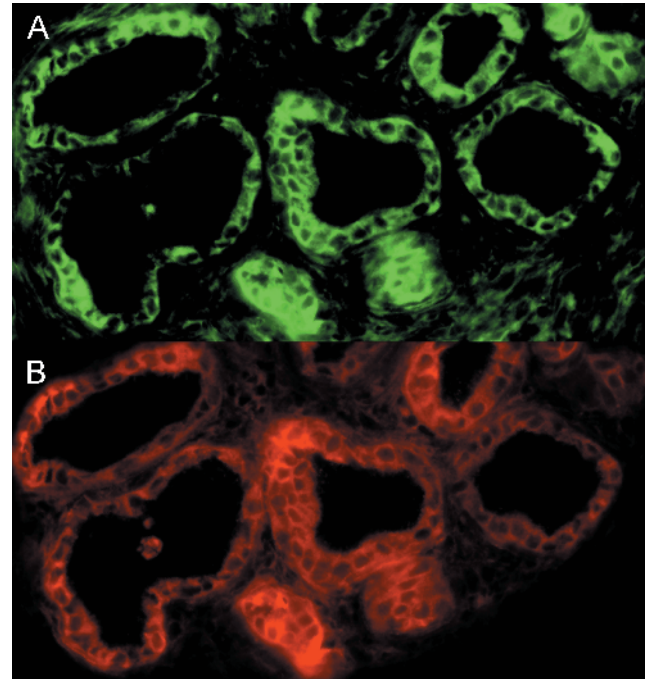
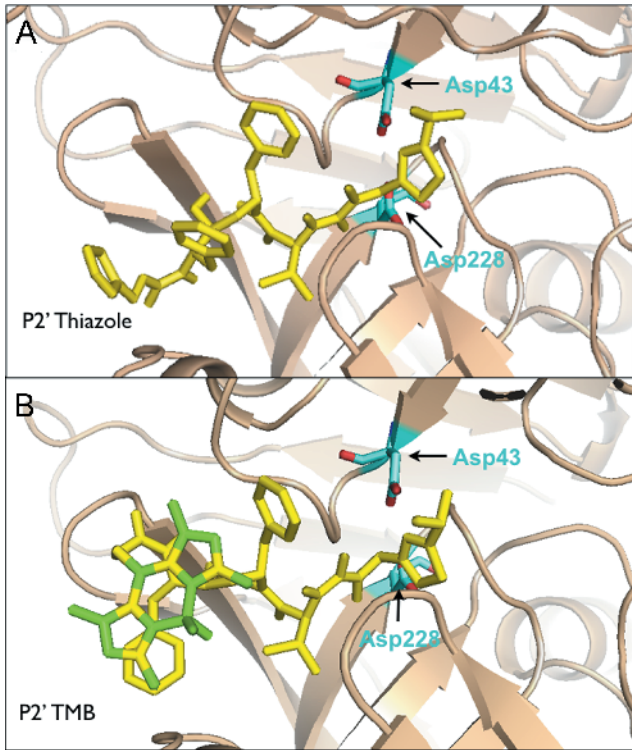
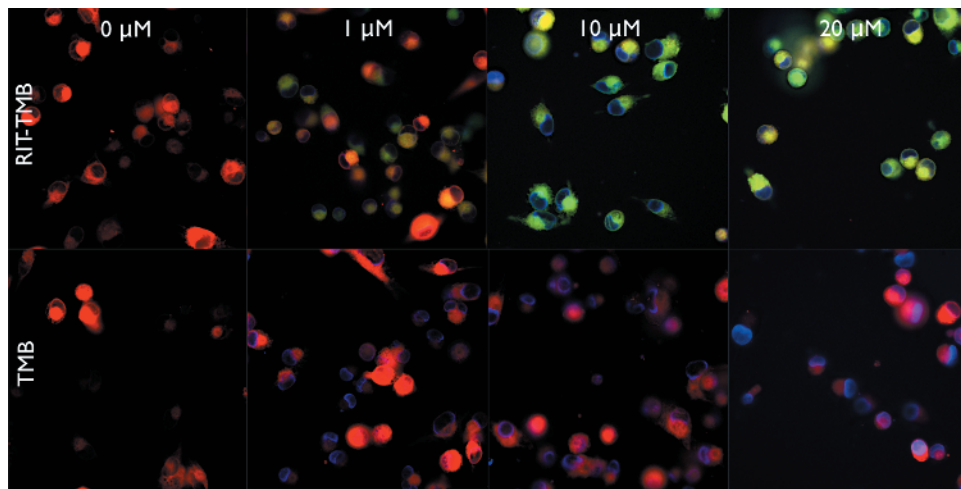


**Figure W1.** Synthesis and characterization of RIT-NH-Ac (**5**) and Ac-NH-RIT (**6**). (A) Synthetic schemes of **5** and **6**. (B) LC-MS analyses of purified of **5** and **6**. (C) Binding affinity data for **5** and **6** against human CTSE. (D) SPR binding data for the interaction of **5** with immobilized CTSE. Red and blue curves depict experimental data (two separate runs); best-fit models overlaid in black.



**Figure W2.** Modeling. Simulated docking of RIT (A) and RIT-TMB (B) with homology model of CTSE.

**Figure W3.** Immunofluorescent anti-CTSE/RIT-TMB double staining of tumor section excised from 10-week-old KRAS p53<sup>-/-</sup> model. (A) RIT-TMB (20  $\mu$ M RIT-TMB for 1 hour). (B) Anti-CTSE immunofluorescence.



**Figure W4.** PaCa-2 CTSE-mCherry cells incubated with RIT-TMB and TMB (fluorochrome only). CTSE-mCherry (red), RIT-TMB and TMB (green), and 4',6-diamidino-2-phenylindole (blue).

	Species	Comment	Western	mRNA
AsPC1	Human		ND	11.9
PANC1			0.3	2.9
PACA2			0.5	1
PACA2-CathE-mCherry		Transduced from PACA2	6.4	354396
PANC02	Mouse		0.5	ND
AH367		Kras <sup>+/+</sup> +Ink4a/Art <sup>-/-</sup>	0.5	ND

**Figure W5.** Relative quantification of CTSE protein and mRNA expression in PDAC cell lines.