

Mitochondrial Targeting of Doxorubicin Eliminates

Nuclear Effects Associated with Cardiotoxicity

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Table S1. Summary of LC₅₀ values (μM) in drug treated H9c2 and A2780 cells

Cell Type	Drug	2 hr	6 hr	24 hr	48 hr
H9c2	Dox	>100	>100	0.6 ± 0.2	0.3 ± 0.1
	mtDox	16.0 ± 3.2	17.5 ± 1.0	12.4 ± 0.9	8.6 ± 1.0
A2780	Dox	>100	>100	0.3 ± 0.2	0.03 ± 0.01
	mtDox	20.3 ± 2.0	14.0 ± 0.6	4.1 ± 0.8	1.0 ± 0.2

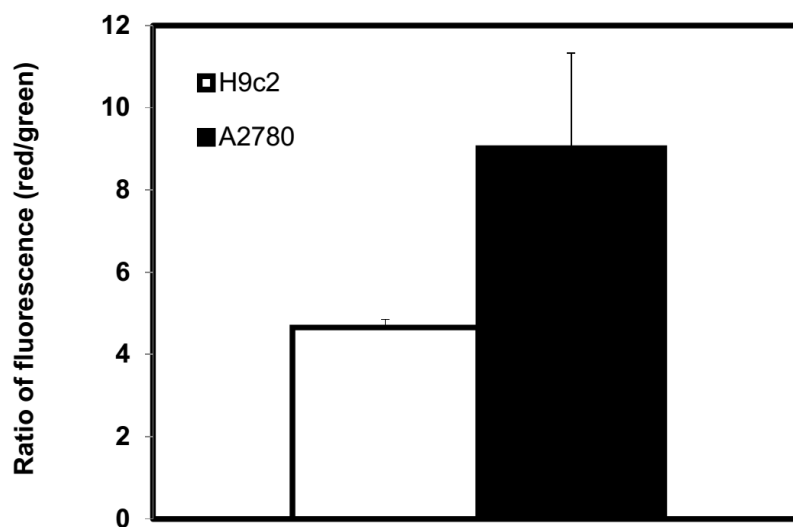
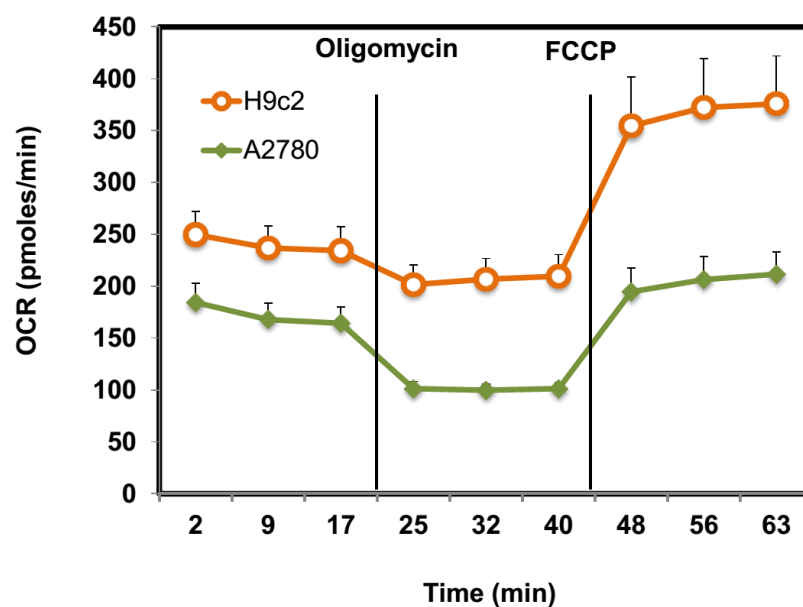
A**B**

Figure S1. Comparison of mitochondrial potential and oxidative metabolism in H9c2 and A2780 cells. (A) Ratio of median red to green fluorescence of JC-1 treated cells measured using flow cytometry (B) Oxygen consumption rate of H9c2 and A2780 cells with sequential treatment of 1.5 μ M oligomycin and 2 μ M FCCP.

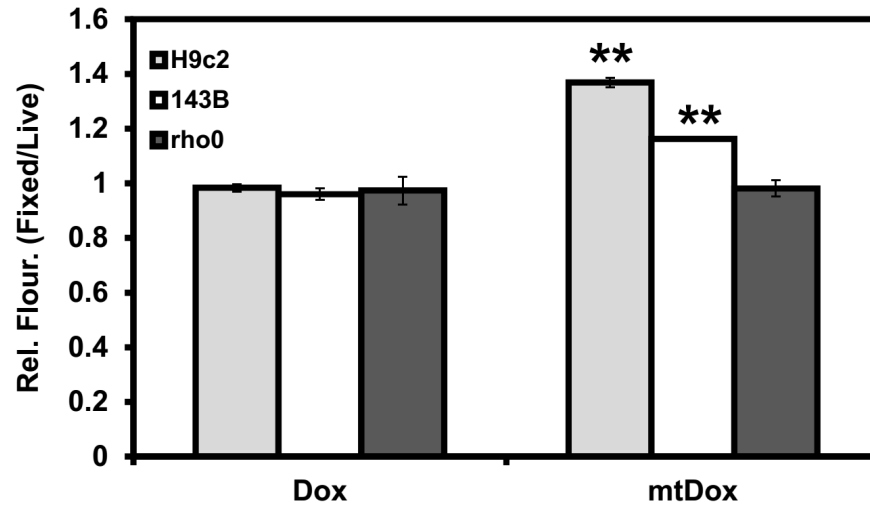


Figure S2. Ratio of total cellular fluorescence prior to and following cell fixation with paraformaldehyde in H9c2 cardiomyocytes, 143B cells, and 143B ρ^0 cells (mtDNA has been depleted by chronic treatment with ethidium bromide). Student's t test, versus untreated control * $p < 0.05$, versus 143B ρ^0 cells ** $p < 0.05$.

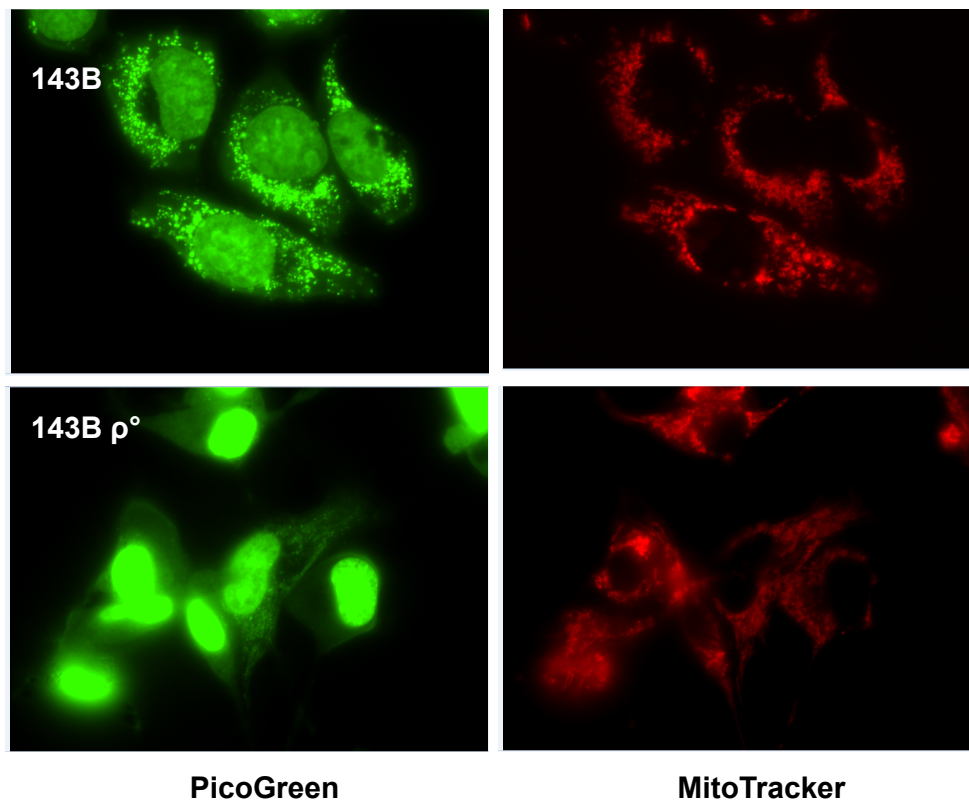


Figure S3. Comparison of mtDNA content by fluorescence microscopy using PicoGreen dye

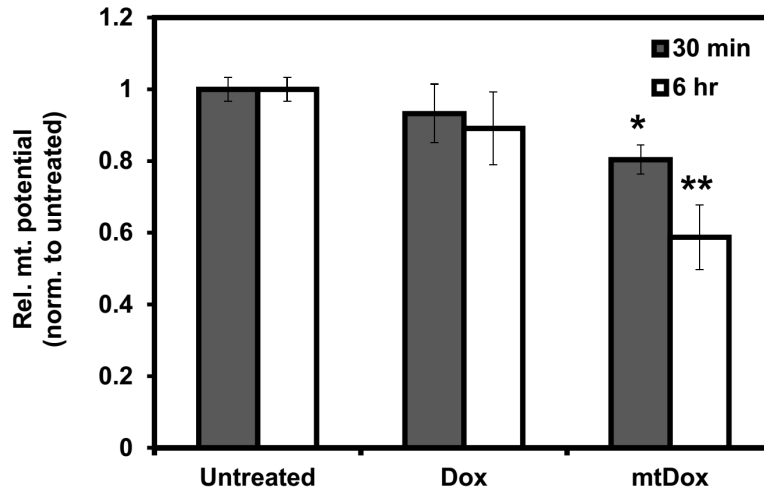


Figure S4. Relative mitochondrial potential following drug treatment. Levels of uptake of a mitochondrial potential sensitive dye were normalized to untreated controls. Student's t test, versus untreated control * $p < 0.05$, versus 30 min ** $p < 0.05$.

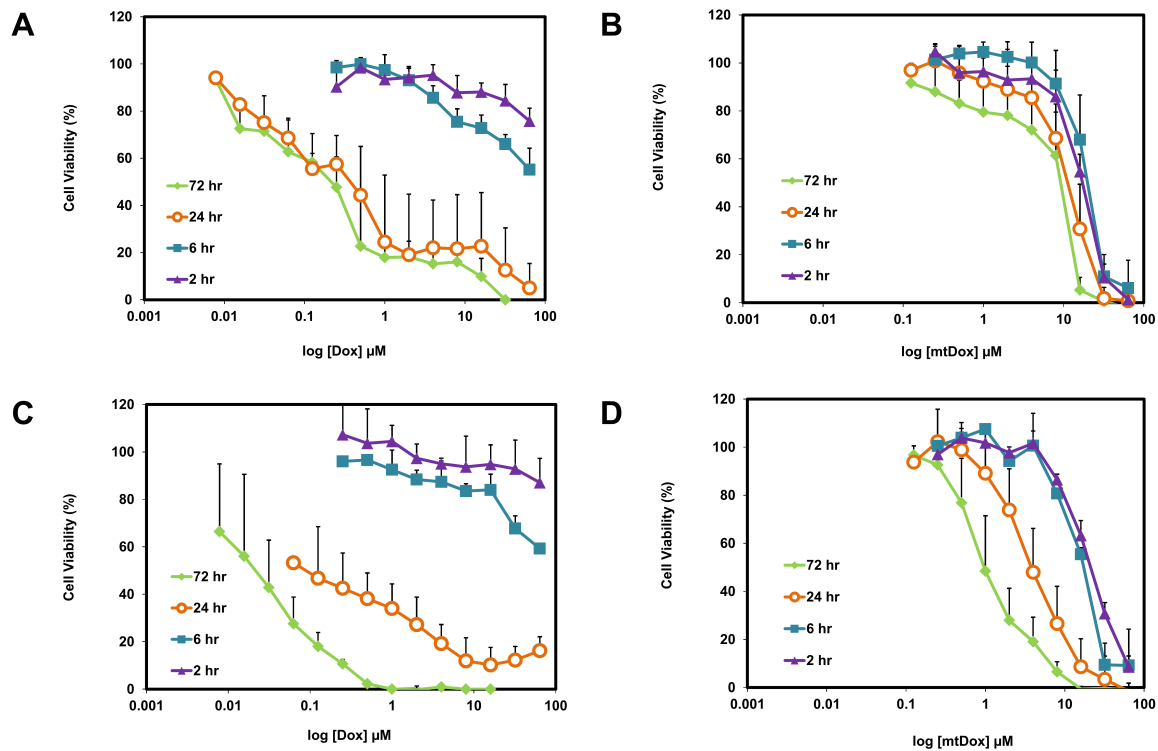


Figure S5. Cell viability curves of H9c2 and A2780 cells with varying drug treatment periods. (A) Dox treated H9c2 cells (B) mtDox treated H9c2 cells (C) Dox treated A2780 cells (D) mtDox treated A2780 cells