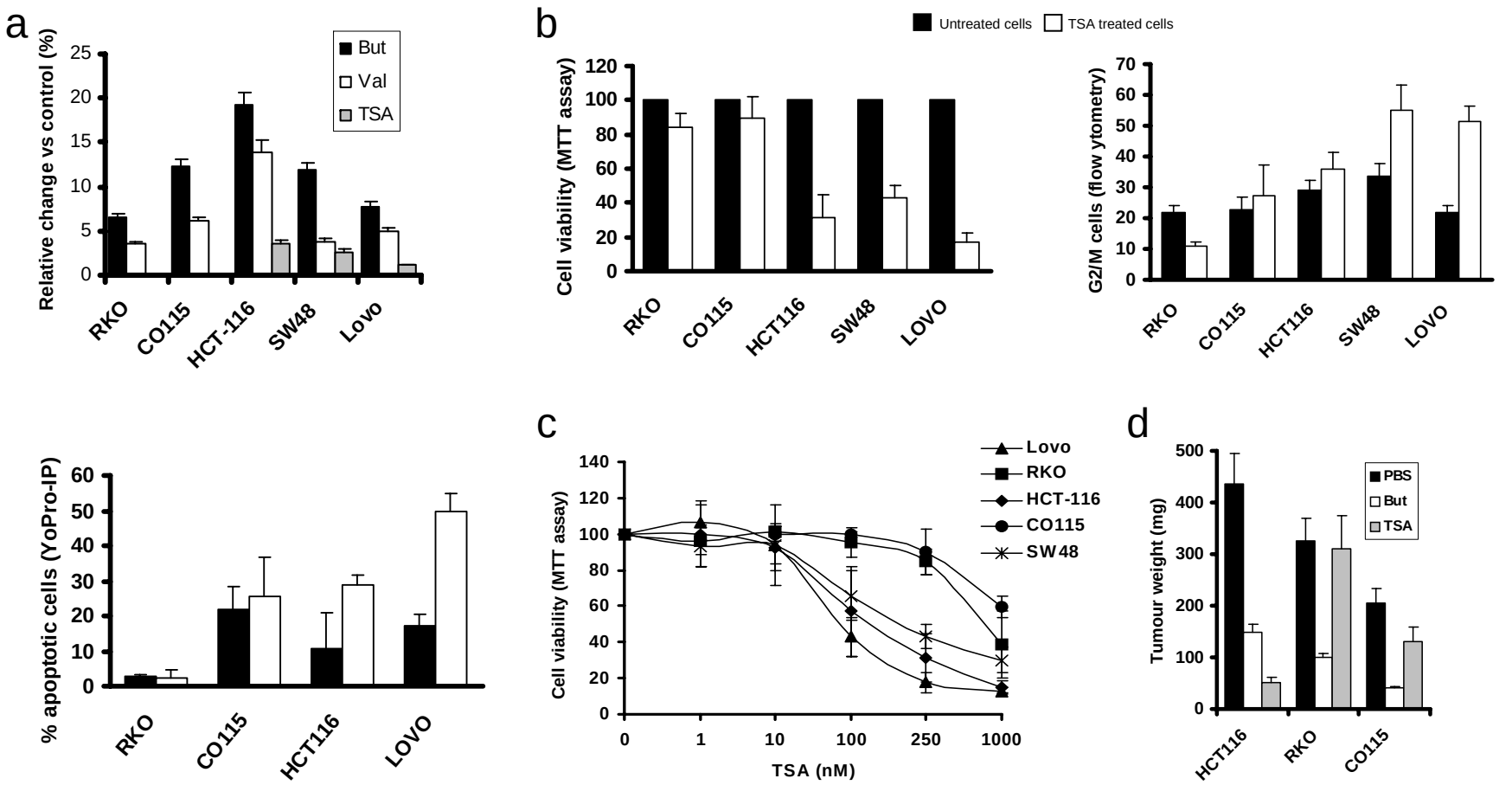

Supplementary Figure 3. **a,** Quantification of histone H4 acetylation levels using high performance capillary electrophoresis after treatment with HDAC inhibitors. The hydroxamic acid TSA does not induce histone hyperacetylacion in the HDAC2-deficient RKO and CO115 cells, whilst in HDAC2-proficient cells (HCT-116, SW48 and LoVo) hyperacetylation is achieved. The carboxylic acids valproate (Val) and butyrate (But) induce hyperacetylation in all cells. **b,** TSA induces cell growth inhibition, G2/M cell cycle arrest, and apoptosis in HDAC2-proficient cells HCT-116, SW48 and LoVo, but HDAC2-mutant cells (RKO and Co115) show resistance to the these three typical effects of the administration of a HDAC inhibitor. **c**, Dose response curves of the effects of the HDAC inhibitor TSA on cell viability (MTT assay) of colon cancer cell lines. Cells were treated for 48 h with different concentrations of TSA (0-1000 nM). Experiments were performed in triplicate. The HDAC2-deficients cells lines RKO and CO115 show an enhanced resistance to cell growth inhibition by TSA. **c**, Butyrate induced tumor shrinkage in all cancer cells xenografted in nude mice independently of their HDAC2 status, whereas TSA was only able to accomplish these effects in the HDAC2-proficient cell line (HCT-116), whilst RKO and CO115 remained resistant.