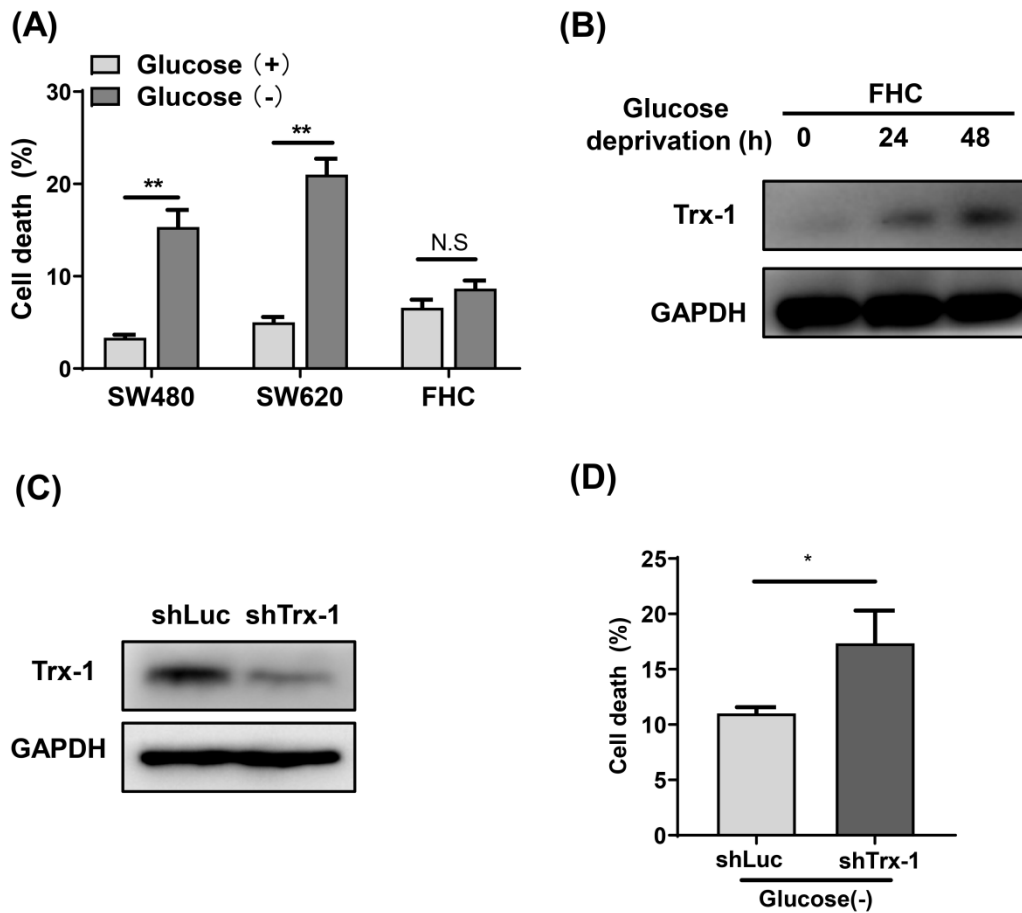
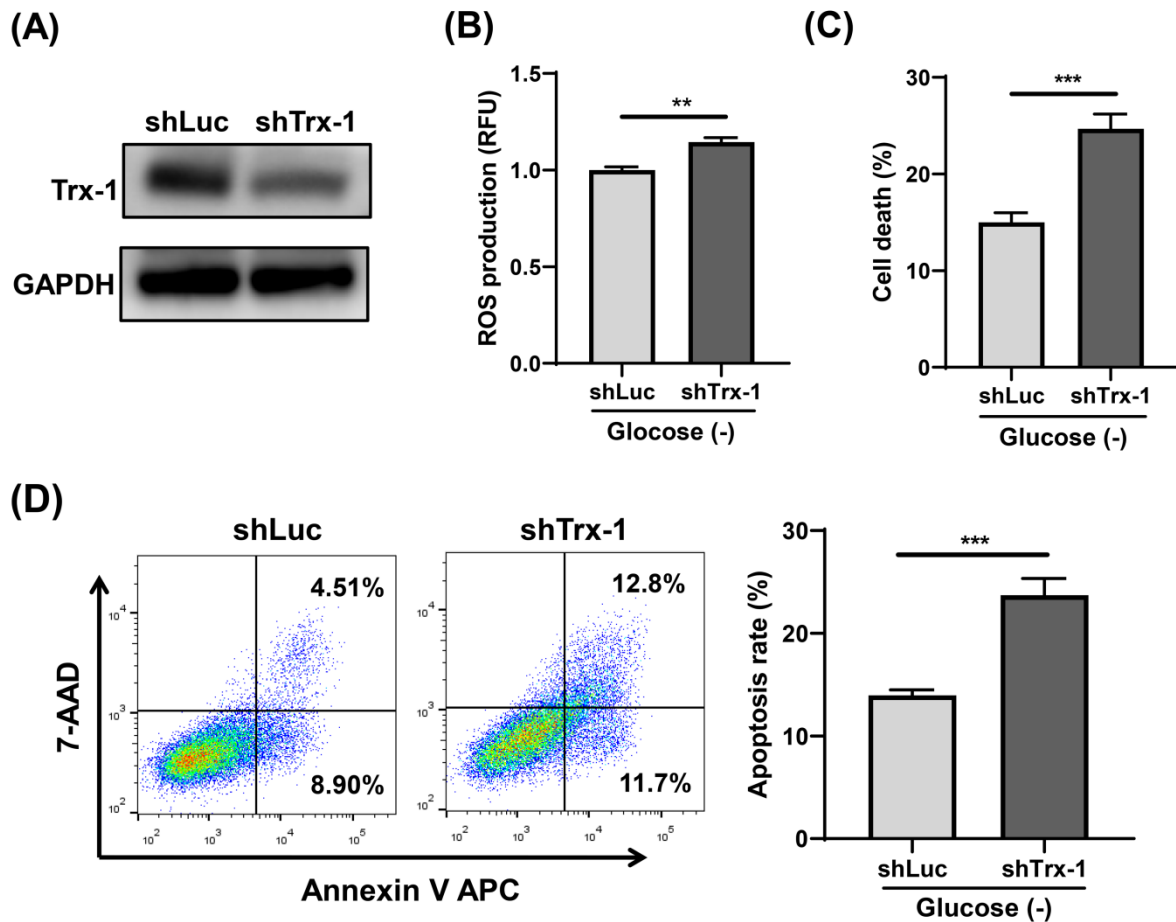


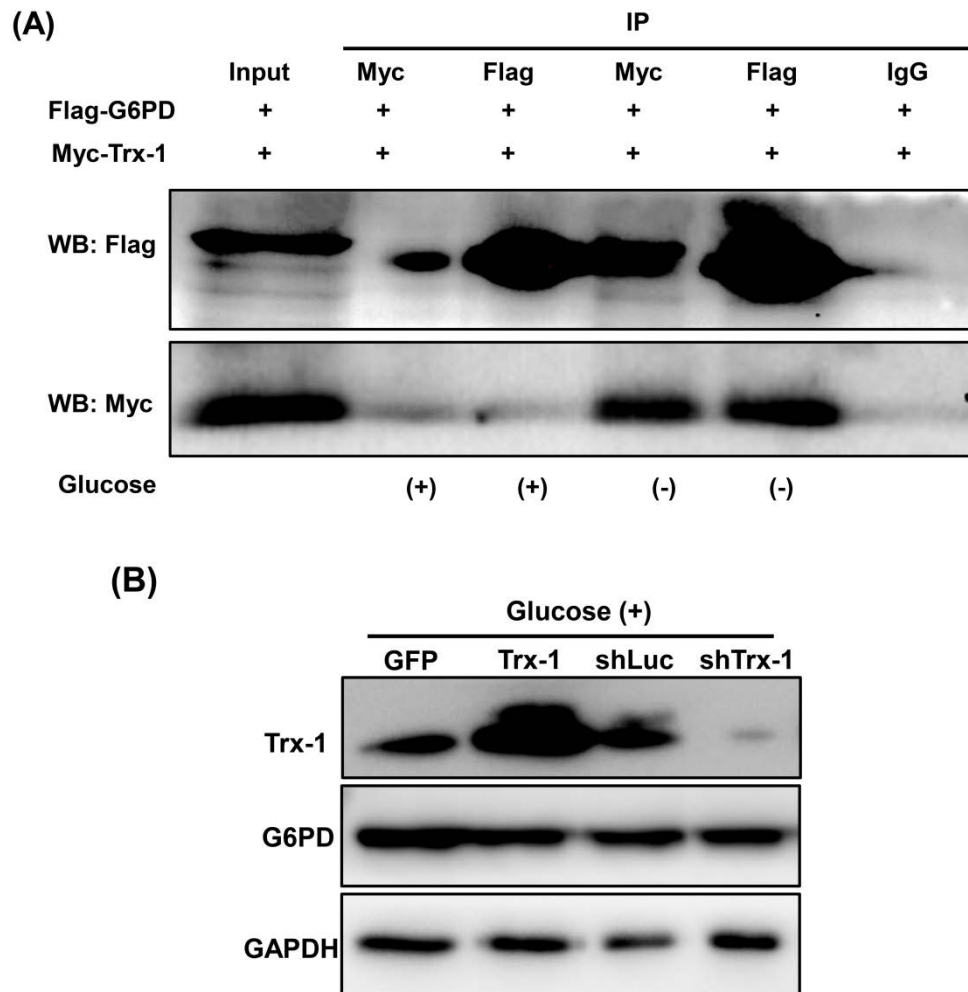
Supplemental data



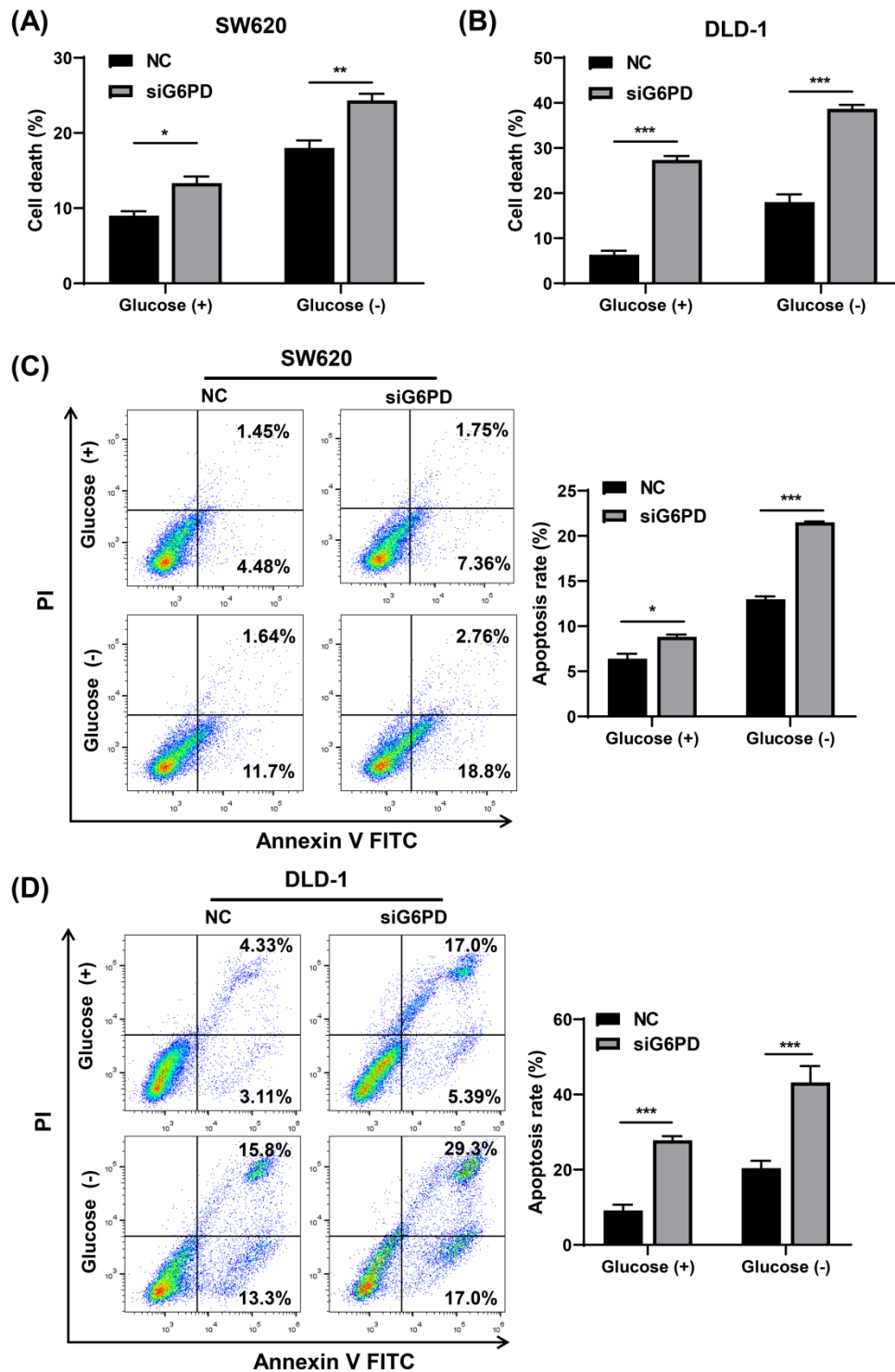
**Figure S1** Toxicity of glucose deprivation in normal (FHC) cells. (A) Cell death assessed by trypan blue assays in SW480, SW620 and FHC cells grown for 24 h without glucose. (B) Trx-1 protein expression detected by Western blotting in FHC cells incubated for 24 h and 48 h in glucose-free medium. (C) Trx-1 protein expression detected by Western blotting in FHC cells transfected with shLuc or shTrx-1. (D) Cell death detected by the trypan blue assays in FHC cells transfected with shLuc or shTrx-1 for 24 h incubated in glucose-free medium. \* $p < 0.05$ .



**Figure S2** Knockdown of Trx-1 sensitizes colorectal cancer cells to glucose deprivation-induced cell death. (A) Trx-1 protein expression detected by Western blotting in SW620 cells stably expressing shLuc or shTrx-1. (B) The ROS level in SW620 cells stably expressing shLuc or shTrx-1 incubated in glucose-deprived medium for 24 h. (C) Cell death in SW620 cells stably expressing shLuc or shTrx-1 incubated for 24 h in glucose-free medium was determined using the trypan blue assays. (D) Cell apoptosis assessed by flow cytometry with Annexin V staining in SW620 cells stably expressing shLuc or shTrx-1 incubated in glucose-deprived medium for 24 h.  $**p < 0.01$ , and  $***p < 0.001$ .

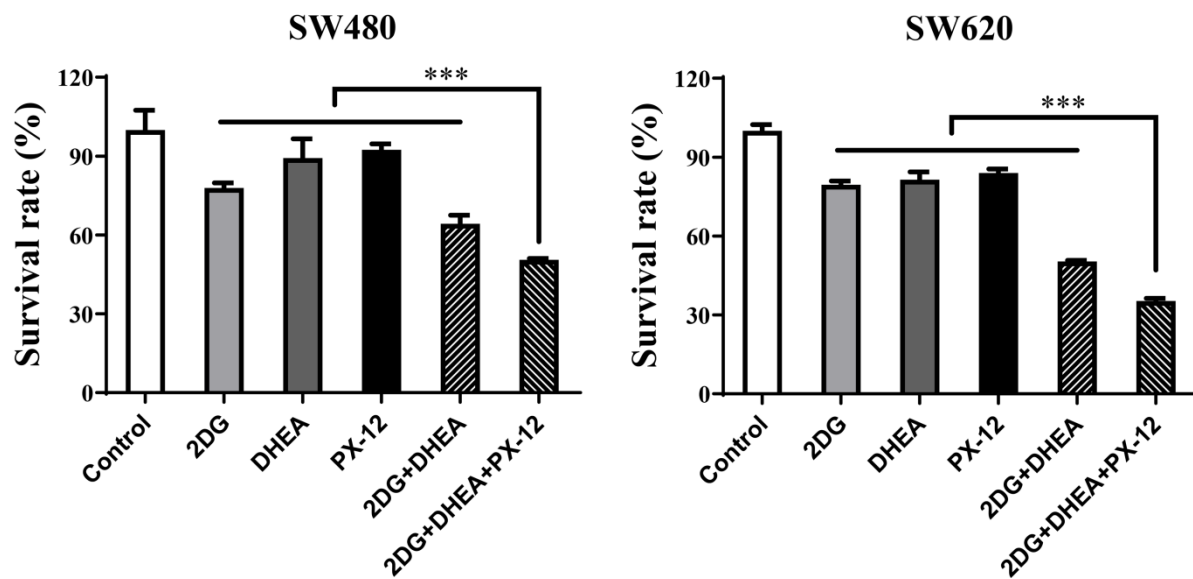


**Figure S3** The interaction between Trx-1 and G6PD in colorectal cancer cells. (A) Co-immunoprecipitation (Co-IP) analysis of the interaction between Trx-1 and G6PD in SW480 cells transfected with Flag-G6PD and Myc-Trx-1 in the absence and presence of glucose. (B) Protein expressions of G6PD and Trx-1 determined by Western blotting in SW480 cells stably expressing GFP, Trx-1, shLuc or shTrx-1 in normal medium.



**Figure S4** Knockdown of G6PD sensitizes colorectal cancer cells to glucose deprivation-induced cell death. (A-B) Cell death assessed by trypan blue assays in SW620 and DLD-1 cells transfected with NC or siG6PD, after 24 h incubation in complete medium or glucose-deprived medium. (C-D) Cell apoptosis assessed by flow cytometry using

Annexin V/propidium iodide (PI) staining in SW620 and DLD-1 cells transfected with NC or siG6PD, after 24 h incubation in complete medium or glucose-deprived medium.



**Figure S5** Combined treatment with PX12, DHEA, and 2DG increases cytotoxicity in human colorectal cancer cells. SW480 and SW620 cells were treated with PX12 (2.5  $\mu$ M), DHEA (75  $\mu$ M), 2DG (2.5 mM), or the combination for 24 h, and cell viability was measured by CCK-8 assay.