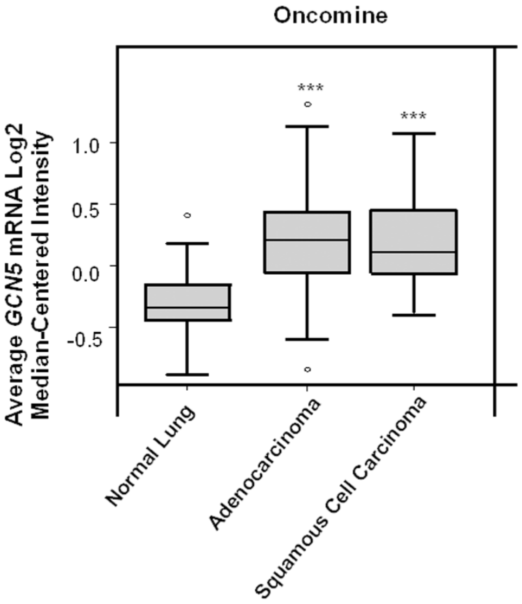

Figure S1. *GCN5* mRNA levels are upregulated in human NSCLC tissues. *GCN5* mRNA expression data from Oncomine [38] was compared between human adjacent normal lung (n = 65), lung adenocarcinoma (n = 45) and lung squamous cell carcinoma (n = 27) tissues, as depicted by a box-and-whisker plot. Symbols refer to ***$P < 0.001$.

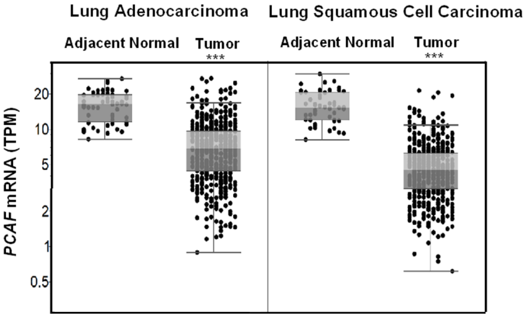

Figure S2. *PCAF* mRNA levels are not upregulated in human NSCLC tissues. Public repositories of TCGA were analyzed for *PCAF* mRNA levels in human adjacent normal lung (n = 59) and lung adenocarcinoma (n = 517) as well as adjacent normal lung (n = 51) and lung squamous cell carcinoma (n = 501) tissues. Symbols refer to ***$P < 0.001$.

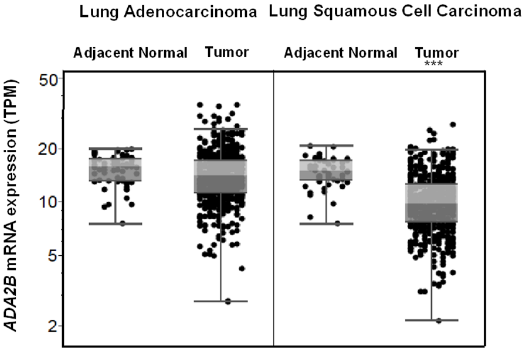

Figure S3. *ADA1B* mRNA levels are not upregulated in human NSCLC tissues. Public repositories of TCGA were analyzed for *ADA2B* mRNA levels in human adjacent normal (n = 59) and lung adenocarcinoma (n = 517) as well as adjacent normal lung (n = 51) and lung squamous cell carcinoma (n = 501) tissues. Symbols refer to ***$P < 0.001$.

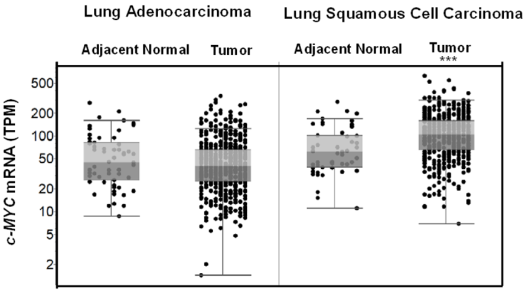

Figure S4. *c-MYC* mRNA levels are not upregulated in human NSCLC tissues. Pubic repositories of TCGA were analyzed for *c-MYC* mRNA levels in human adjacent normal lung (n = 59) and lung adenocarcinoma (n = 517) as well as adjacent normal lung (n = 51) and lung squamous cell carcinoma (n = 501) tissues. Symbols refer to ***$P < 0.001$.

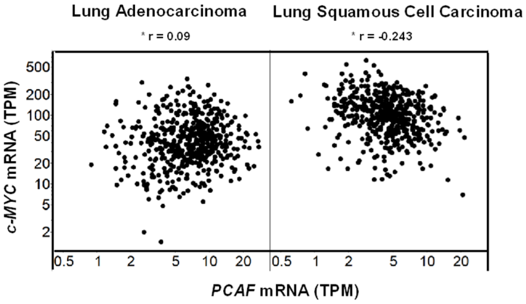

Figure S5. *PCAF* mRNA levels are not associated with *c-MYC* in human NSCLC tissues. TCGA repositories were analyzed for associations between *PCAF* and *c-MYC* mRNA levels in human lung adenocarcinoma and squamous cell carcinoma tissues. Symbols refer to *$P < 0.05$ and ***$P < 0.001$.

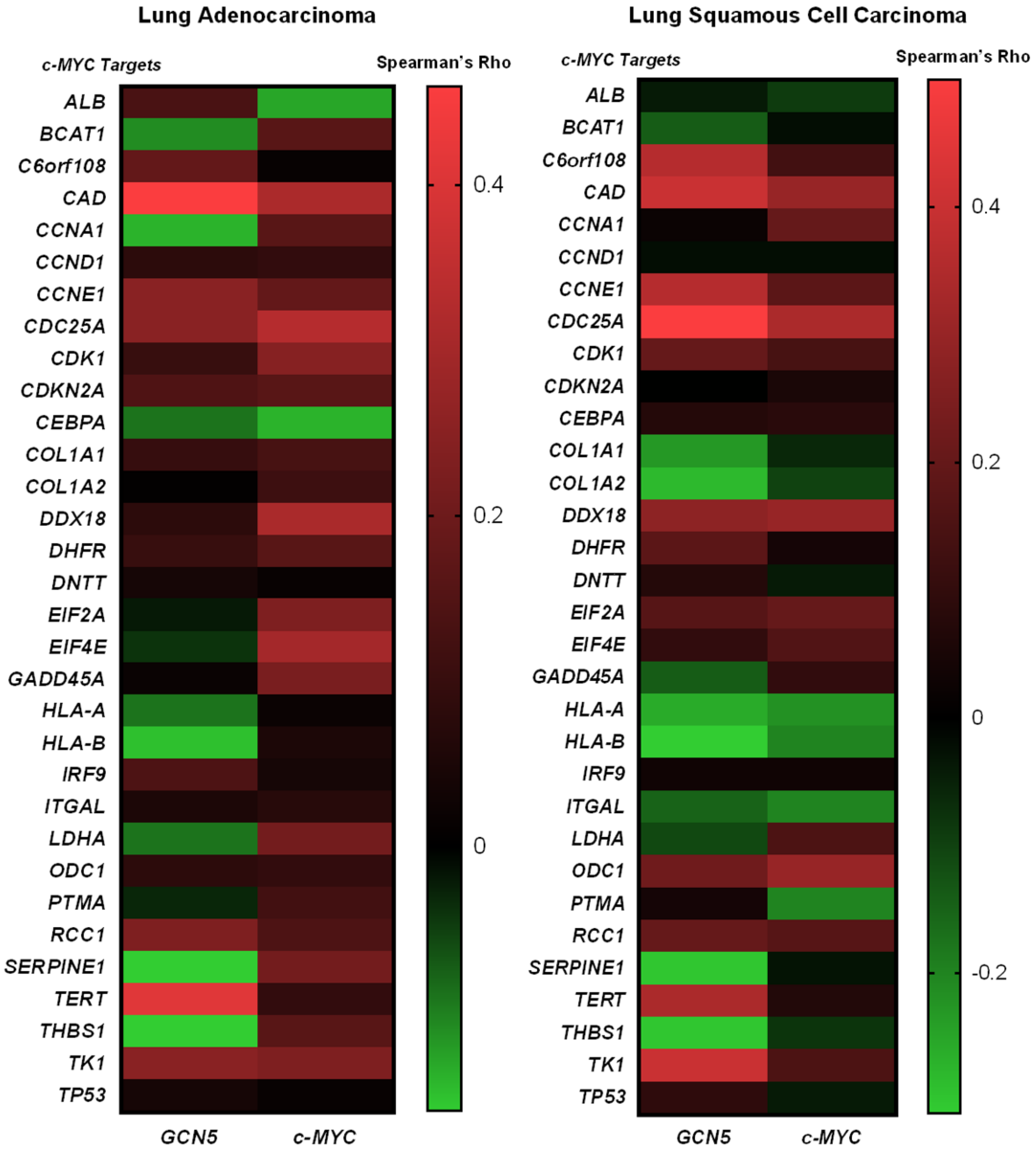

Figure S6. Associations between *c-MYC* target genes and *GCN5* or *c-MYC* mRNA levels in human NSCLC tissues. Associations between *GCN5* and *c-MYC* mRNA levels in human lung adenocarcinoma and lung squamous cell carcinoma tissues are depicted using a heatmap representing negative (green) versus positive (red) associations.

Table S1. Known *c-MYC* target genes associated with both *GCN5* and *c-MYC* in human NSCLC tissues from TCGA repositories

A. Lung Adenocarcinoma (n = 517)

c-MYC Target	Gene 1	Spearman Rho	Gene 2	Spearman Rho	*p*-value
CAD	GCN5	0.462	c-MYC	0.312	0
CCNE1	GCN5	0.254	c-MYC	0.176	4.6e-009
CDC25A	GCN5	0.251	c-MYC	0.333	6.7e-009
CDK1	GCN5	0.103	c-MYC	0.244	0.02
CDKN2A	GCN5	0.143	c-MYC	0.162	0.001
CEBPA	GCN5	-0.0878	c-MYC	-0.139	0.046
COL1A1	GCN5	0.0978	c-MYC	0.126	0.03
DHFR	GCN5	0.104	c-MYC	0.160	0.02
SERPINE1	GCN5	-0.162	c-MYC	0.211	0.00021
TERT	GCN5	0.414	c-MYC	0.0923	0
TK1	GCN5	0.247	c-MYC	0.234	1.1e-008

B. Lung Squamous Cell Carcinoma (n = 501)

c-MYC Target	Gene 1	Spearman Rho	Gene 2	Spearman Rho	*p*-value
C6orf108	GCN5	0.363	c-MYC	0.128	0
CAD	GCN5	0.401	c-MYC	0.299	0
CCNE1	GCN5	0.360	c-MYC	0.175	0
CDC25A	GCN5	0.455	c-MYC	0.337	0
CDK1	GCN5	0.215	c-MYC	0.138	1.2e-006
COL1A2	GCN5	-0.276	c-MYC	-0.107	3.5e-010
DDX18	GCN5	0.283	c-MYC	0.322	1.09e-010
EIF2A	GCN5	0.171	c-MYC	0.182	0.00012
EIF4E	GCN5	0.097	c-MYC	0.162	0.030
HLA-A	GCN5	-0.255	c-MYC	-0.217	6.61e-009
HLA-B	GCN5	-0.310	c-MYC	-0.204	1.20e-012
ITGAL	GCN5	-0.153	c-MYC	-0.181	0.000570
ODC1	GCN5	0.218	c-MYC	0.268	8.63e-007
RCC1	GCN5	0.202	c-MYC	0.169	4.92e-006
TK1	GCN5	0.355	c-MYC	0.152	2.22e-016

Public repositories of TCGA were analyzed for significant associations between *GCN5* and *c-MYC* to known *c-MYC* target genes (Refer to **Figure 1D**).

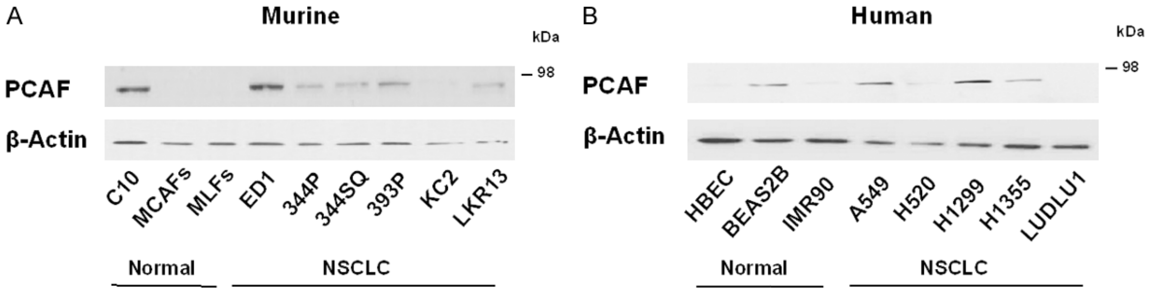

Figure S7. PCAF protein levels are not upregulated in NSCLC cell lines. Steady state levels of PCAF were analyzed in (A) murine and (B) human immortalized epithelial and fibroblast lung controls and NSCLC cell lines. Immunoblotting was performed using an anti-PCAF antibody. β-Actin served as a loading control in these studies.

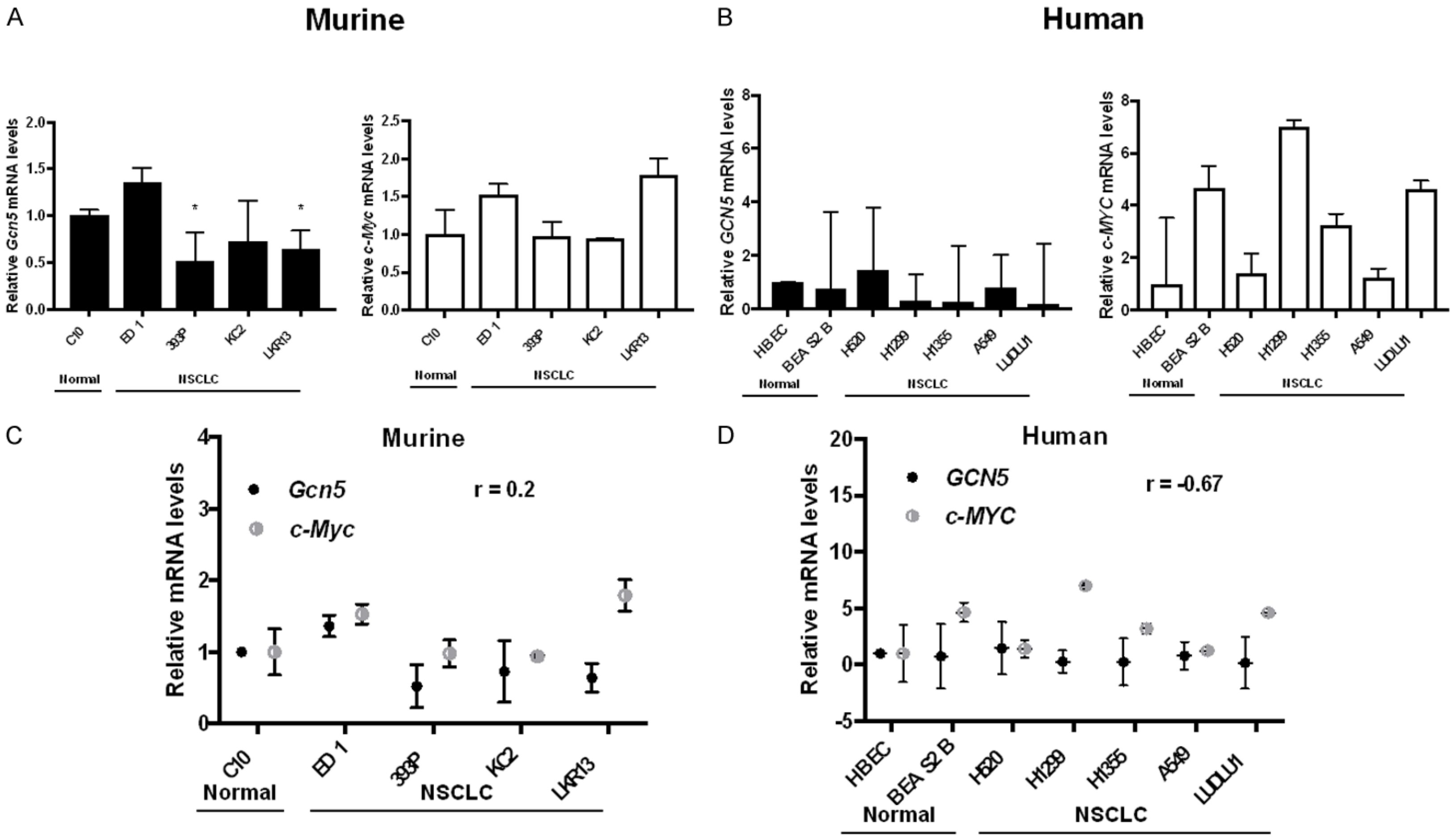

Figure S8. *GCN5* and *c-MYC* mRNA levels are weakly associated. Expression of *GCN5* and *c-MYC* mRNA was analyzed by qRT-PCR assays for (A) murine and (B) human normal immortalized epithelial and *NSCLC* cell lines. *GCN5* and *c-MYC* mRNA expression was quantified relative to *GAPDH* and normalized to immortalized epithelial lung control C10 in murine cells and immortalized epithelial lung control HBEC in human cells. The association between *GCN5* and *c-MYC* mRNA levels were plotted and compared for (C) murine and (D) human lung cell lines.

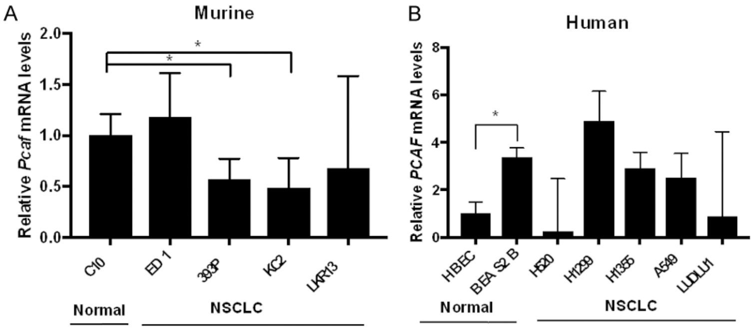

Figure S9. Lack of clear, consistent changes in *PCAF* mRNA levels when comparing normal lung and NSCLC cell lines. Expression of *PCAF* mRNA was analyzed by qRT-PCR assays for (A) murine and (B) human normal immortalized epithelial and NSCLC cell lines. *PCAF* mRNA expression was quantified relative to *GAPDH* and normalized to immortalized epithelial lung control C10 in murine cells and immortalized epithelial lung control HBEC in human cells.

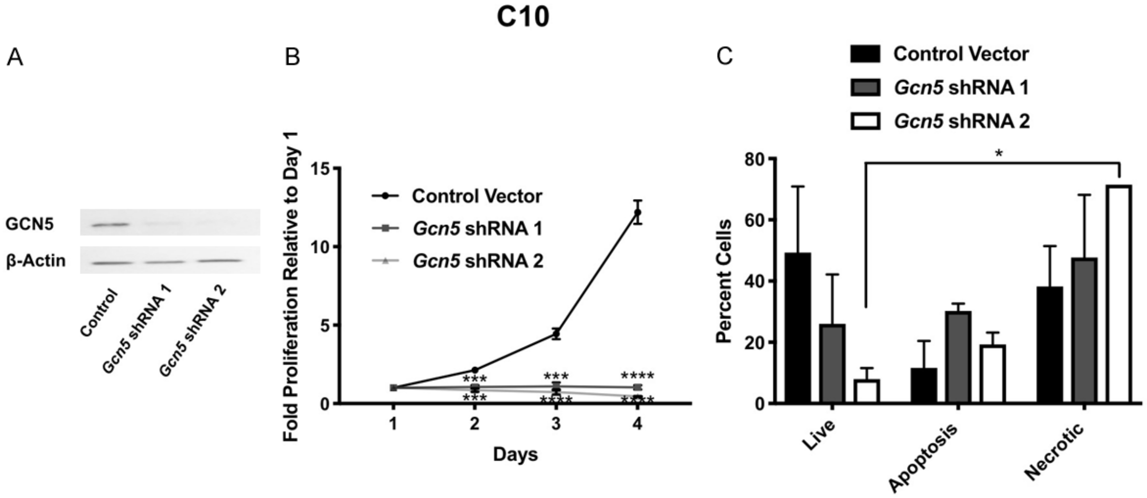

Figure S10. Reduction of GCN5 represses cell proliferation and increases the population of necrotic cells in normal immortalized epithelial cells. A. Confirmation of stable endogenous GCN5 knockdown by two independent shRNAs introduced into C10 murine normal immortalized epithelial lung cells. Immunoblotting was performed using an anti-GCN5 antibody. β-Actin served as a loading control. B. Proliferation of murine C10 cells with stable knockdown of GCN5 by two independent shRNAs was monitored over 4 days. Proliferation rate was normalized to day 1. C. Apoptosis assays were performed in the C10 cell line with stable knockdown of GCN5 by shRNAs 3 days after seeding cells. Percentage of live, apoptotic, and necrotic cells are shown. Symbols refer to $^{*}P < 0.05$, $^{***}P < 0.001$, and $^{****}P < 0.0001$.

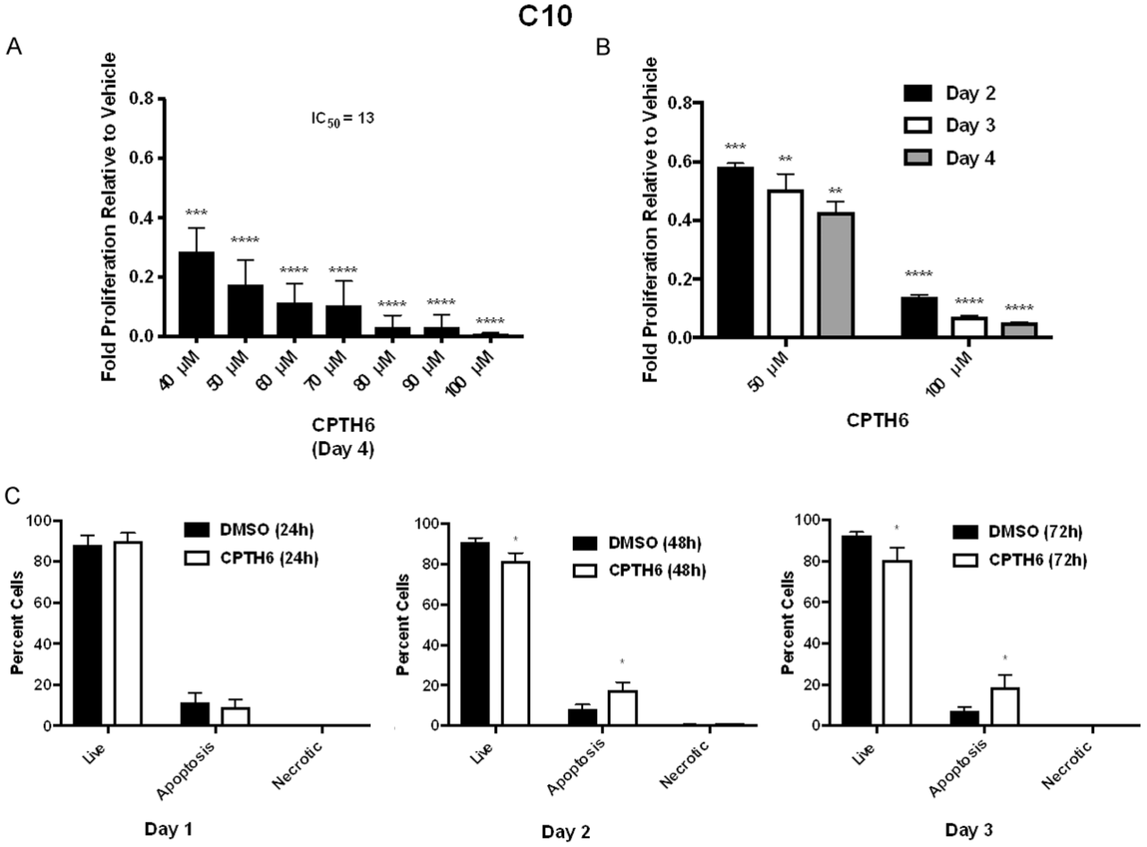

Figure S11. Inhibition of GCN5 activity by CPTH6 treatment represses cell proliferation and increases apoptosis in normal immortalized epithelial cells. A. Proliferation of C10 murine normal immortalized epithelial lung cells at multiple doses (40-100 mM) of CPTH6 treatment was normalized to proliferation of vehicle (DMSO) treated cells after 4 days. B. Proliferation of C10 cells at 50 mM and 100 mM of CPTH6 treatment was normalized to proliferation of vehicle control after 2, 3 or 4 days of treatment. C. Apoptosis assays were performed using 100 mM of CPTH6 or vehicle control and analyzed after 1, 2, or 3 days of treatment. Percentage of live, apoptotic and necrotic cells are shown. Symbols refer to **P* < 0.05, ***P* < 0.01, ****P* < 0.001, and *****P* < 0.0001.