



Supplementary Materials

Smart Design of Mitochondria-Targeted and ROS-Responsive CPI-613 Delivery Nanoplatform for Bioenergetic Pancreatic Cancer Therapy

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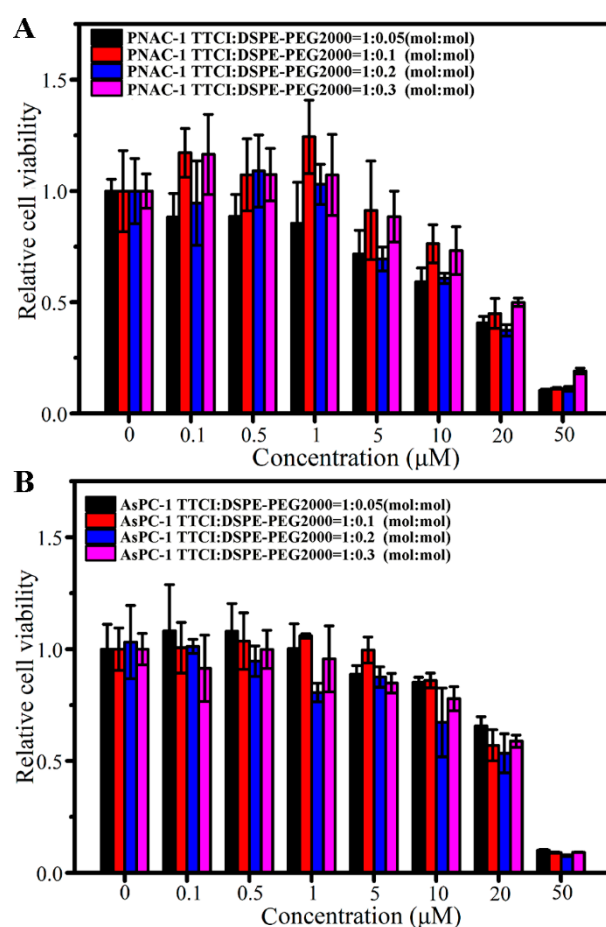


Figure S1. In vitro cytotoxicity of TTCl NPs constructed with different molar ratios of TTCl:DSPE-PEG2000 in PNAC-1 (A) and AsPC-1 (B) cells treated with various concentrations for 48 h. Data represent mean \pm SD ($n = 3$).

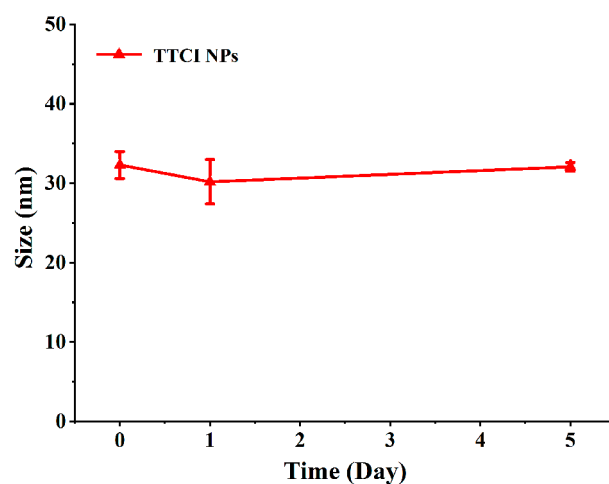


Figure S2. Mean particle sizes of TTCl NPs constructed with TTCl:DSPE-PEG2000 at a molar ratio of 1:0.2 at different time points (DLS at room temperature). Data represent mean \pm SD ($n = 3$).

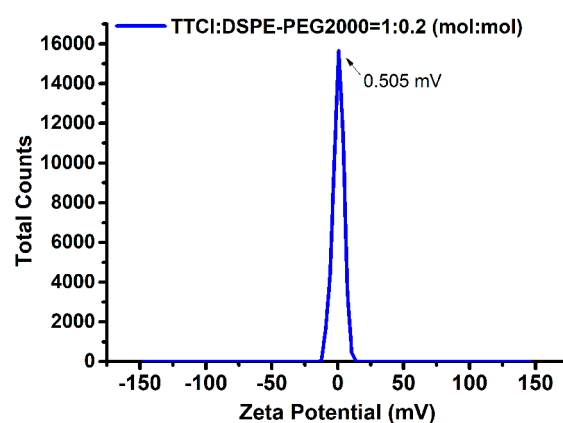


Figure S3. Zeta-potentials of TTCl NPs constructed with TTCl:DSPE-PEG2000 at a molar ratio of 1:0.2 (DLS at room temperature).

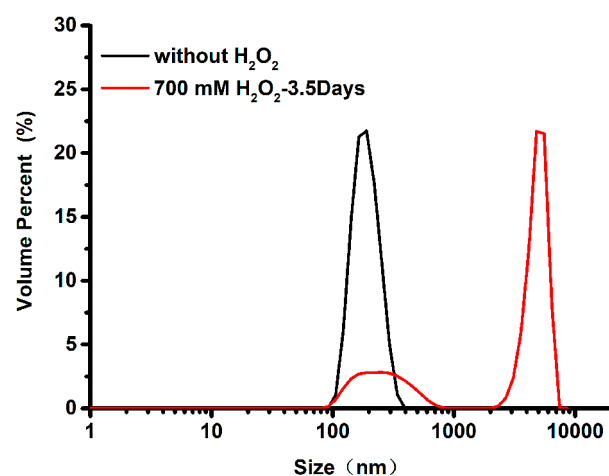


Figure S4. Size distribution of TTCh NPs after treatment with 700 mM H₂O₂ for different time.

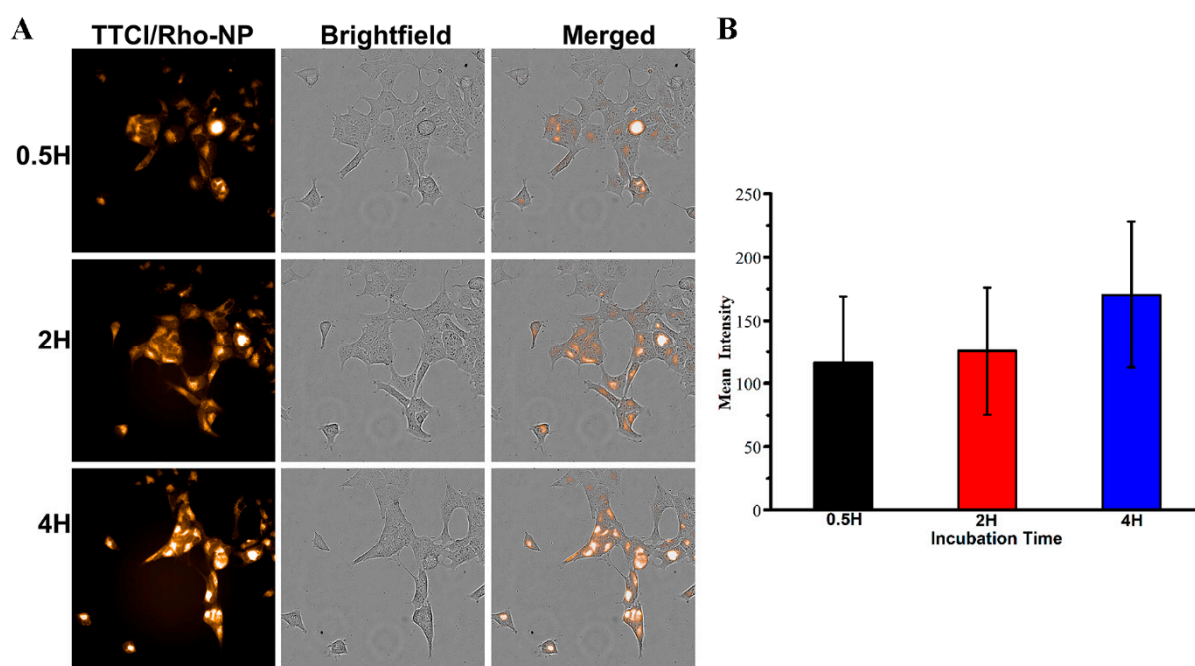


Figure S5. Images of the BxPC-3 cells treated with Rhodamine B-loaded **TTCI/Rho** NPs at the concentration of 20 μ M for 0.5, 2, 4 h, respectively. For each row, left: **TTCI/Rho** NPs; middle: bright field; right: merged image. The images were captured by high content analysis system-operetta CLSTM (A). Scale bars: 50 μ m. the mean intensity of rhodamine fluorescent in the images at different incubation times calculated by the imageJ software (B).

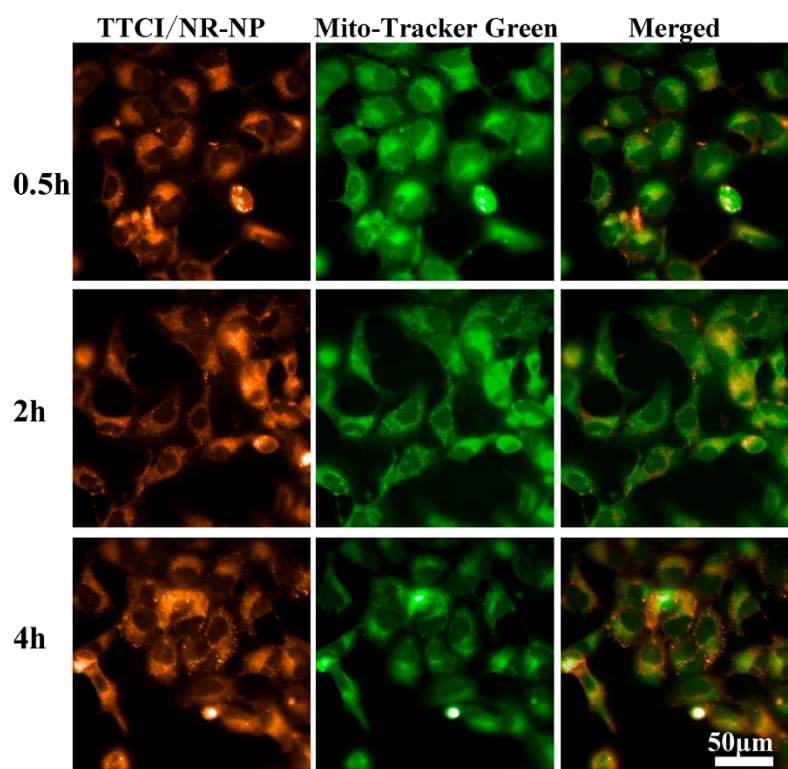


Figure S6. Mitochondria-targeting ability of **TTCI/NR** NPs in vitro: Images of the BxPC3 cells treated with **TTCI/NR** NPs at the concentration of 20 μ M for 0.5, 2 and 4 h captured by high content analysis system-operetta CLSTM. For each row, from left to right: **TTCI/NR** NPs; mitochondria stained by MitoTracker Green; merged image. Scale bars: 50 μ m.

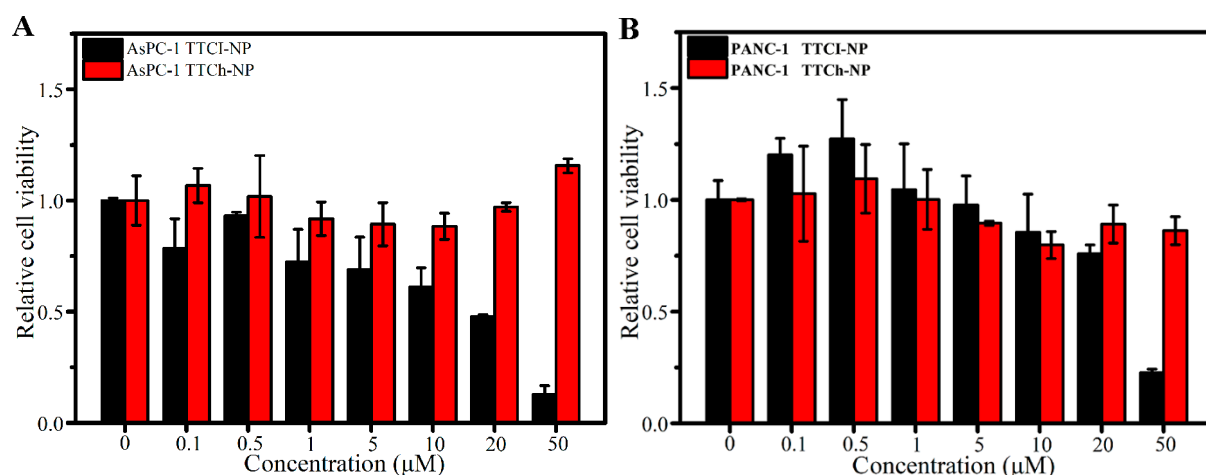


Figure S7. Cell viability of AsPC-1 (A) and PANC-1 (B) cells after being treated with different concentration of TTCl NPs and TTCh NPs for 48 h. Data represent mean \pm SD ($n = 3$).

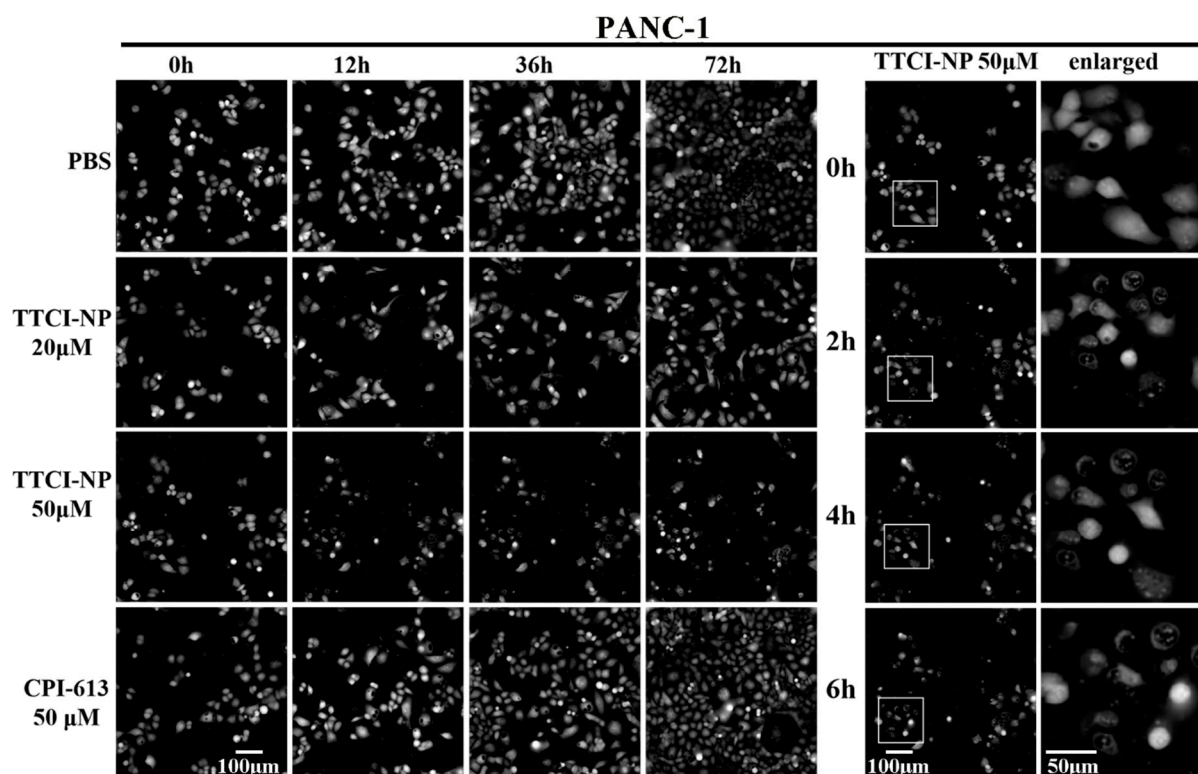


Figure S8. Digital phase contrast images of living PANC-1 cells treated with PBS, 20 μM TTCl NPs, 50 μM TTCl NPs and 50 μM CPI-613 at different times. Digital phase contrast images were captured by high content analysis system-operetta CLSTM. Scale bar: 100 μm and 50 μm (for enlarged images).

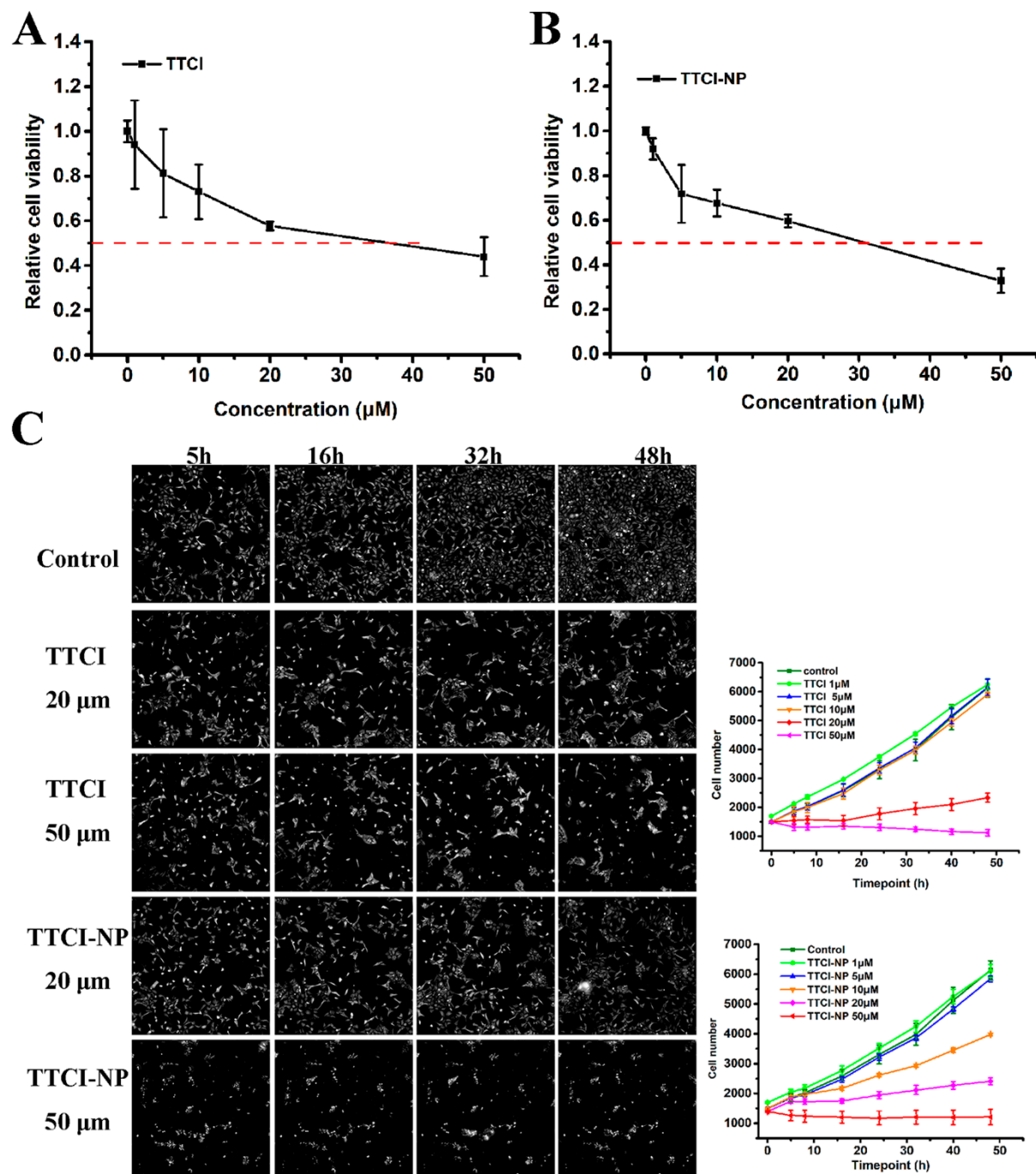


Figure S9. In vitro cytotoxicity of TTCl prodrugs (A) and TTCl NPs (B) at various concentrations against BxPC3 cells after 48 h incubation. Digital phase contrast images of living BxPC3 cells were captured by high content analysis system-operetta CLS™ treated with TTCl prodrugs and TTCl NPs at various concentrations (C).