SUPPLEMENTAL DATA

Genotypes	rs121434569*	p.Thr790Met
PC9ER1	C/C	no
PC9ER3	C/C	no
PC9ER4	C/C	no
HCC827ER9	C/C	no

*Mutation information is as following.

SNP IN dbSNP	rs121434569
Position in Cutted Seq.	162347
Position in NC_000007	55249071
Reference Allele (A1)	C
The Other Allele (A2)	T
SNP Property (NM_005228.3)	EXON20, missense
base on db cDNA (NM_005228.3)	c.2369C>T
base on db protein (NP_005219.2)	p.Thr790Met
5' Flanking reference seq	ctccaccgtgcagctcatca
SNP	C/T
3' Flanking reference seq	gcagctcatgcccttcggct

Table S1. Determination of EGFR T790M mutation by SNP sequence in the indicated cells. All cells were EGFR T790M negative.

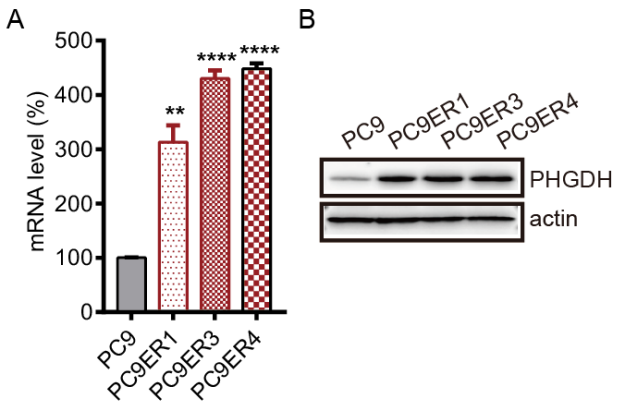

Figure S1. Level of PHGDH in PC9 and PC9 erlotinib resistant cells were determined by qRT-PCR (A) and immunoblotting (B) respectively. Results were shown in mean ± SEM of triplicates. **, $p < 0.01$; ****, $p < 0.0001$.

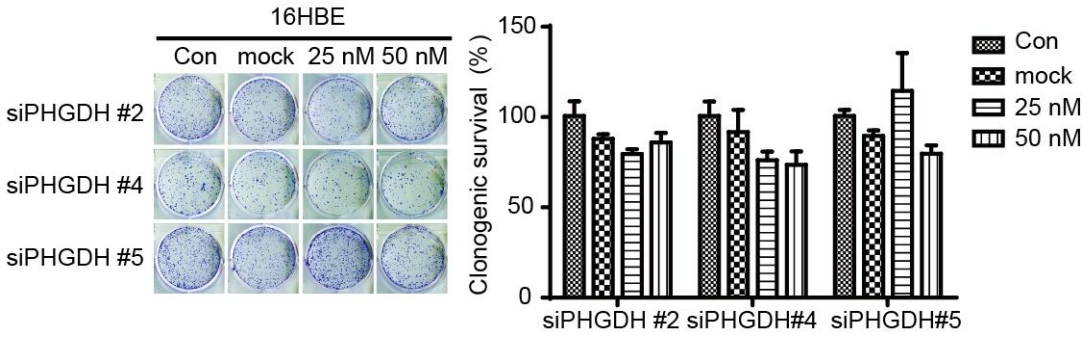

Figure S2. Clonogenic assays. 16HBE cells were transfected with siPHGDH candicates, then the clonogenic proliferation was analyzed after 14 days incubation.

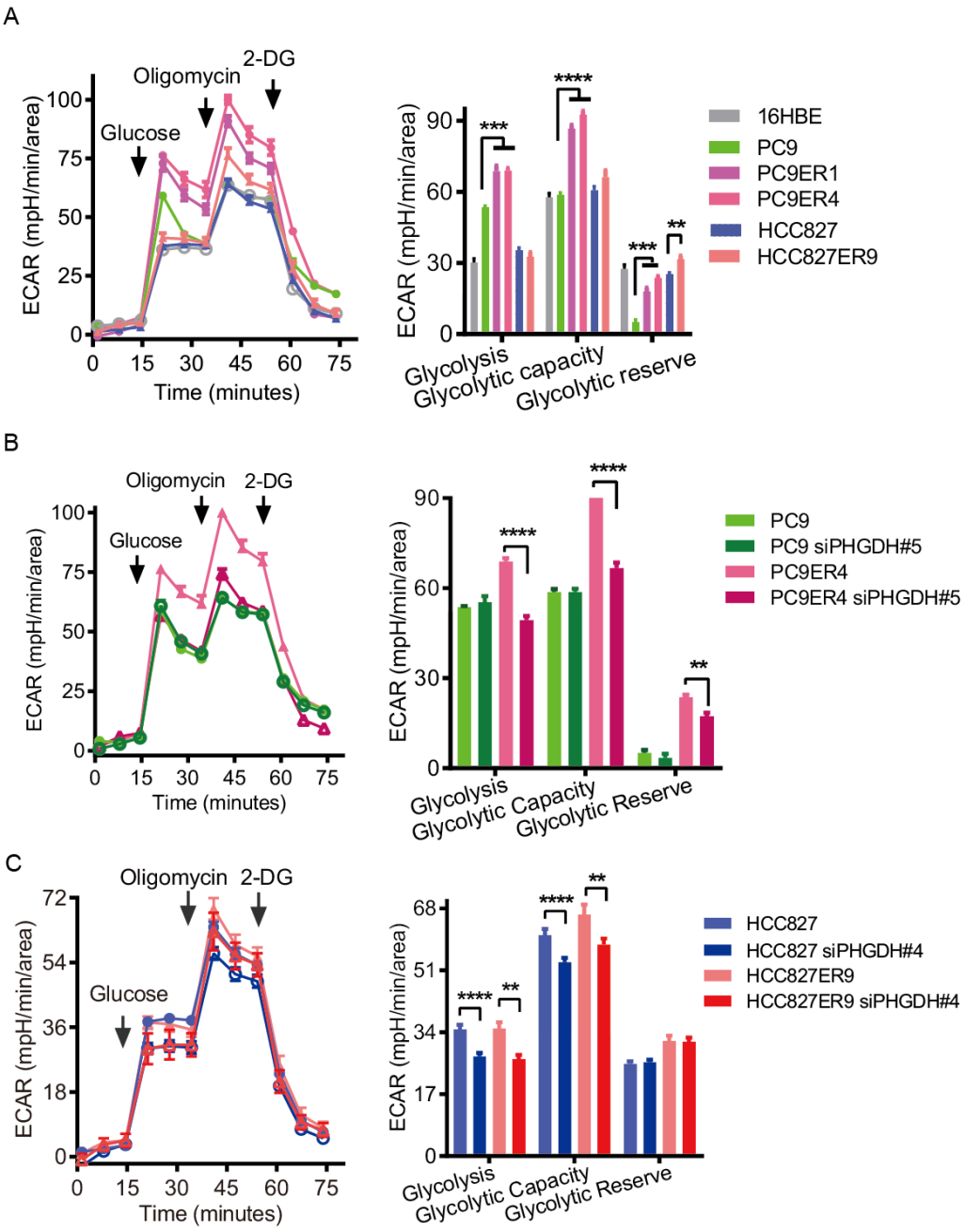

Figure S3. Downregulation of PHGDH suppressed the metabolic activity in the erlotinib resistant cells. (A) Extracellular acidification rates (ECAR) normalized to cellular confluency (area) showed enhanced glycolysis level in erlotinib resistant cells, PC9ER1, PC9ER4 and HCC827ER9 compared to their parental PC9 and HCC827 cells respectively. Low activity of glycolysis was observed in 16HBE cells. (B and C) Cells were transfected with 20 nM siPHGDH#5 or siPHGDH#4 for 48 h, the ECAR level was analyzed by glycolysis stress kit. Error bars represent mean ± SEM of triplicates. **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$.

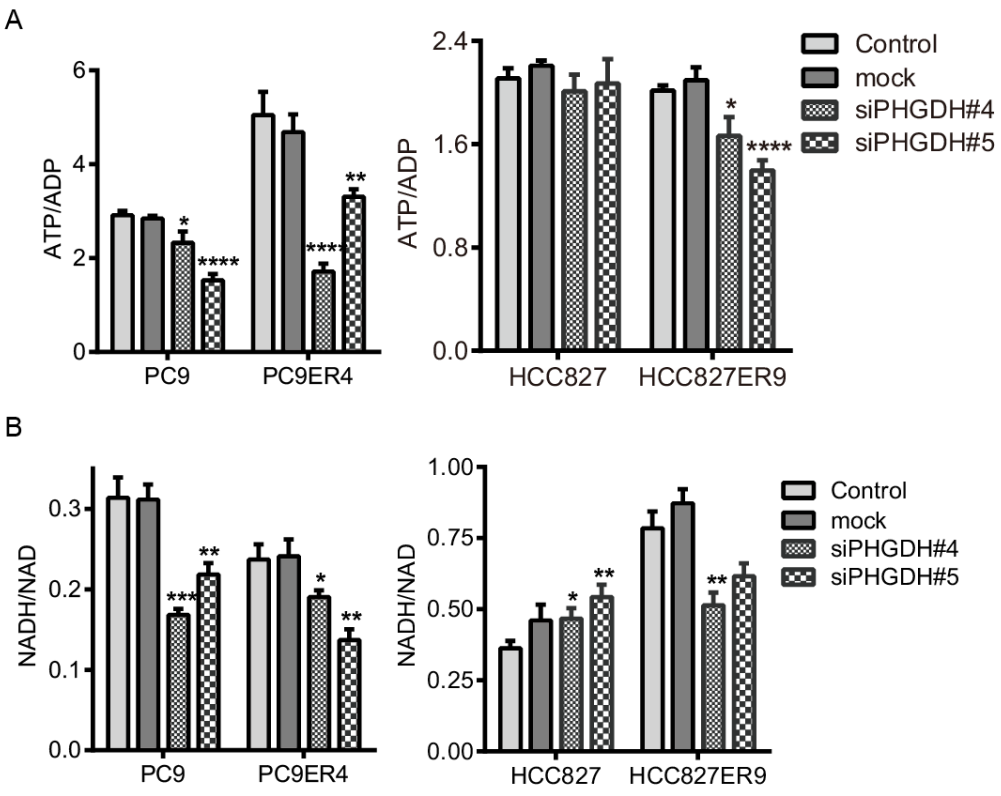

Figure S4. (A) Intracellular ATP/ADP ratio was quantified by LC-MS/MS after cells were transfected with 25 nM siPHGDH#4 and siPHGDH#5 for 72 h. (B) Intracellular NADH/NAD ratio was quantified by LC-MS/MS after cells were transfected with 25 nM siPHGDH#4 and siPHGDH#5 for 72 h. Error bars represent mean ± SEM of triplicates. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$.

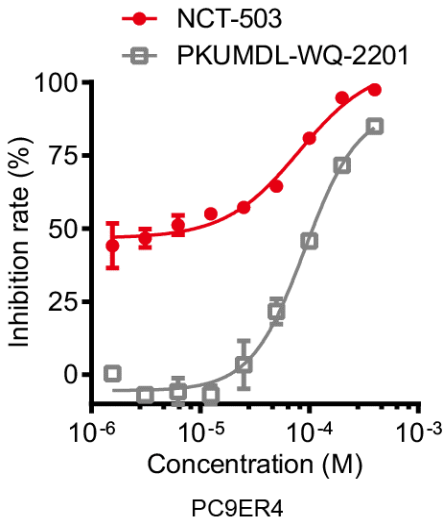

Figure S5. CCK8 assays. The PC9ER4 cells were dosed with NCT-503 or PKUMDL-WQ-2201 at various concentrations for 72 h. Error bars show as mean ± SEM of triplicates.

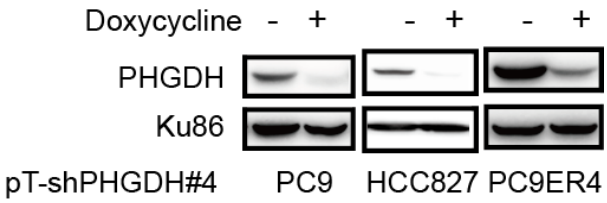

Figure S6. Immunoblotting of PHGDH and Ku86 after cells were incubated with 1 μg/mL doxycycline for 72 h.

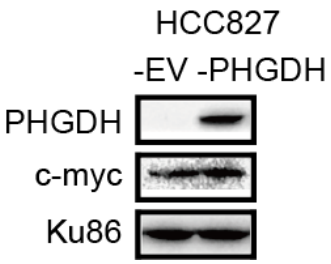

Figure S7. Immunoblotting of PHGDH, c-myc and Ku86 after cells were infected with c-myc tagged PHGDH lentivirus in HCC827 cells. EV, empty vector as infect control.