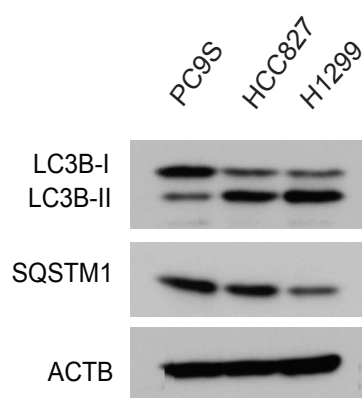


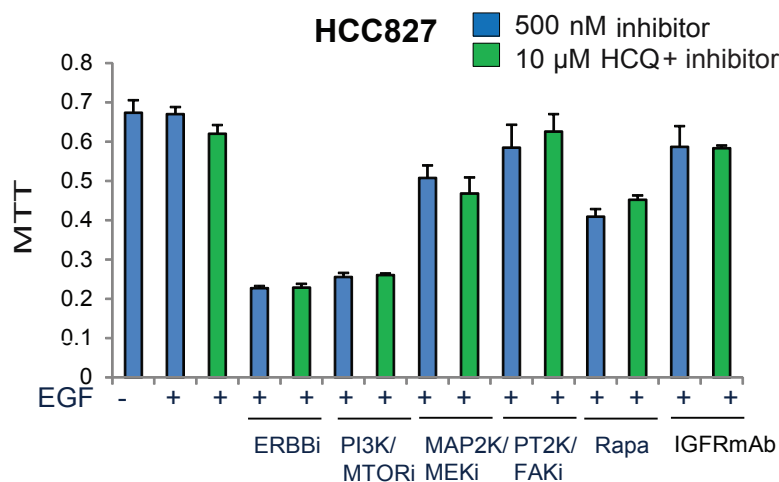
Figure S1. Autophagy induction predicts augmented cytotoxicity from autophagy inhibition only in certain cell lines. **(A)** Immunoblotting against SQSTM1/p62 and LC3 in LN229 and PC9 cells treated as indicated for 24 h in the presence of EGF (epidermal growth factor) + inhibitor (500 nM). **(B)** A375P mCherry-EGFP-LC3 cells treated with the indicated inhibitors (24 h); red puncta reflects induction of autophagy. **(C)** MTT (96 h) assays. Mean \pm SD is shown; * p <0.05.

A

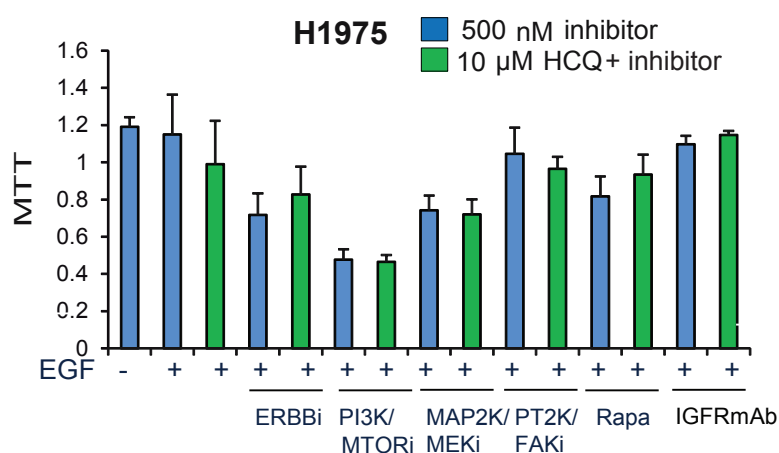


B

IGFR mab – Figitumumab PI3K/ MTORi -PF4691502
 PT2K/FAKi -PF562271 ERBBi- Dacomitinib
 MAP2K/MEKi-PD325901



C



D

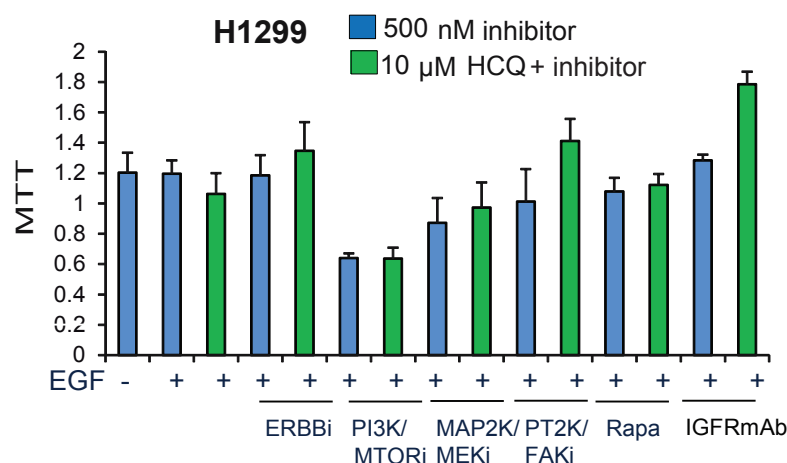


Figure S2. Addition of HCQ to targeted therapies in EGFR mutant lung cancer cell lines. (A) immunoblotting against LC3 and SQSTM1/p62 in the indicated cell lines. (B-D) MTT (96 h) assays were performed in the indicated cells simultaneously treated with inhibitor (blue), or inhibitor + HCQ (green) in the presence of EGF. Rapa, rapamycin; * $p < 0.05$

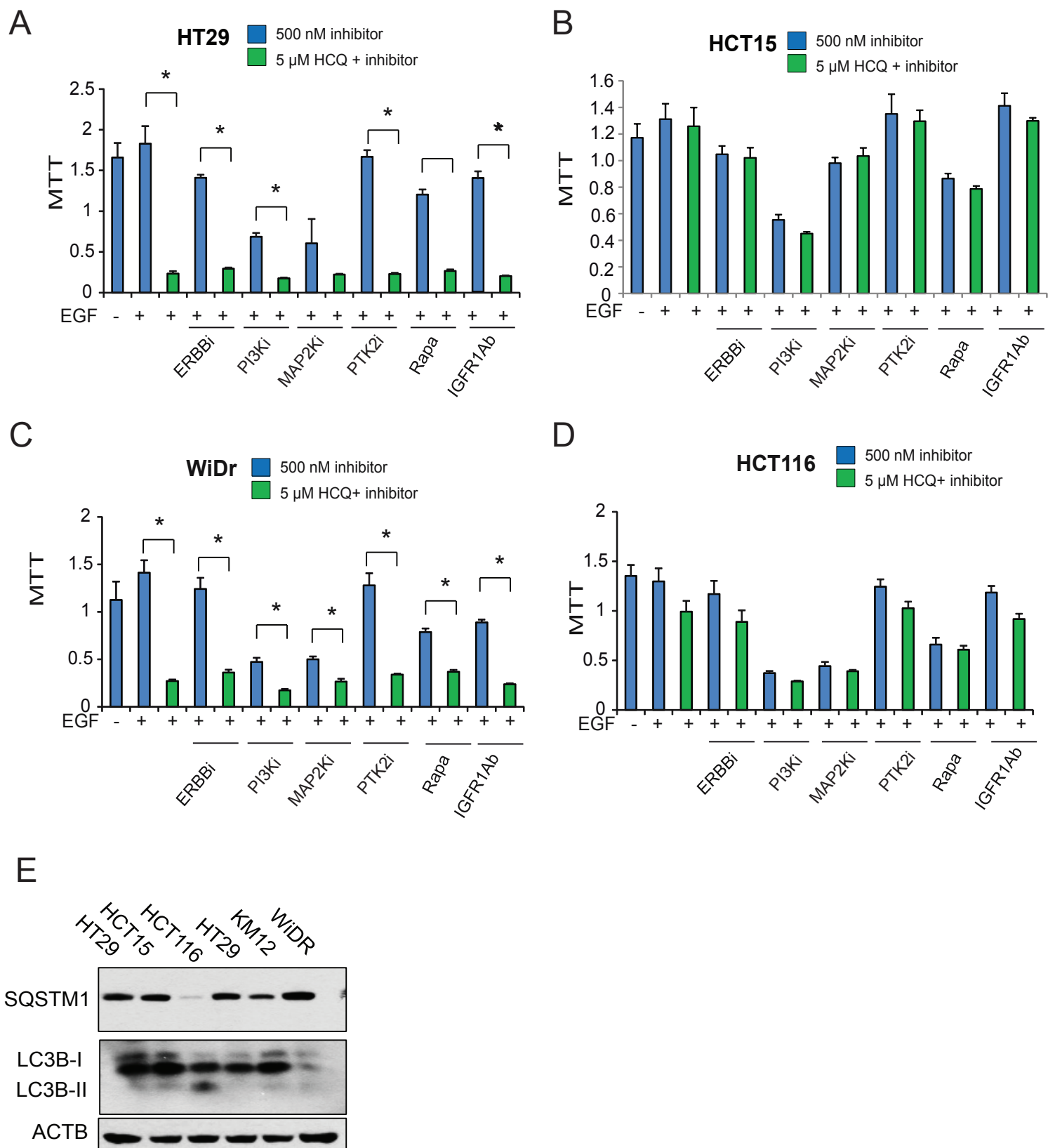


Figure S3. Colon cancer cell lines sensitive to HCQ. (A-D) MTT (96 h) assays were performed in the indicated cells simultaneously treated with inhibitor (blue), or inhibitor + HCQ (green) in the presence of EGF. Rapa, rapamycin; (E) Immunoblotting against LC3 and SQSTM1/p62 in the indicated cell lines. * $p < 0.05$.

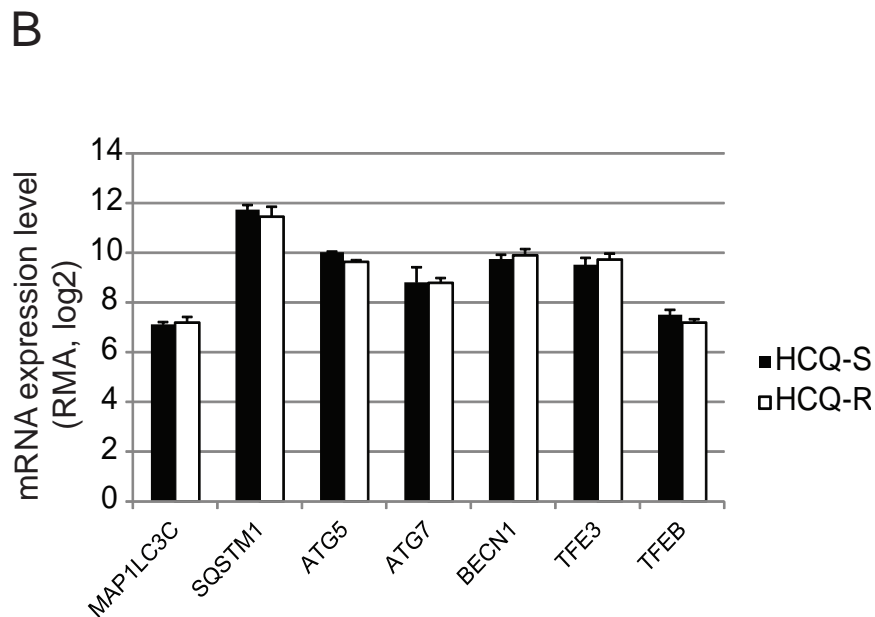
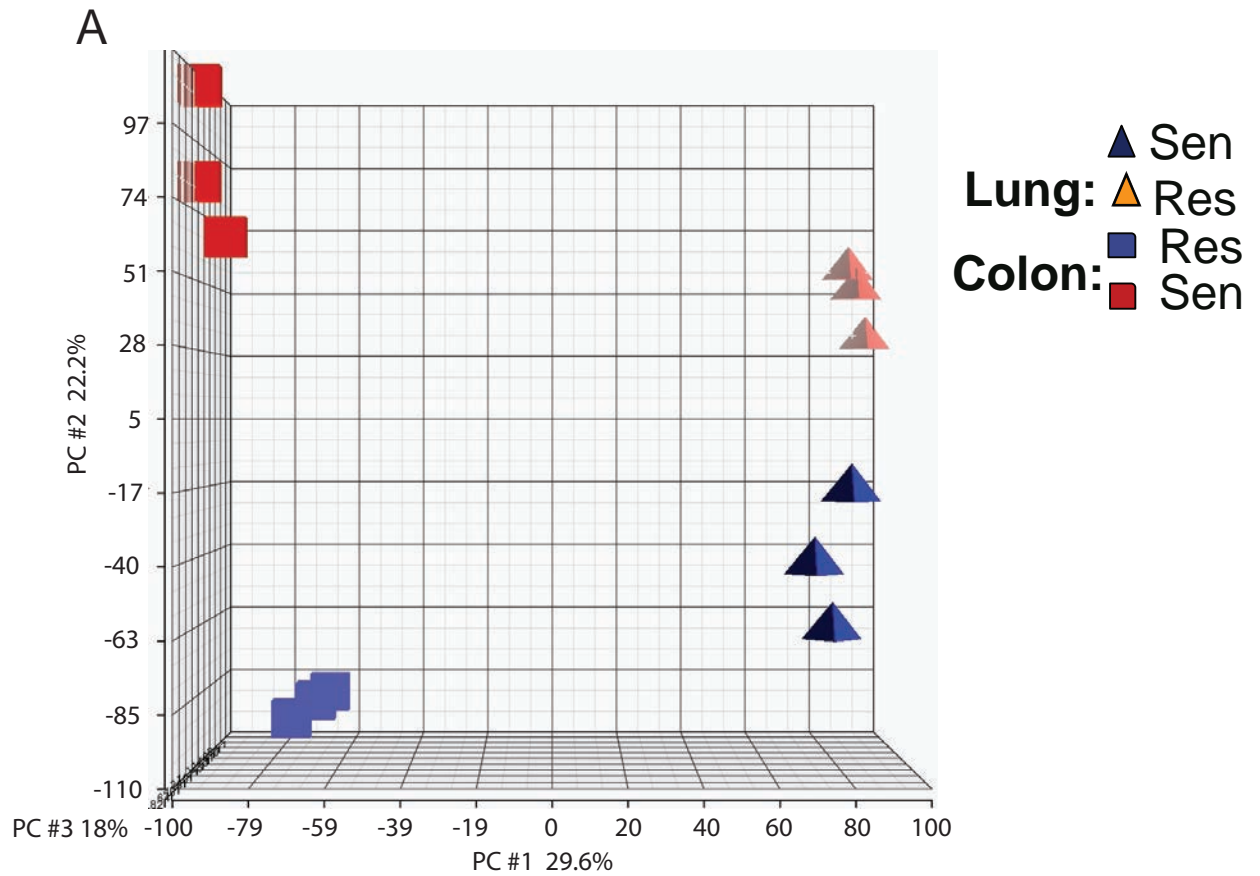


Figure S4. Expression microarray analysis in HCQ-sensitive and HCQ-resistant cells (A) Principal component analysis (PCA) of gene expression profile for 4 cancer cell lines (B) mRNA expression of essential autophagy and lysosomal biogenesis genes in 4 cancer cell lines. HCQ-S, HCQ sensitive; HCQ-R, HCQ resistant.

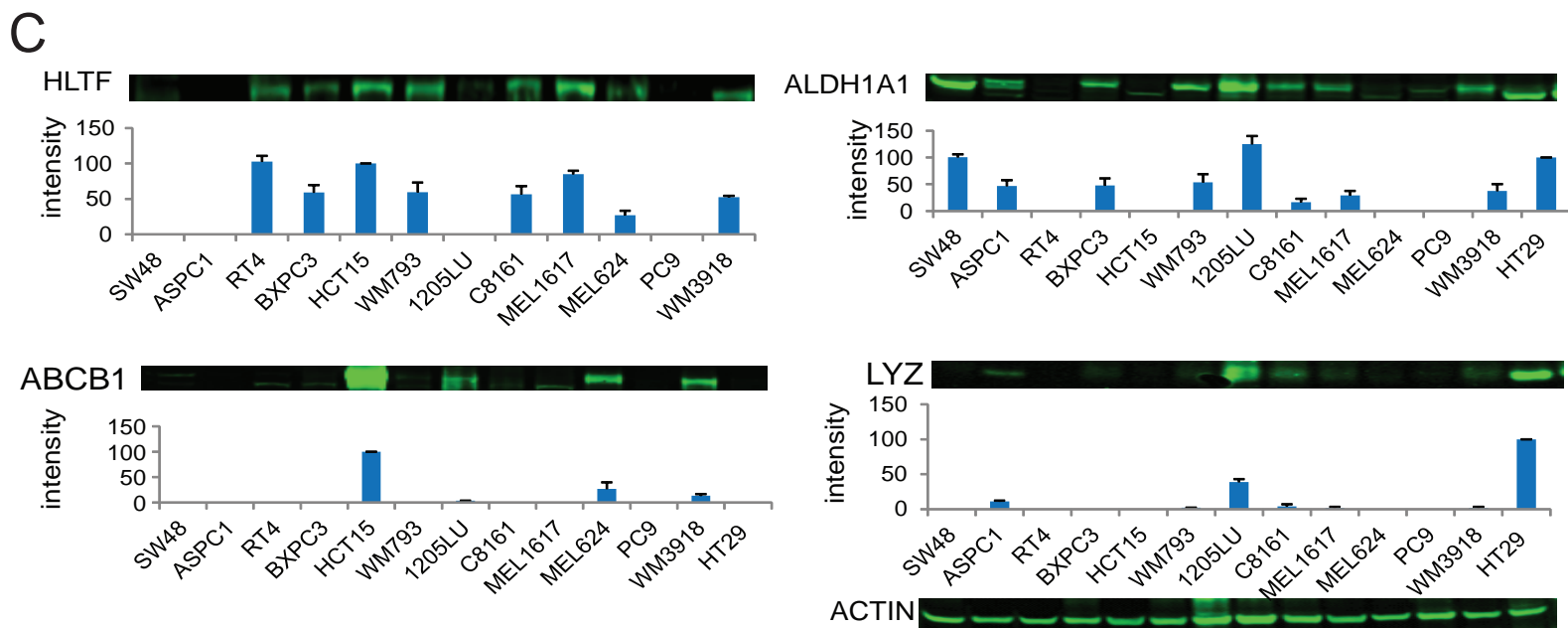
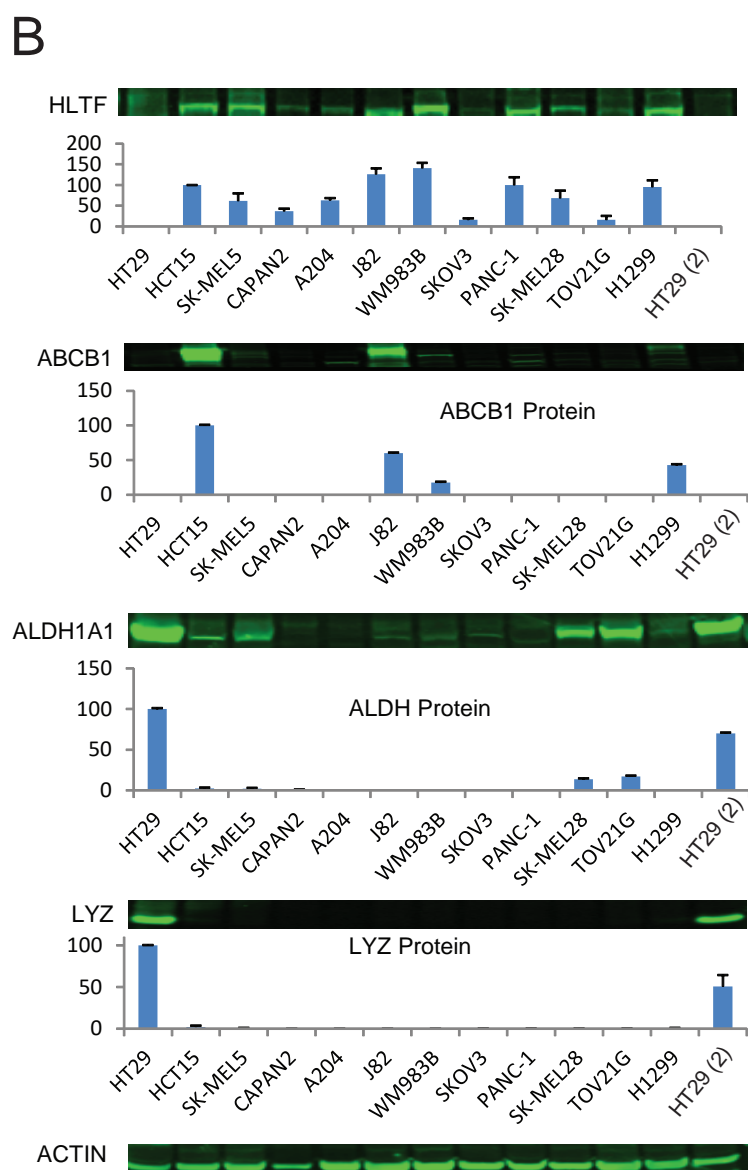
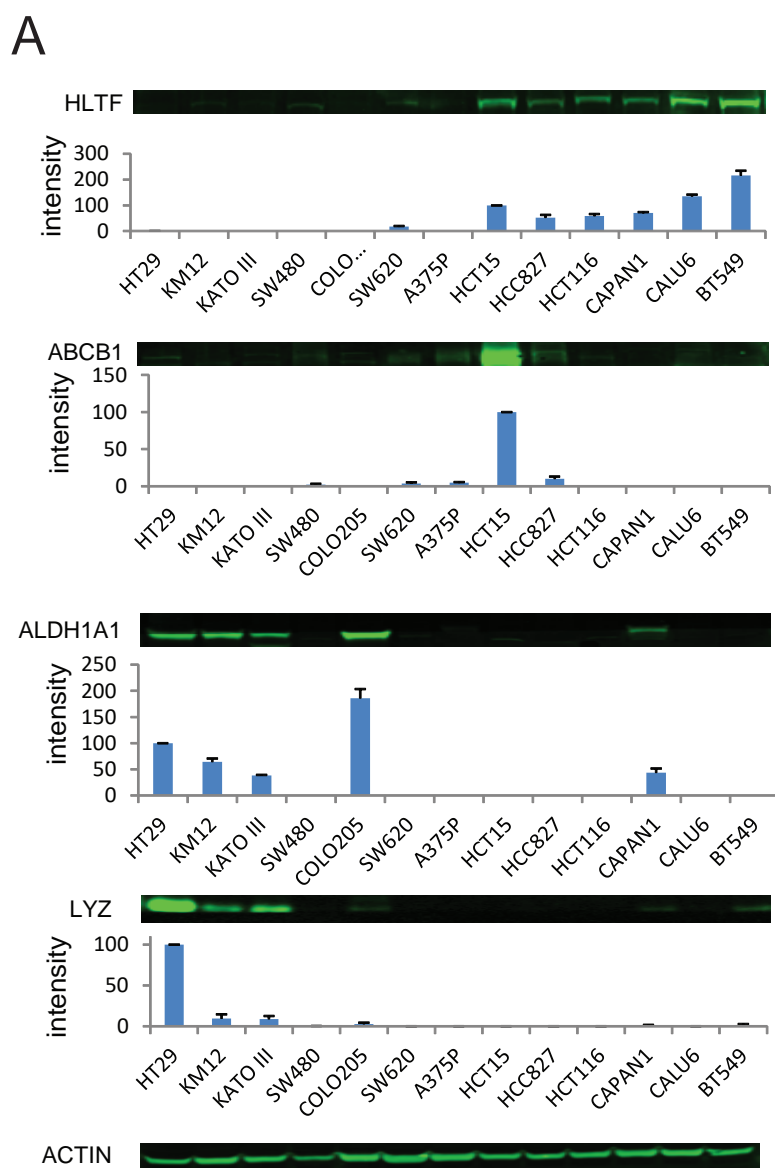


Figure S5. Licor Odyssey detection of protein expression of 4 differentially expressed genes in 33 HCQ-S and HCQ-R cell lines. (A-C) Separate cell lines.

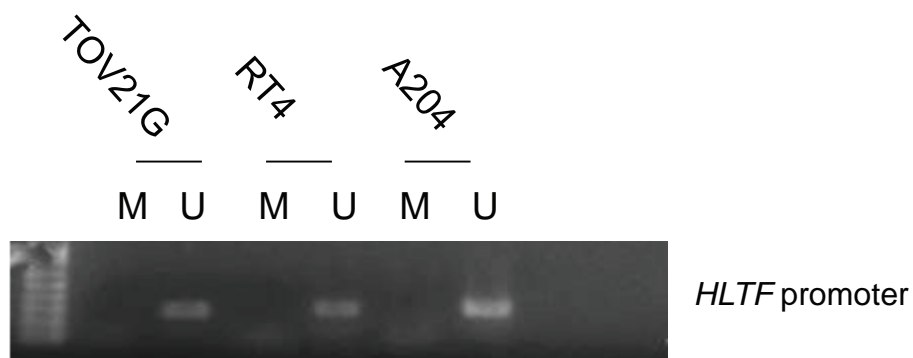
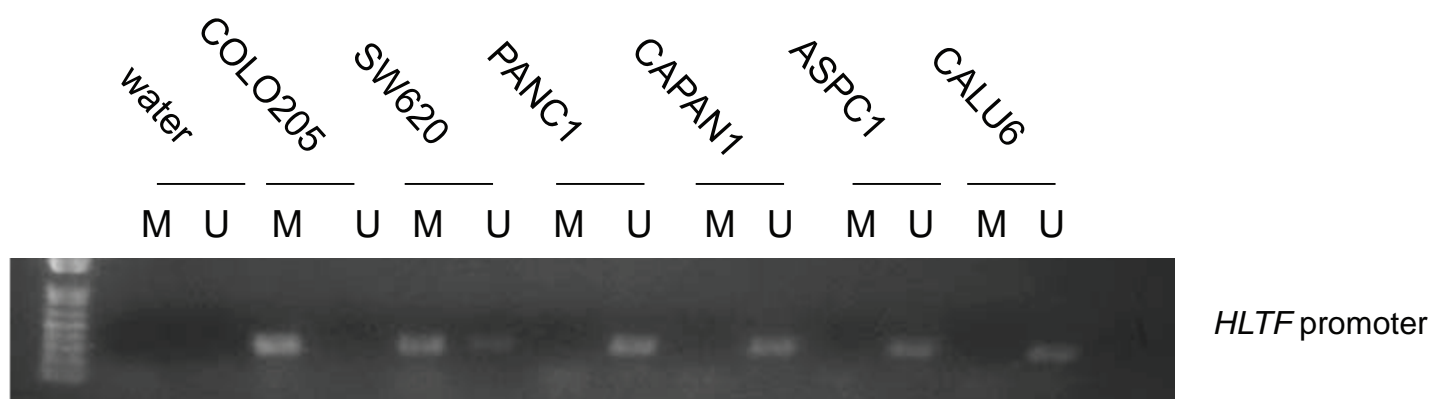
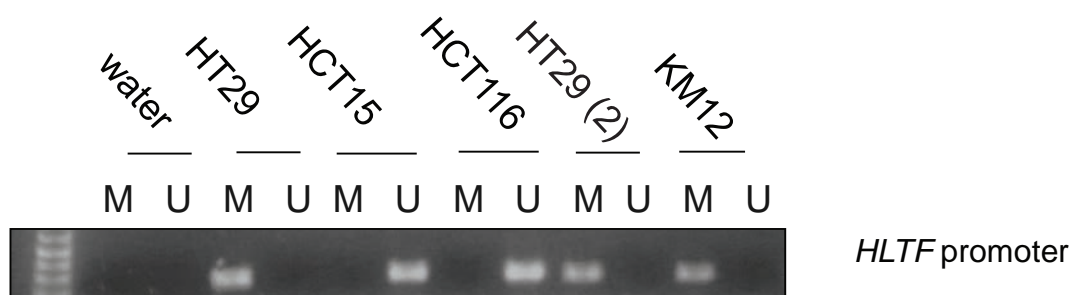
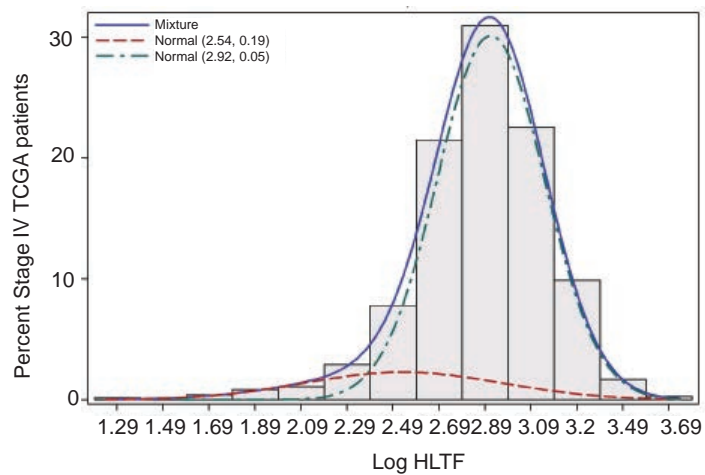
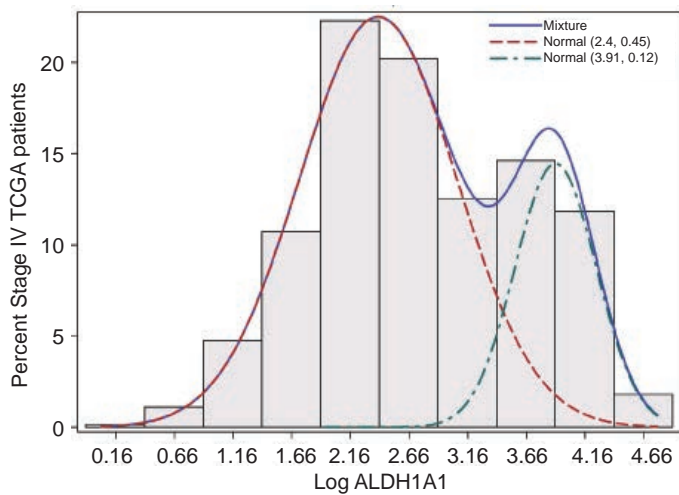
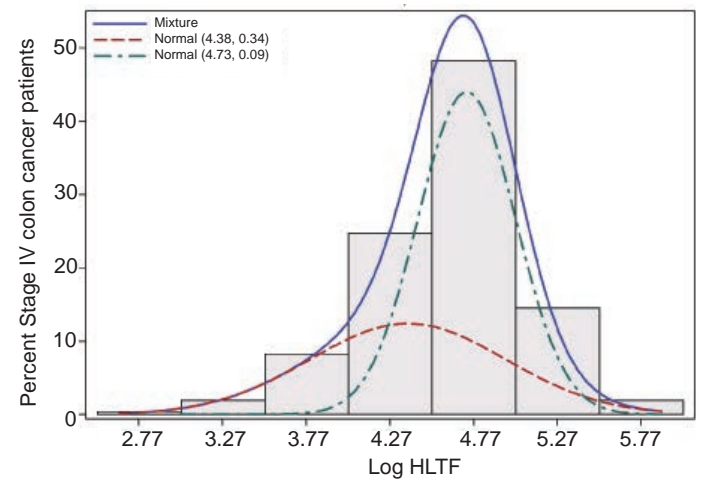
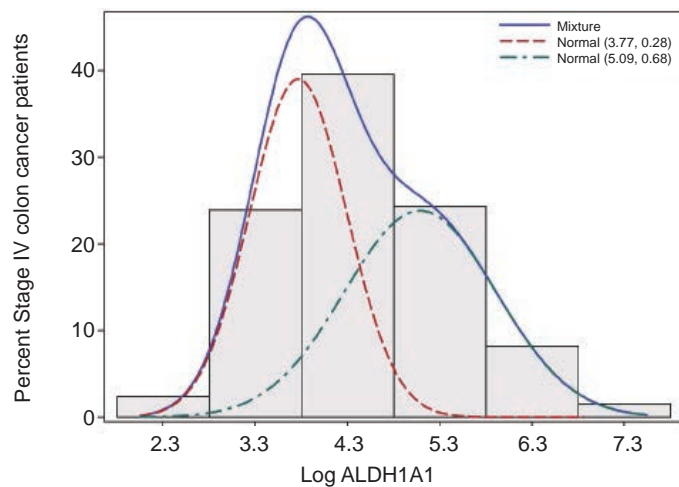


Figure S6. Methylation-specific PCR of the *HLTF* promoter in the indicated cell lines. M, methylated; U, unmethylated.

A



B



C

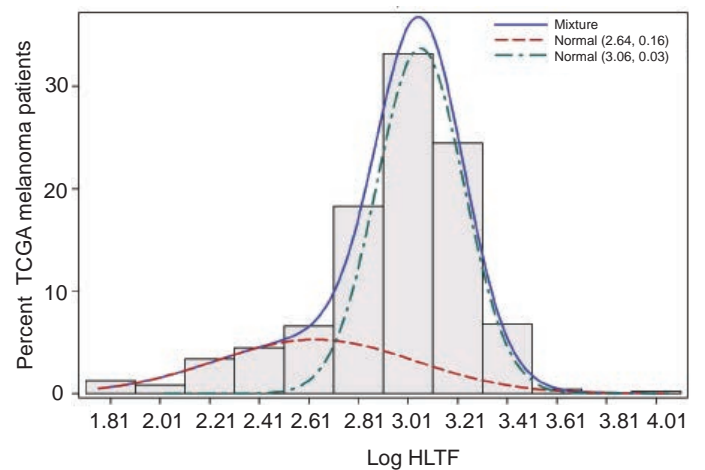
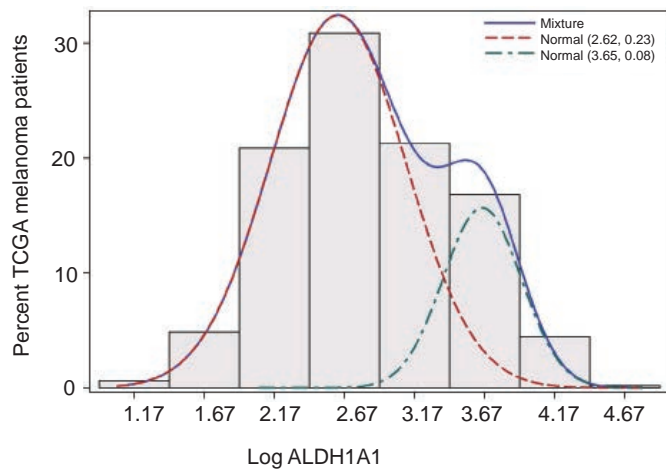


Figure S7. Histograms of expression of ALDH1A1 and HLTF. **(A)** TCGA stage IV tumors with >25 samples (N=718); **(B)** stage IV colon cancers from GSE41258, (n=255) **(C)** TCGA melanoma stage I-IV patients, (N=461). Black line, mixture model; red line, low expression; green line, high expression