

Figure S1. Validation of the repeated sphere-forming and recovery assay using HCT116 clone 2 based on the stemness marker Nanog. Expression levels of Nanog mRNA in SDCSCs and SDACs from G0 (parental) to G8, as analyzed by reverse transcription-quantitative PCR. Data are presented as the mean  $\pm$  SD (n=3). GAPDH was used as the reference gene. SDCSCs, sphere-derived cancer stem cell-like cells; SDACs, sphere-derived adherent cells; G, generation.

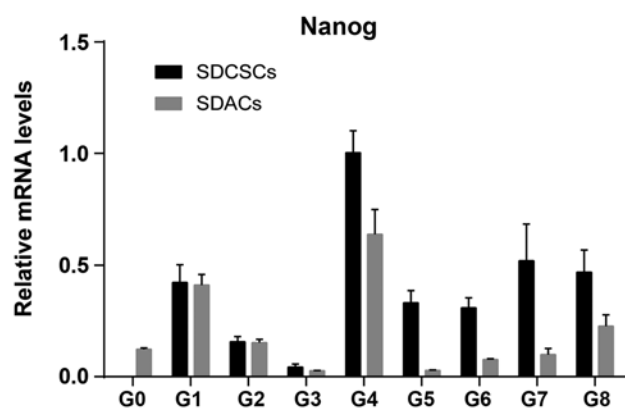


Figure S2. DPEP1 upregulation in HCT116 clone 2. DPEP1 mRNA expression between G0 (parental) and G8D cells was confirmed by reverse transcription-quantitative PCR. Data are presented as the mean  $\pm$  SD (n=3). GAPDH was used as the reference gene. Significant differences were determined using unpaired t-tests. \*\*P<0.01. G8D, eighth-generation sphere-derived adherent cells; DPEP1, dipeptidase 1.

