Figure S1. Effects of CPT on the three-dimensional spheroid formation of human PDAC (MIAPaCa-2 and BxPC3) and human CRC (DLD-1 and DKO4) cancer cell lines *in vitro*. (A) Spheroid morphology of PDAC and CRC cell lines treated with CPT. x4 magnification, Scale bar=500 μm. (B) Quantitative analysis of protein expression levels of K-ras protein after CPT treatment in MIAPaCa-2, BxPC3, DLD-1 and DKO4 cells. Blotting images were shown in Fig. 1B. A protein expression was quantitated using ImageJ v1.51 software. Bars indicate the relative expression value normalized to that of GAPDH and are presented as mean ± standard deviation of three independent assays. $^{*}P<0.05$ compared with control (0 μM) by Tukey's test. CPT, cryptotanshinone; PDAC, pancreatic ductal adenocarcinoma; CRC, colorectal cancer; KRAS, Kirsten rat sarcoma viral oncogene homolog.

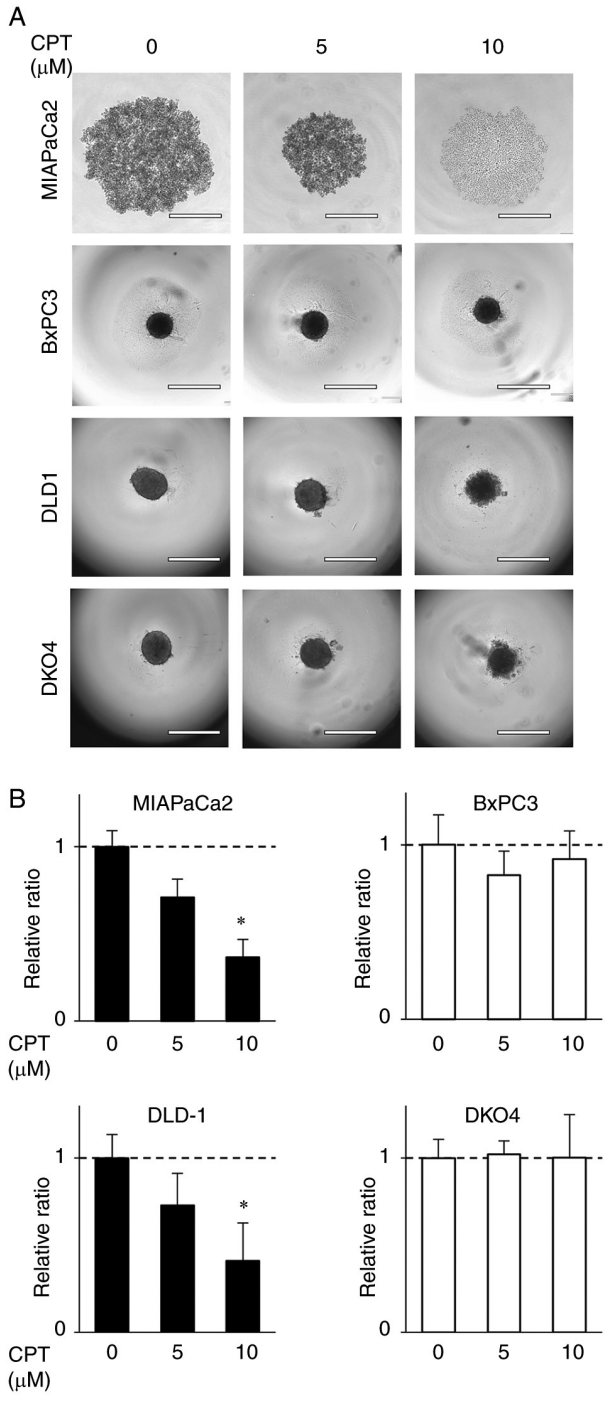

Figure S2. The effects of (A) glutamine depletion and (B) glucose depletion on the antitumor effect of CPT in human pancreatic ductal adenocarcinoma (MIAPaCa-2 and BxPC3) and human colorectal (DLD-1 and DKO4) cancer cell lines *in vitro*. For the three-dimensional (3D) spheroid viability assay, a total of $1x10^3$ cells were seeded into a 96-well V-bottom plate and incubated with CPT for 72 h in triplicate. Spheroid viability was determined by measuring adenosine triphosphate (ATP) content using the CellTiter-Glo 3D assay. Closed and open bars represent the cell lines with mutant KRAS (MIAPaCa-2 and DLD-1) and wild-type KRAS (BxPC3 and DKO4), respectively. Error bars represent the standard deviation. $^{*}P<0.05$, $^{**}P<0.01$ and $^{***}P<0.001$ compared with control (4 mM for glutamine and 25 mM for glucose) using Tukey's test. CPT, cryptotanshinone; KRAS, Kirsten rat sarcoma viral oncogene homolog.

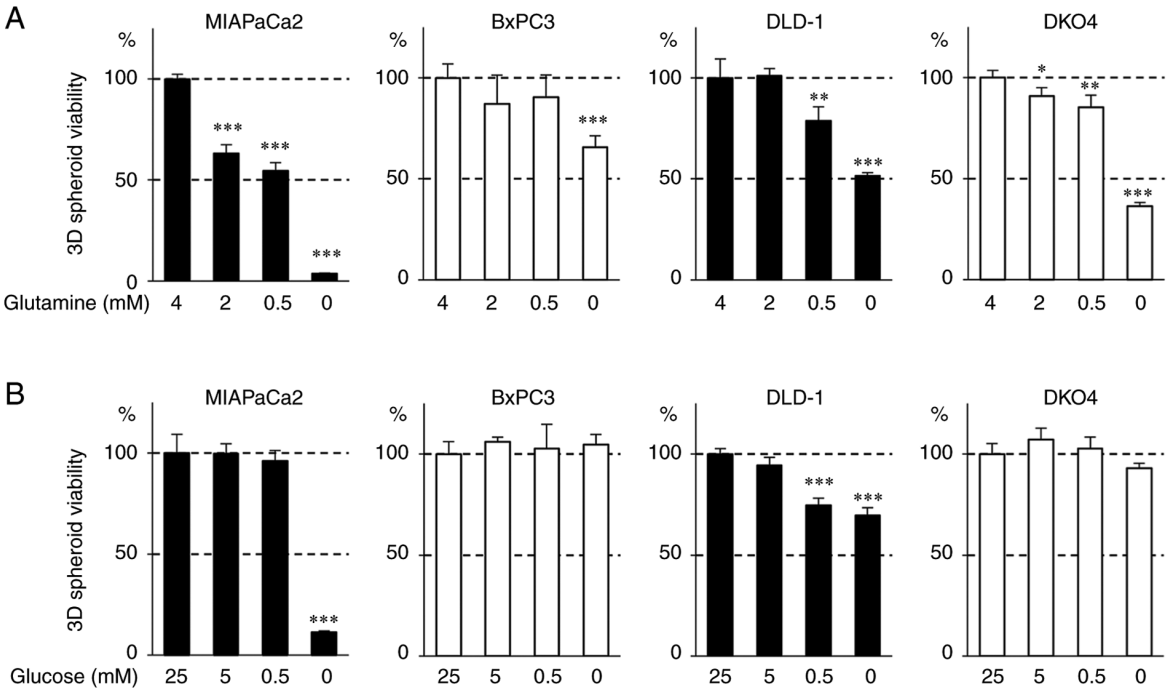

Figure S3. Quantitative analysis of protein expression levels of glutamine and lipid metabolism protein after CPT treatment in MIAPaCa-2 (A) and BxPC3 (B) cells. Blotting images were shown in Figure 2. A protein expression was quantitated using ImageJ v1.51 software. Bars indicate the relative expression value normalized to that of GAPDH and are presented as mean ± standard deviation of three independent assays. *P<0.05, **P<0.01 and ***P<0.001 compared with control (0 μM) by Tukey's test. CPT, cryptotanshinone; KRAS, Kirsten rat sarcoma viral oncogene homolog; GOT, glutamic-oxaloacetic transaminase; GLUD, glutamate transport system permease protein; GLS, glutaminase; IDH, isocitrate dehydrogenase; FASN, fatty acid synthase; ACC1, acetyl-CoA carboxylase 1; ACLY, ATP-citrate lyase; p-, phosphorylated.

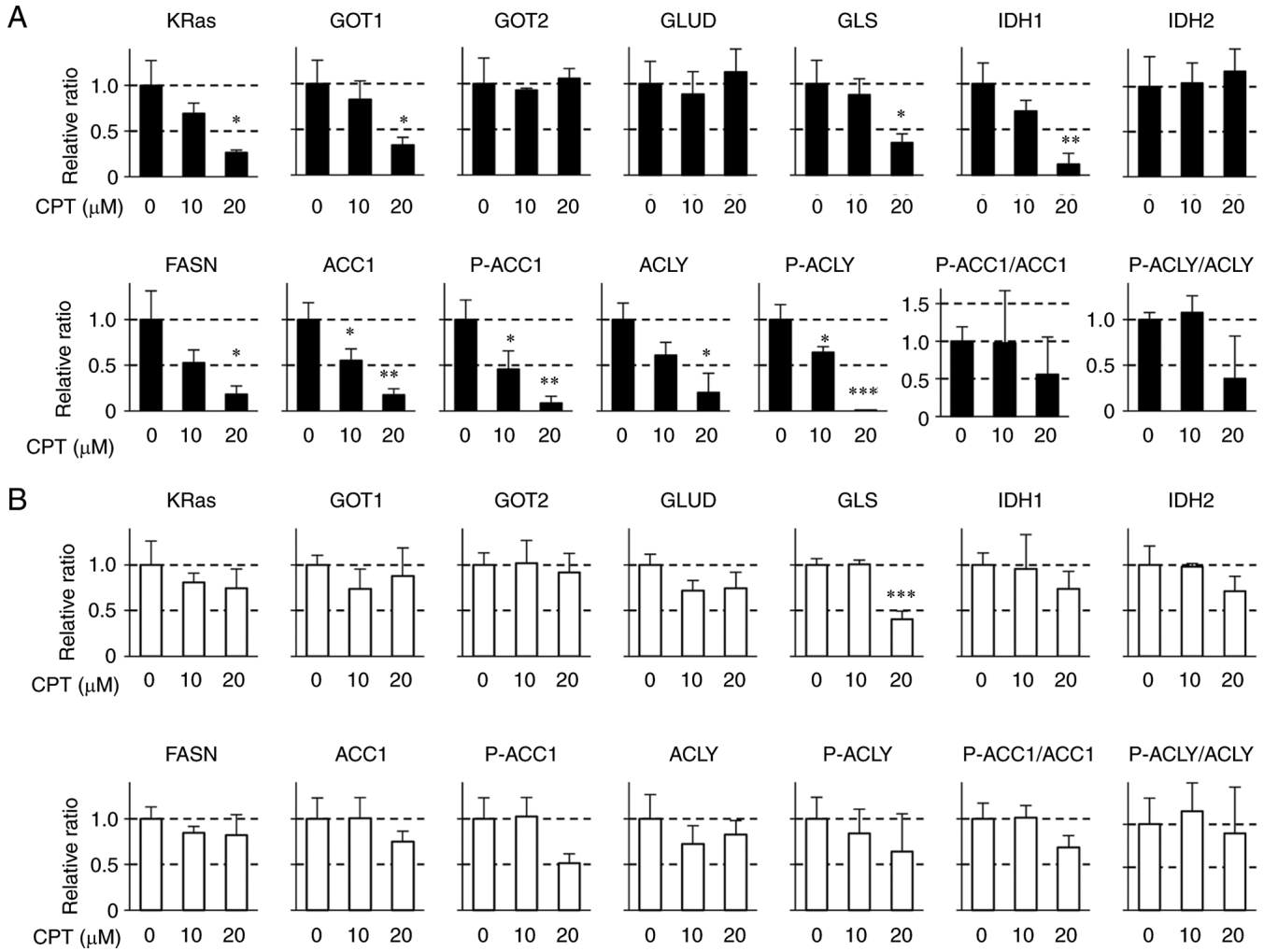

Figure S4. Representative image of lipid droplet formation in CPT-treated pancreatic cancer cell lines. A total of $1x10^5$ cells were treated or untreated with 5 μM CPT for 24 h, followed by staining with LipiDyeII and DAPI. The nuclei of the cells were stained with DAPI (blue) and the lipid droplets were stained with LipiDyeII (red). Scale bars=50 μm. Representative images of lipid droplet formation in (A and B) MIAPaCa-2 and (C and D) BxPC3 cells. The cells were (A and C) treated or (B and D) untreated with 5 μM CPT for 24 h. CPT, cryptotanshinone.

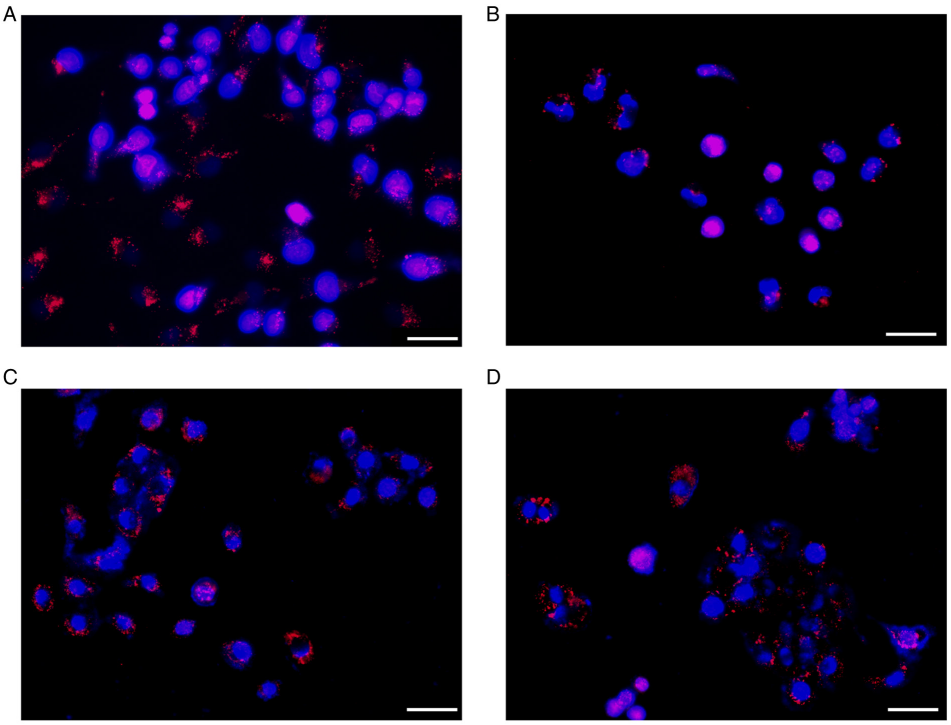

Figure S5. Quantitative analysis of protein expression levels of glutamine and lipid metabolism protein treated KRAS siRNA and FASN siRNA in MIAPaCa-2. (A) Quantitative analysis of proteins regulating glutaminolysis and lipogenesis in MIAPaCa-2 cells treated with control (siC) and KRAS siRNA (siKRAS). Blotting images were shown in Fig. 4A. (B) Quantitative analysis of K-Ras and FASN proteins in MIAPaCa-2 cells treated with control (siC), KRAS siRNA (siKRAS) and FASN siRNA (siFASN). Blotting images were shown in Fig. 5A. A protein expression was quantitated using ImageJ v1.51 software. Bars indicate the relative expression value normalized to that of GAPDH and are presented as mean ± standard deviation of three independent assays. *P<0.05 compared with control (0 μM) by Tukey's test. KRAS, Kirsten rat sarcoma viral oncogene homolog; si, short interfering; FASN, fatty acid synthase; GOT, glutamic-oxaloacetic transaminase; IDH, isocitrate dehydrogenase; GLUD, glutamate transport system permease protein; GLS, glutaminase; ACC1, acetyl-CoA carboxylase 1; ACLY, ATP-citrate lyase; p-, phosphorylated.

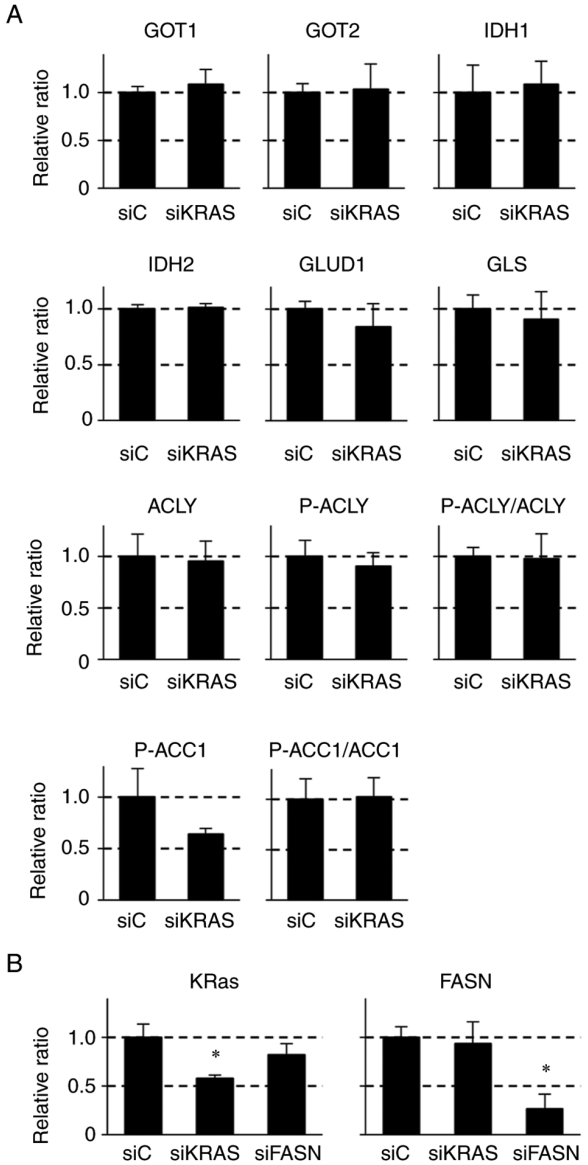

Figure S6. Representative image of lipid droplet formation in MIAPaCa-2 cells treated with siKRAS and siFASN. A total of $1x10^5$ cells were treated with siKRAS and siFASN for 72 h, followed by staining with LipiDyeII and DAPI. The nuclei of the cells were stained with DAPI (blue) and the lipid droplets were stained with LipiDyeII (red). Scale bars=50 μm. Representative image of lipid droplet formation in MIAPaCa-2 cells treated with (A) si control, (B) siKRAS and (C) siFASN. si, short interfering; KRAS, Kirsten rat sarcoma viral oncogene homolog; FASN, fatty acid synthase.