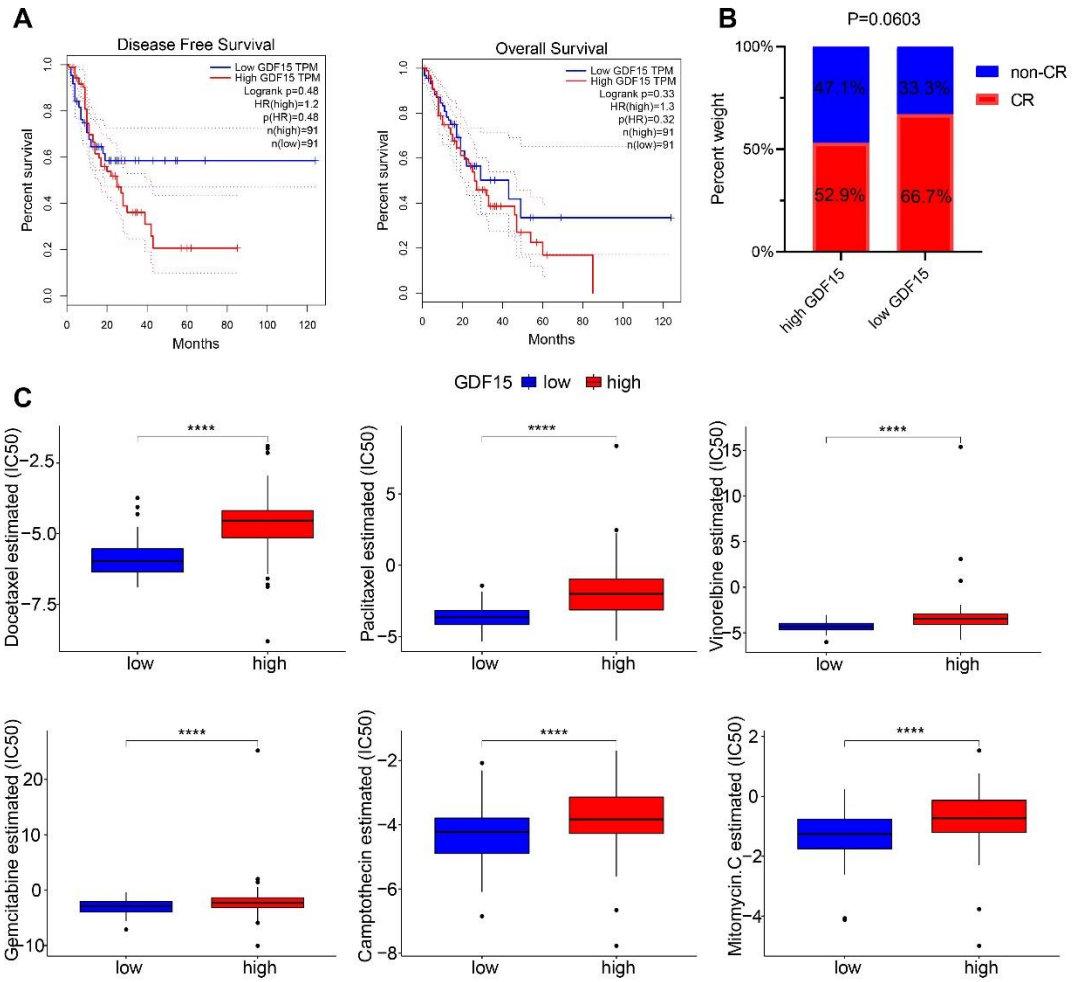

Fig. S1 Differential chemotherapy responses in GDF15 low and high groups

(A) Kaplan-Meier survival curves showing disease free survival and overall survival of patients with GDF15 low and high expression. (B) The proportion of chemotherapy response in high versus low GDF15 expression groups. non-CR, non-complete response; CR, complete response. (C) GDF15 high expression was related to higher IC50 for some common chemotherapy drugs.

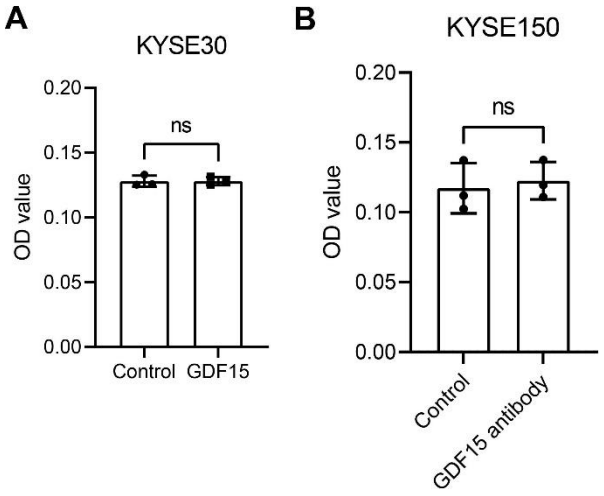

Fig. S2 Cell viability of KYSE30 and KYSE150 under treatment with GDF15

(A) Cell viability was measured in KYSE30 treated with GDF15 for two days. (B) Cell viability was measured in KYSE150 treated with anti-GDF15 antibody for two days.

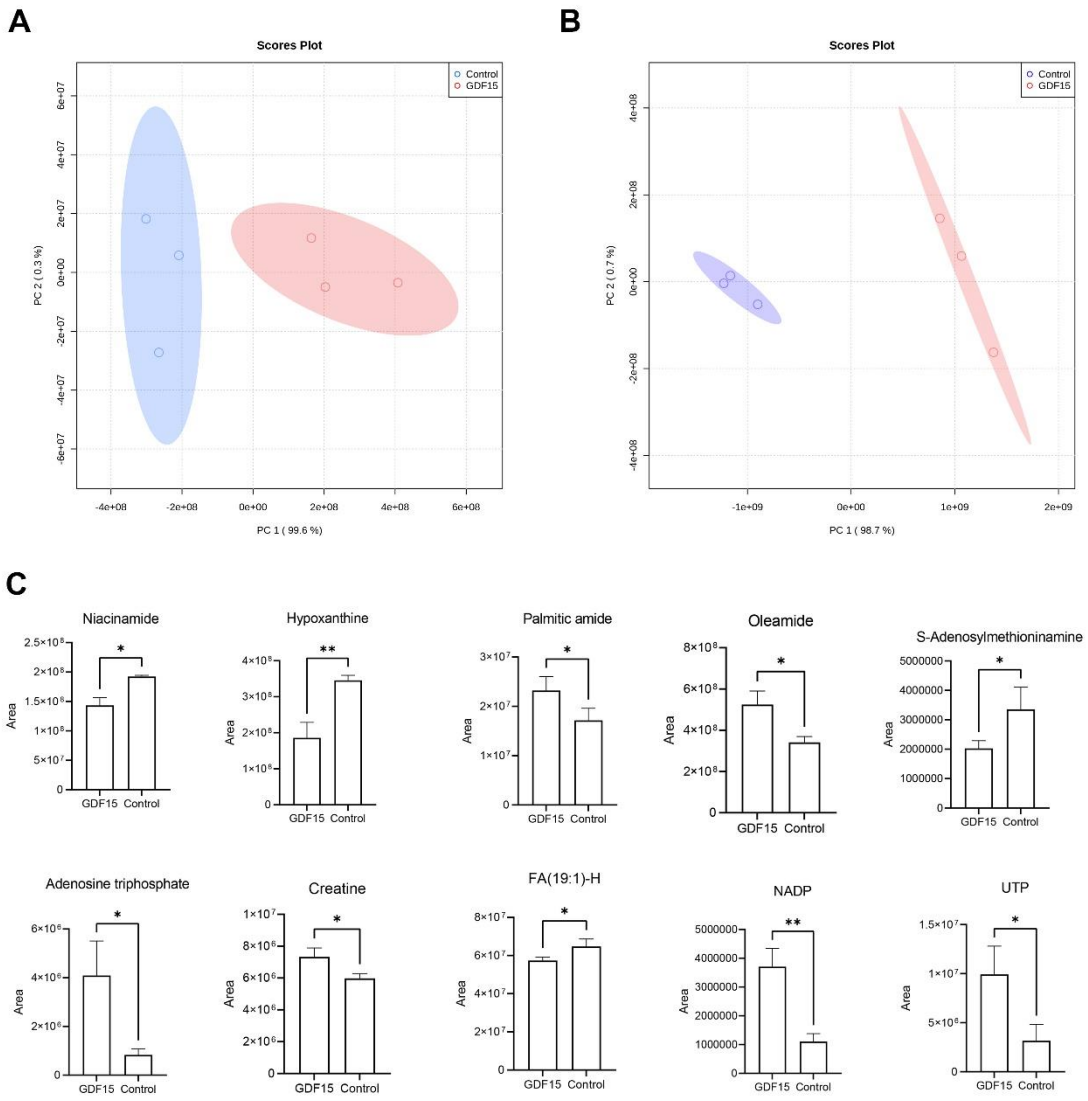

Fig. S3 GDF15 changed the metabolome of cancer cells

(A, B) Principal component analyses of the metabolome of the treatment group and control group in the negative (ESI-) ion mode and the positive (ESI-) ion mode. (C) Levels of indicated metabolites in KYSE30 cells treated with GDF15 for two days. Data are shown as the mean ± SD.

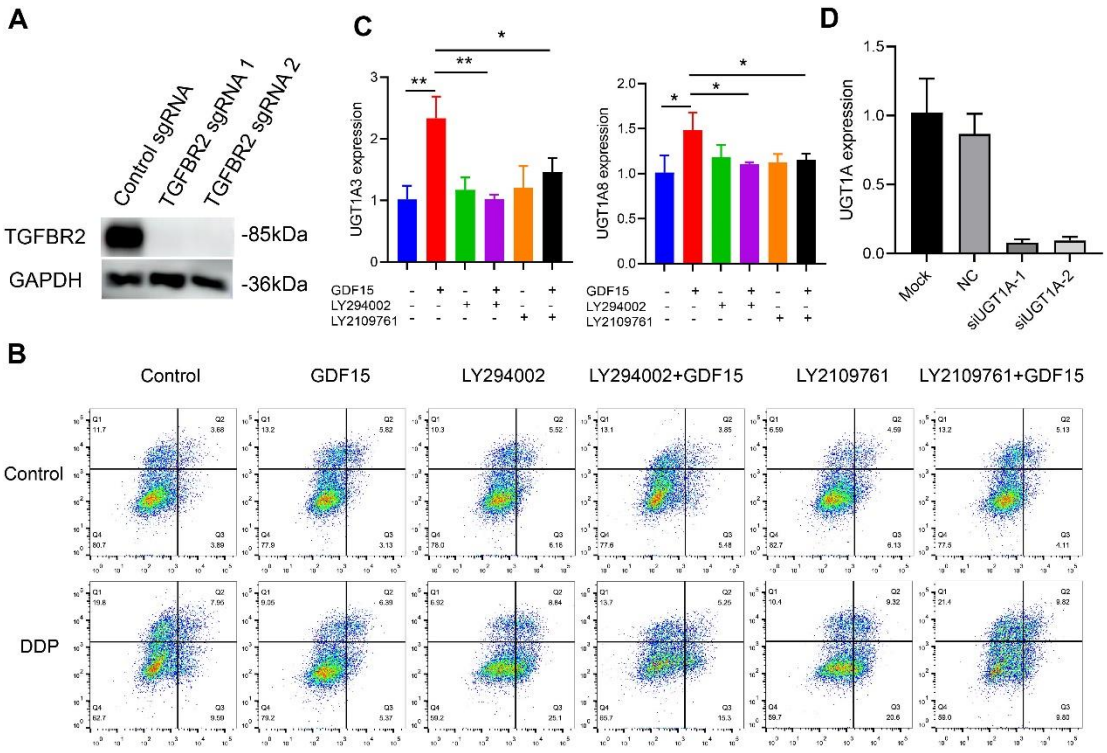

Fig. S4 GDF15 regulated UGT1A through the TGFBR2-AKT pathway

(A) Western blot for TGFBR2 and GAPDH after transfection with either control or TGFBR2-targeting sgRNAs. (B) Flow cytometry analysis of apoptosis in KYSE30 cells under the treatment of GDF15, LY294002, and LY2109761, in combination and alone. (C) The expression level of UGTs following GDF15 treatment. (D) Silencing efficiency of siUGT1A-1 and siUGT1A-2 was verified by qRT-PCR.