA5 overexpressed cell with L-OHP treatment. All cells were exposed to 2 μM L-OHP for 48 h. After propidium iodide staining, the proportion of cells in cell cycle phases G1, S and G2/M was measured by flow cytometry and quantified by FlowJo.



Supplementary Figure 3. APOA5 alleviates ROS production in PIK3CA-E454K cCRC cells with L-OHP treatment. (**A**) Relative APOA5 and PPARγ mRNA expression was analyzed in control or shAPOA5 plasmids infected HCT116-E454K cells by qRT-PCR. β-actin was used as control. (**B**) Flow cytometry was performed to determine cell apoptosis of HCT116/E454K control and APOA5 overexpressed cells, which was combined with L-OHP (2 μM) and LY294002 or NAC for 48 h.



Supplementary Figure 4. Elevated APOA5 attenuates stemness traits of colorectal cancer cells. (**A**) Relative LGR5 and ALDH1A1 mRNA expression was analyzed in parental or APOA5 overexpressing plasmids infected HCT116 and SW480 cells by qRT-PCR. β-actin was used as control. (**B**) The percentage of LGR5 positive cells in APOA5 overexpressed and parental cells were analyzed with flow cytometry analysis. (**C**) Representative tumorosphere images of APOA5 overexpressed and parental cells which were treated with L-OHP (1 μM). (**D**) Flow cytometry analysis was performed to evaluate the ROS production of APOA5 overexpressing and control cells with a gradient concentration of L-OHP treatment. Displayed as mean ± SD (*n* = 3). (**E**) Representative dissected tumors of CC1/APOA5 and parental cells (1 × 10^7 cells injected) were shown. Bar = 1 cm.



Supplementary Figure 5. Increased APOA5 mRNA expression predicts favored survival estimation. (**A**, **B**) Kaplan-Meier analysis of the disease-free survival (DFS, **A**) and overall survival (OS, **B**) between APOA5 positive and negative tumors in colorectal cancer patients with TCGA database. *P*-value was obtained from two-sided log-rank tests.