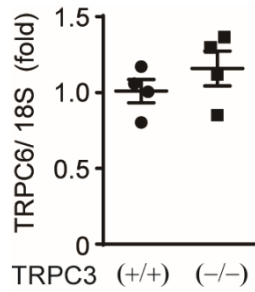
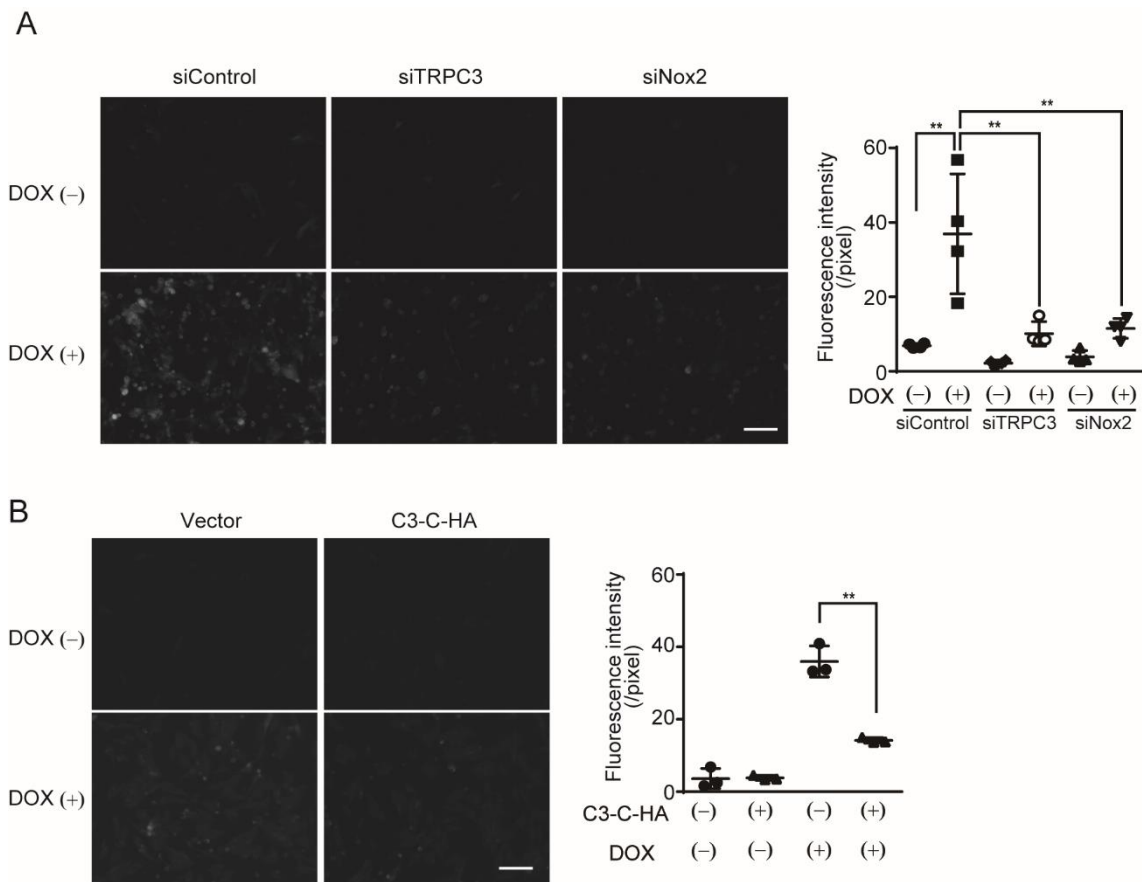


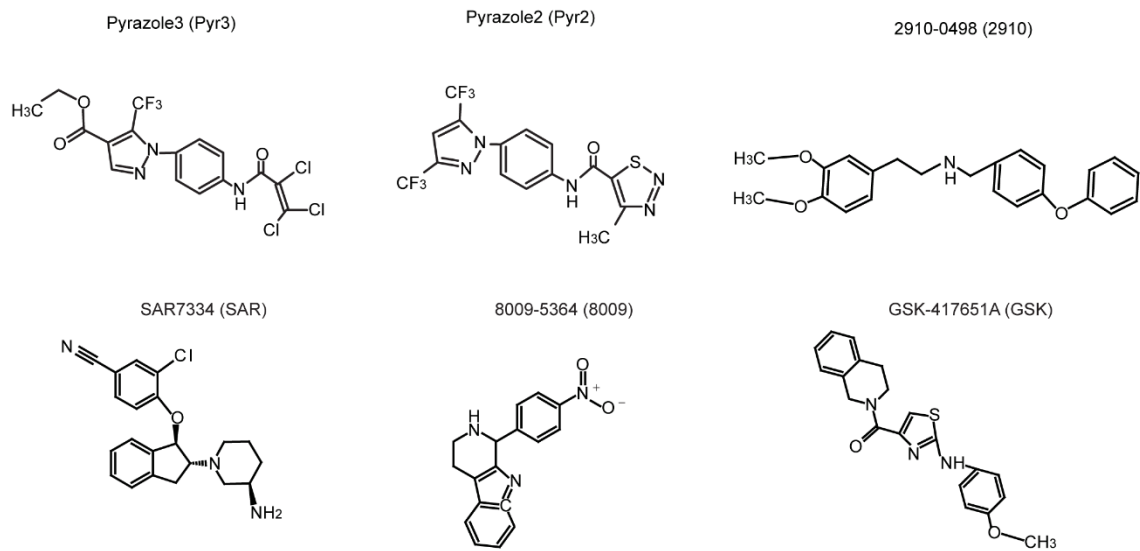
Supplemental Figures and Figure legends



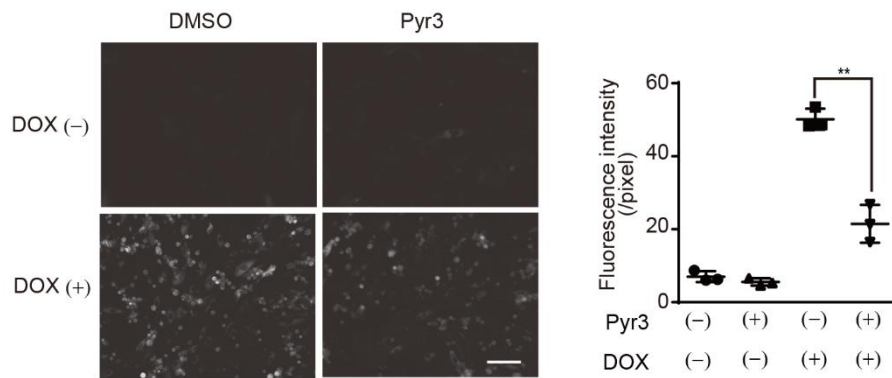
Supplemental Figure 1. TRPC6 mRNA levels in TRPC3^(+/+) or TRPC3^(-/-) mouse hearts. n=4. Data are shown as mean ± SEM.



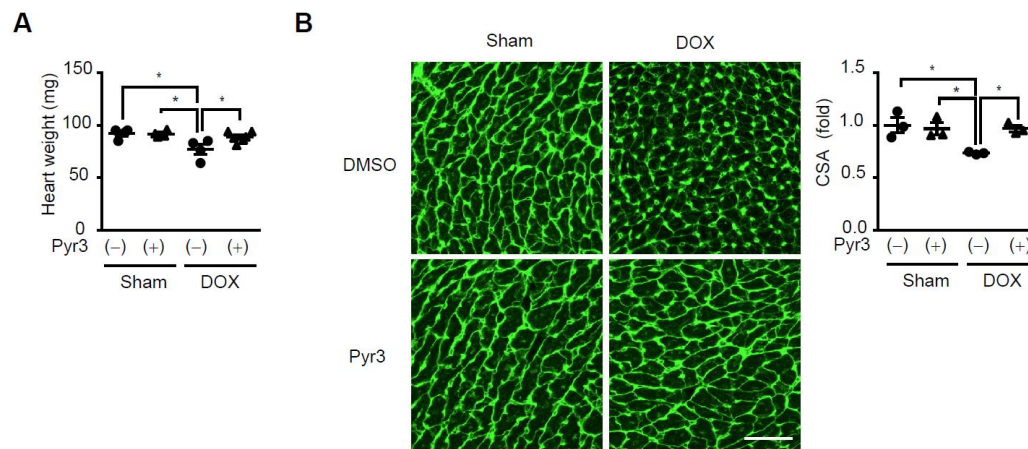
Supplemental Figure 2. DOX-induced ROS production in H9c2 cells expressing Hyper. (A and B) Effect of siRNAs for TRPC3 or Nox2 (n=4, A) and HA-tagged C3-C fragment (C3-C-HA, n=3; B) on DOX-induced ROS production in H9c2 cells. Scale bar: 50 μ m. Data are shown as mean \pm SEM. Significance was determined by one-way ANOVA followed by Tukey's comparison test. * P <0.05, ** P <0.01



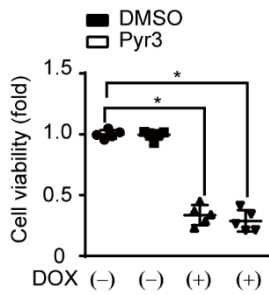
Supplemental Figure 3. Chemical structures of TRPC3/6 inhibitors.



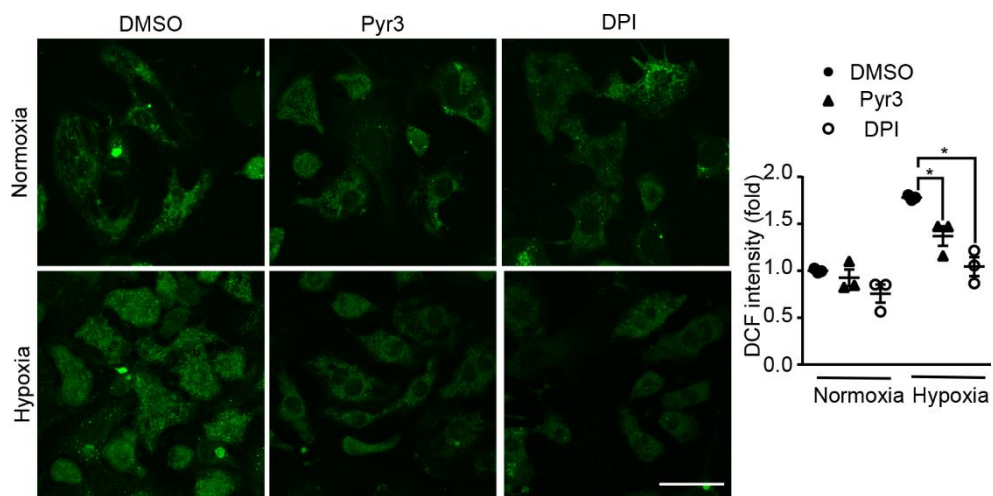
Supplemental Figure 4. DOX-induced ROS production in H9c2 cells expressing Hyper in the presence or absence of Pyr3. Scale bar: 50 μm . $n=3$. Data are shown as mean \pm SEM. Significance was determined by one-way ANOVA followed by Tukey's comparison test. $**P<0.01$



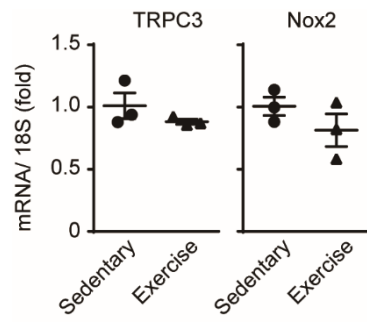
Supplemental Figure 5. Prevention of DOX-induced cardiac atrophy by Pyr3 treatment. (A and B) Decreases in heart weight (A) and cross sectional area (CSA) of cardiomyocytes (B) in C57BL/6J mouse hearts 2 weeks after administration of vehicle (Sham) or DOX (n=3). Scale bar: 50 μ m. * P <0.05



Supplemental Figure 6. Effect of Pyr3 on the anti-tumor actions by DOX. A549 cells were treated with DOX (10 μ M) and Pyr3 (3 μ M) for 24 h and cell viability was measured by MTT assay (n=5). Data are shown as mean \pm SEM. Significance was determined by one-way ANOVA followed by Tukey's comparison test. * P <0.05.



Supplemental Figure 7. Effects of Pyr3 and DPI on hypoxia-induced ROS production. NRCMs were exposed to 1% hypoxia for 12 h. Pyr3 (300 nM) or DPI (1 μ M) was applied 30 min prior to the hypoxia (n=3). Scale bar: 40 μ m. Data are shown as the mean \pm SEM. Significance was determined using one-way ANOVA followed by Tukey's comparison test. * P <0.05.



Supplemental Figure 8. Expression levels of TRPC3 and Nox2 mRNAs in sedentary or exercised mouse hearts. n=3. Data are shown as mean \pm SEM.