Figure S1. Correlation between SVCT2 expression and clinical characteristics. SVCT2 expression levels of patients with PDAC in different clinical stages is shown using a histogram (left). The Kaplan-Meier method was used to analyze the association between SVCT2 expression and disease-free survival rate of patients with pancreatic cancer (right). Data were collected from TCGA datasets and are shown as the mean ± standard error of the mean. ***P<0.001. SVCT2, sodium-dependent VC transporter 2.

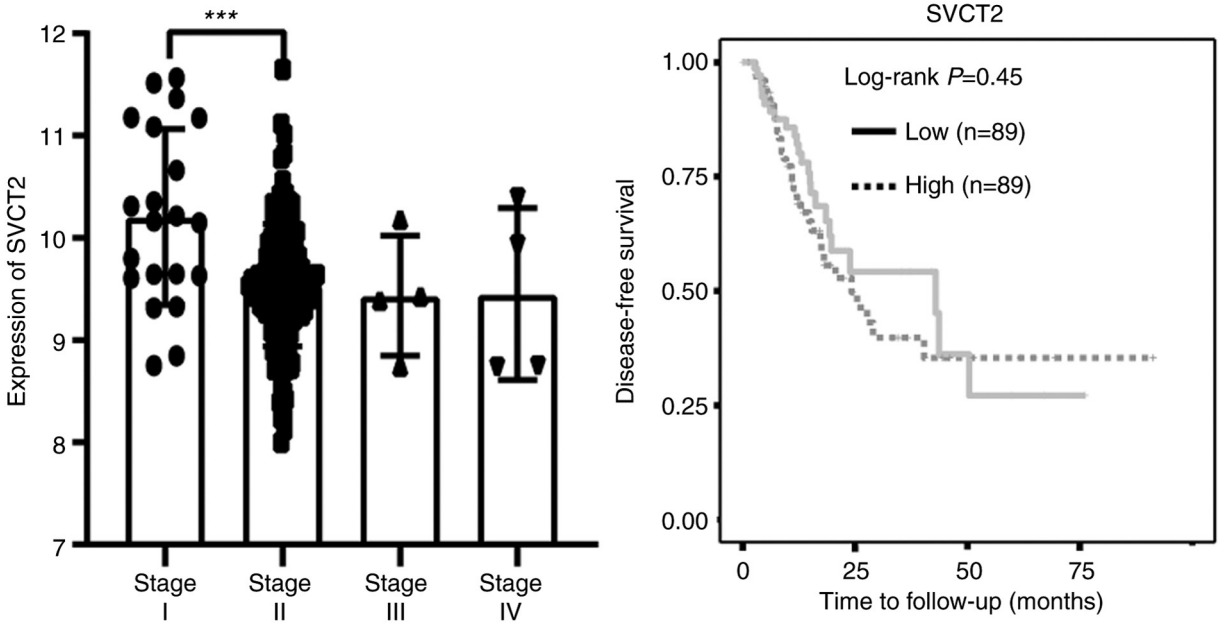

Figure S2. VC shows no potent killing activity when applied to human normal cells. peripheral blood mononuclear cells were treated with 4 mM VC for 48 h, and then examined by flow cytometry for assessment of apoptosis. Data are shown as the mean ± standard error of the mean of three independent experiments. VC, vitamin C; 7-AAD, 7-aminoactinomycin D.

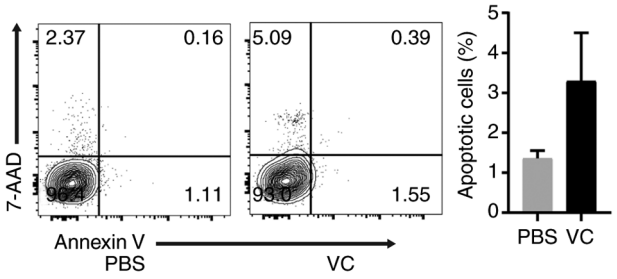

Figure S3. siRNA-mediated knockdown of TET2 and PHLPP2 in Capan-1 and PANC-1 cells lines. (A) Quantitative changes in the mRNA expression levels of TET2 were detected by RT-qPCR 48 h post-transfection. (B) Quantitative changes in the mRNA expression levels of PHLPP2 were detected by RT-qPCR 48 h post-transfection. Data are presented as the mean ± standard error of the mean of three independent experiments. ***P<0.001. PHLPP2, PH domain leucine-rich repeat protein phosphatase 2; si, small interfering RNA; TET2, ten-eleven translocation 2; NC, negative control; RT-qPCR, reverse transcription-quantitative PCR.

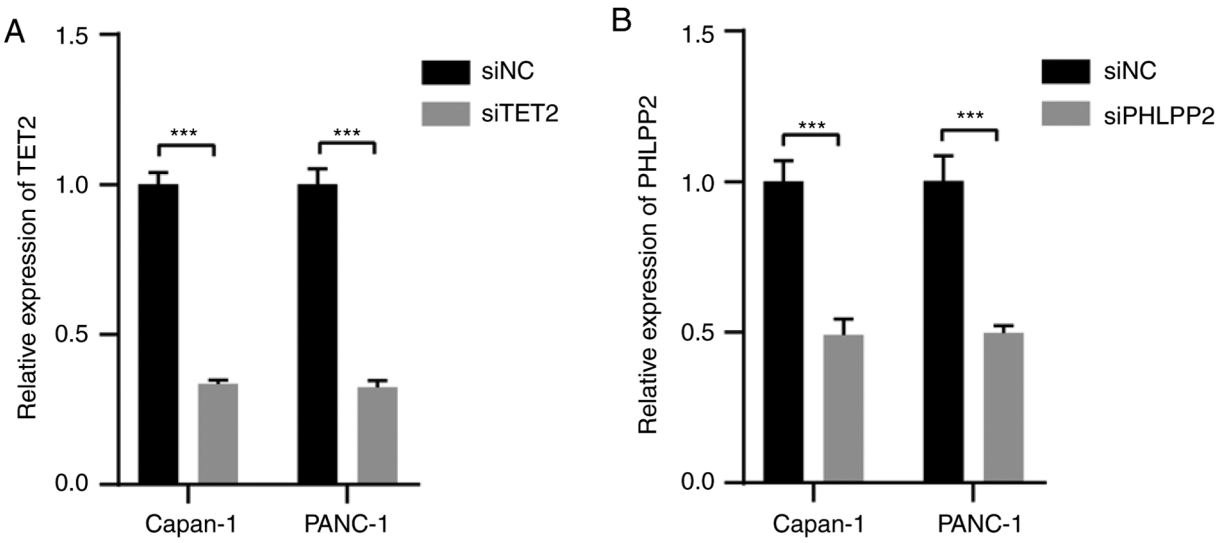

Figure S4. VC-induced cell necrosis relies on PHLPP2 only in Capan-1 cells. Following PHLPP2-knockdown, Capan1 or PANC-1 cells were treated with 4 mM VC for 48 h, and then the percentages of necrotic cells were examined by flow cytometry. Data were shown as mean ± standard error of the mean of three independent experiments. *P<0.05, ***P<0.001. VC, vitamin C; PHLPP2, PH domain leucine-rich repeat protein phosphatase 2; NC, negative control; si, small interfering RNA.

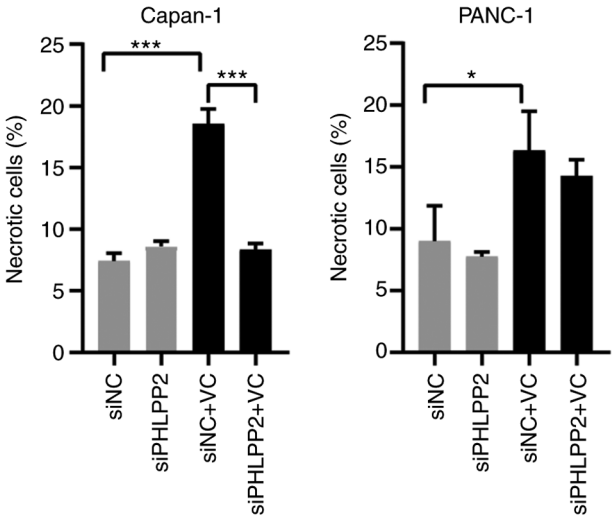

Figure S5. Correlation between the expression of PHLPP2/TET2 and C-Raf pS338. The correlation between the expression of PHLPP2/TET2 and C-Raf pS338 was determined using Pearson's correlation analysis. Data were collected from the Cancer Genome Atlas datasets and analyzed by R software. PHLPP2, PH domain leucine-rich repeat protein phosphatase 2; TET2, ten-eleven translocation 2; SVCT2, sodium-dependent VC transporter 2.

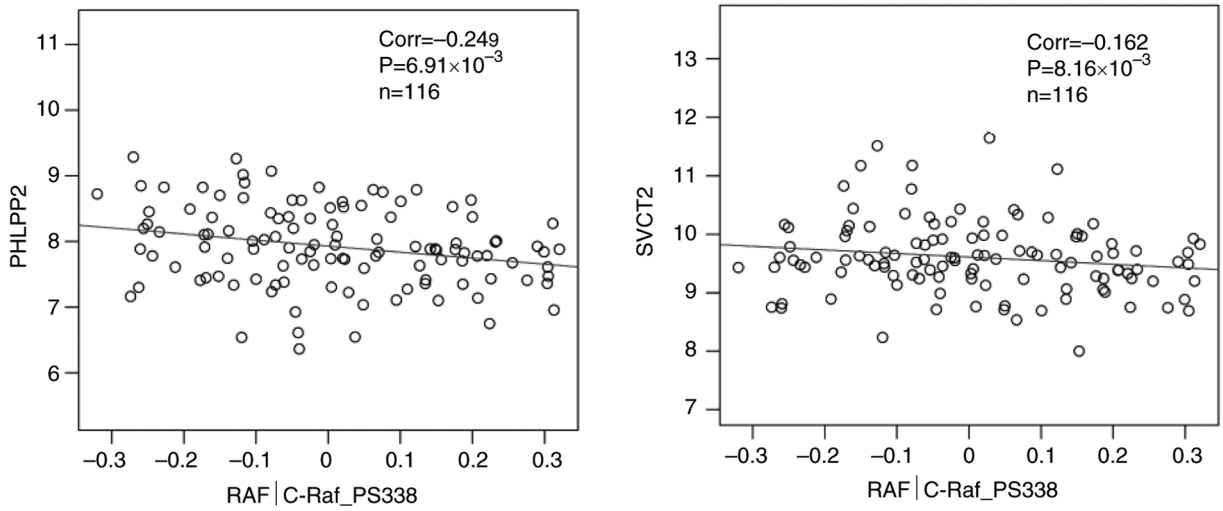

Table SI. Patient characteristics.

Characteristic	No. of patients (%)
Total	178
Age	
Range, years	35-88
Median, years	65
Sex	
Male	98 (55.1)
Female	80 (44.9)
Histology	
Pancreas-adenocarcinoma ductal type	147 (82.6)
Pancreas-colloid (mucinous non-cystic) carcinoma	4 (2.2)
Pancreas-undifferentiated carcinoma	1 (0.6)
Pancreas-adenocarcinoma-other subtype	25 (14.0)
Stage	
I	21 (11.8)
II	147 (82.6)
III	4 (2.2)
IV	4 (2.2)
Chemotherapy treatment	33 (18.5)
Radiotherapy treatment	43 (24.2)