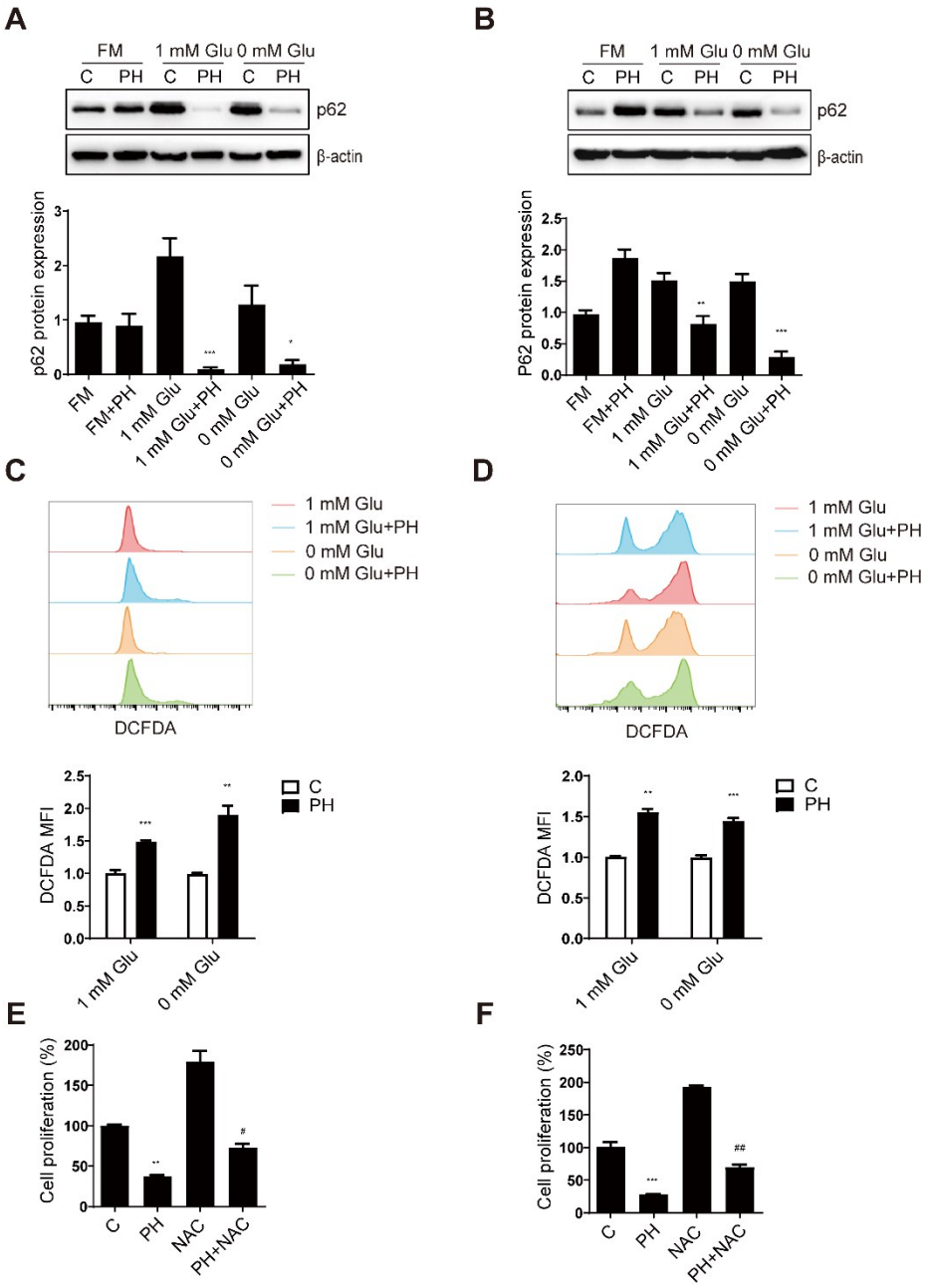

Figure S1. Phloretin triggered oxidative stress in breast cancer cells cultured in glucose-limiting media. (A-B) Immunoblot analyses of p62 expression in MCF7 (A) and MDA-MB-231 cells (B) exposed to phloretin under full media and 1 mM glucose and 0 mM glucose media. The results from quantitative analyses were shown in the lower panels. **p<0.01, ***p<0.001 1 mM Glu+PH compared with 1 mM Glu, *p<0.05, ***p<0.001 0 mM Glu+PH compared with 0 mM Glu. (C-D) Flow cytometry analyses of ROS levels in MCF7 (C) and MDA-MB-231 (D)

cells stained with DCFH-DA after phloretin treatment in 1 mM or 0 mM glucose media. Quantitative analyses of ROS levels were shown in lower panels, respectively. **p<0.01, ***p<0.001 PH compared with vehicle. (E-F) The effect of co-treatment with NAC (10 mM) and phloretin on MCF7 (E) and MDA-MB-231 (F) cell proliferation was analyzed by CCK8 assay. **p<0.01, ***p<0.001 PH compared with control, #p<0.05, ##p<0.01 PH+NAC compared with PH.

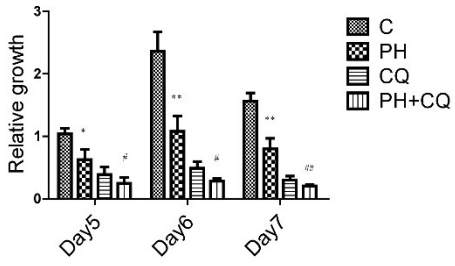

Figure S2. MDA-MB-231 cells were treated with phloretin and CQ for the time intervals as indicated. CCK8 assay was performed. *p<0.05, **p<0.01 PH versus control, #p<0.05, ##p<0.01 PH+CQ versus PH.

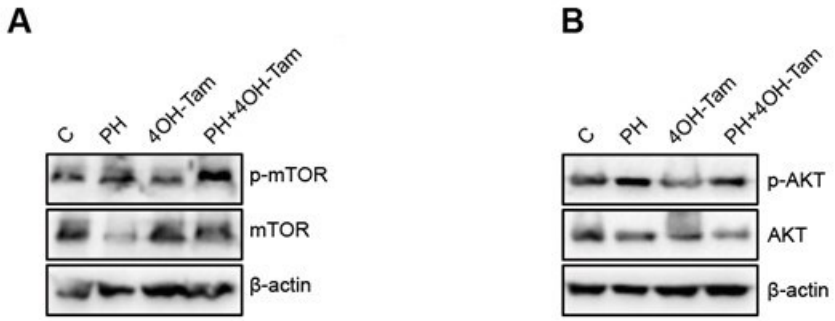

Figure S3. PH inhibited autophagy by modulating mTOR/AKT signaling in MCF7 re cells. (A, B) Immunoblot analyses of p-mTOR, mTOR, p-AKT, and AKT expression in MCF7 re cells treated with 4OH-Tam in the presence or absence of PH.

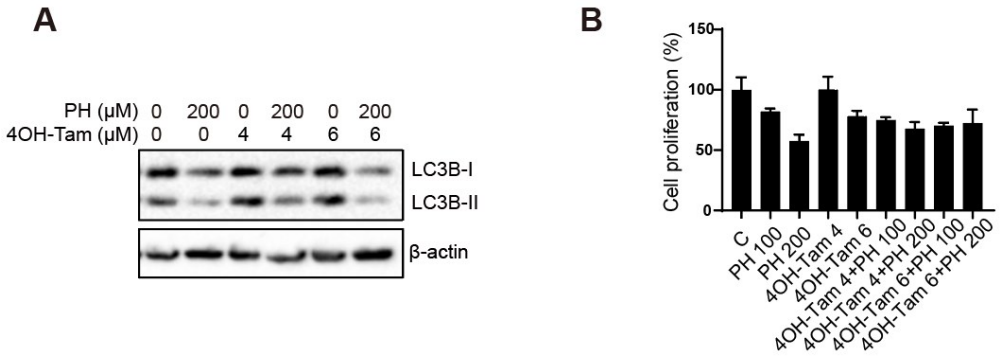

Figure S4. PH failed to enhance sensitivity of MCF7 parental cells to 4OH-Tam in 1 mM glucose-limiting media. (A) Immunoblot analyses of LC3B-II expression in MCF7 parental cells treated with 4OH-Tam in the presence or absence of PH. (B) MCF7 parental cells were treated with PH (100, 200 μM), 4OH-Tam (4, 6 μM) or their combinations in 1 mM Glu media and cell proliferation was measured by the CCK-8 assay.

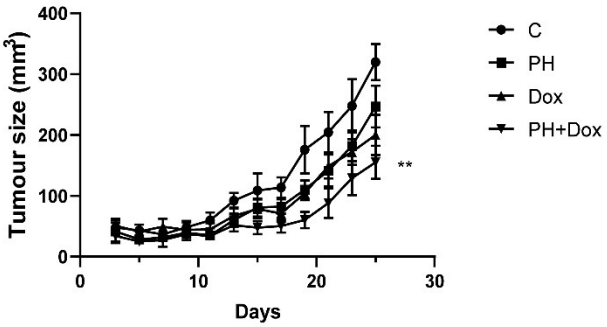

Figure S5. PH displayed a synergetic inhibitory effect with Dox on the growth of subcutaneous xenografts (MDA-MB-231 cells) in Balb/c nude mice. ***p<0.01* compared with control.

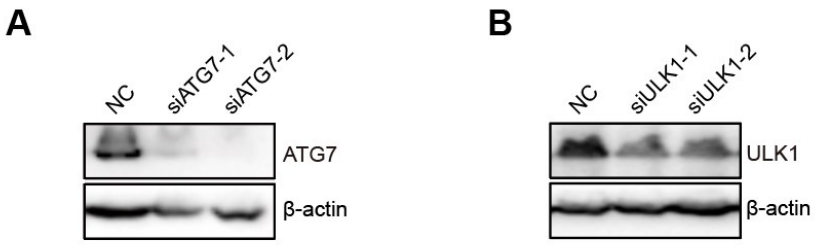

Figure S6. Validation of ATG7 and ULK1 knockdown in MCF7 re cells transfected with siATG7, siULK1 or their scrambled control.