

# Supplementary Information

## **The Anti-Cancer Multikinase Inhibitor Sorafenib Impairs Cardiac Contractility by Reducing Phospholamban Phosphorylation and Sarcoplasmic Calcium Transients**

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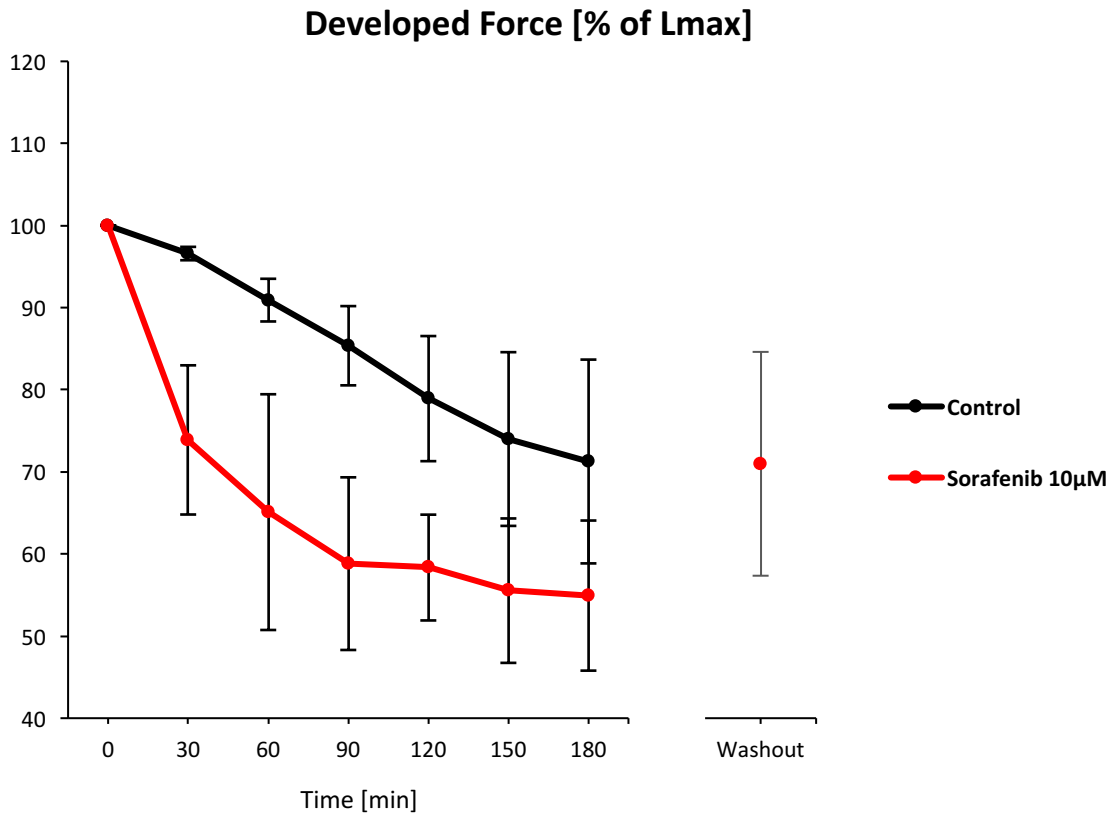
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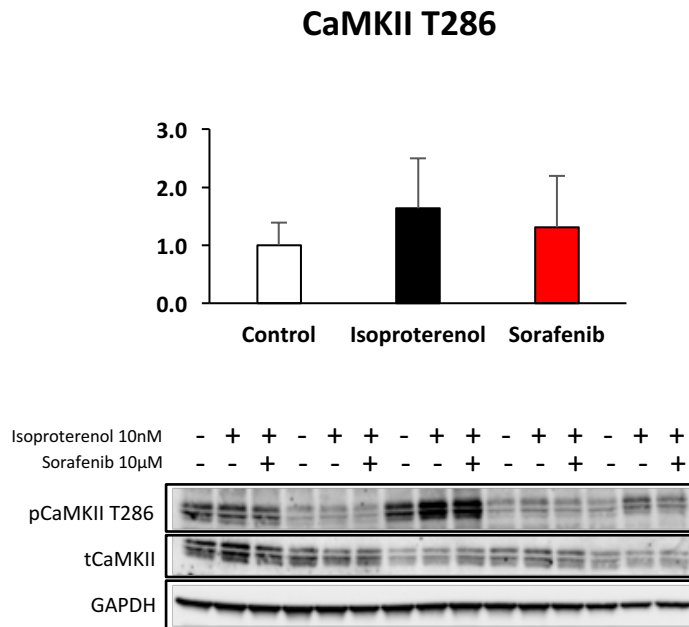
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## Supplementary Figure S1



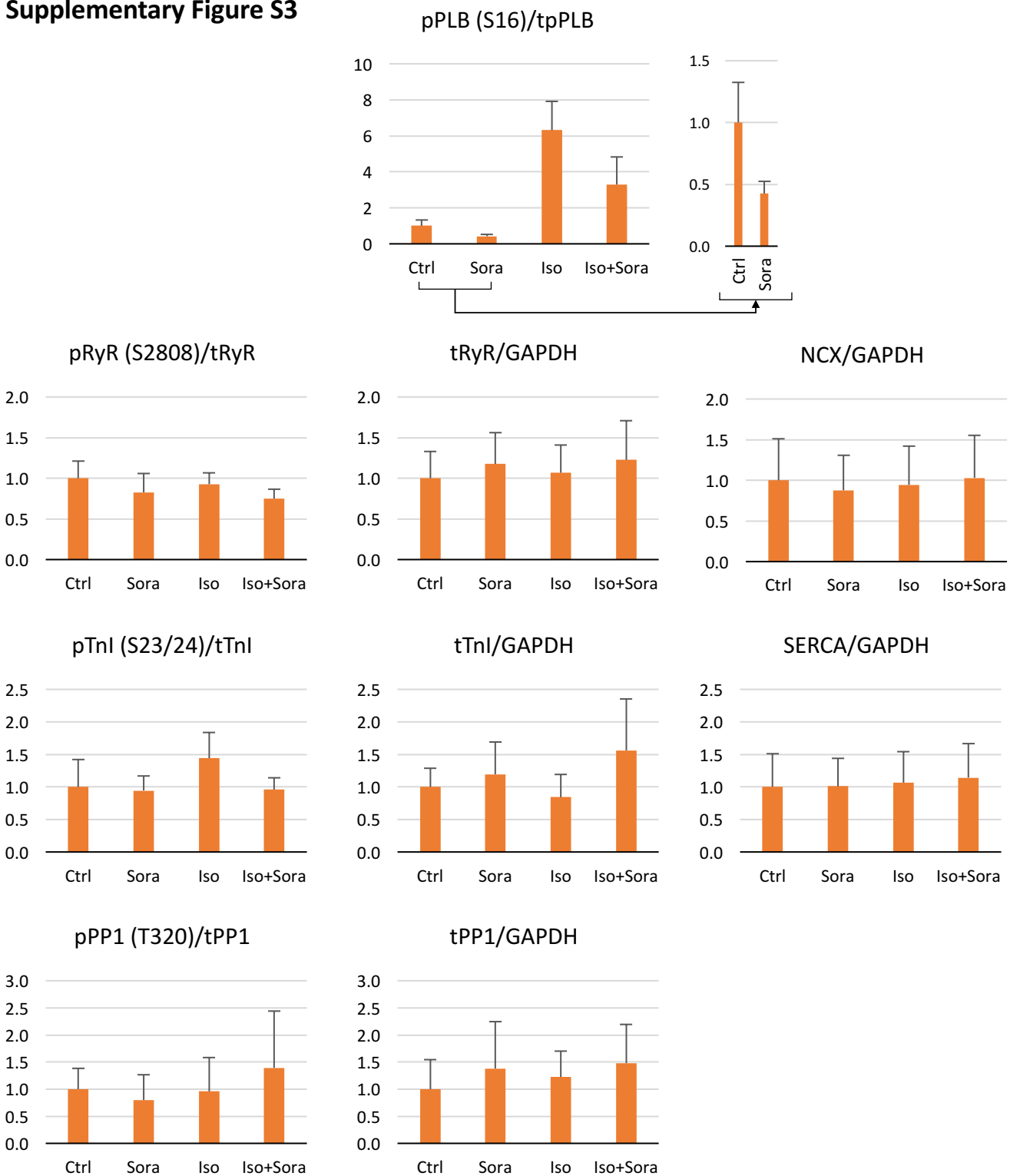
**Fig. S1. Sorafenib-induced negative inotropy is sustained over several hours and remains reversible.**  $n=3/4$  trabeculae from 4 hearts,  $p<0.05$  for all sorafenib time-points vs. baseline and for the 150- and 180-minute time points for control vs. baseline (inherent natural run-down of atrial muscle preparations in the organ bath). Developed force of sorafenib-treated muscles did not differ from control after wash-out ( $p=0.94$ ).

## Supplementary Figure S2



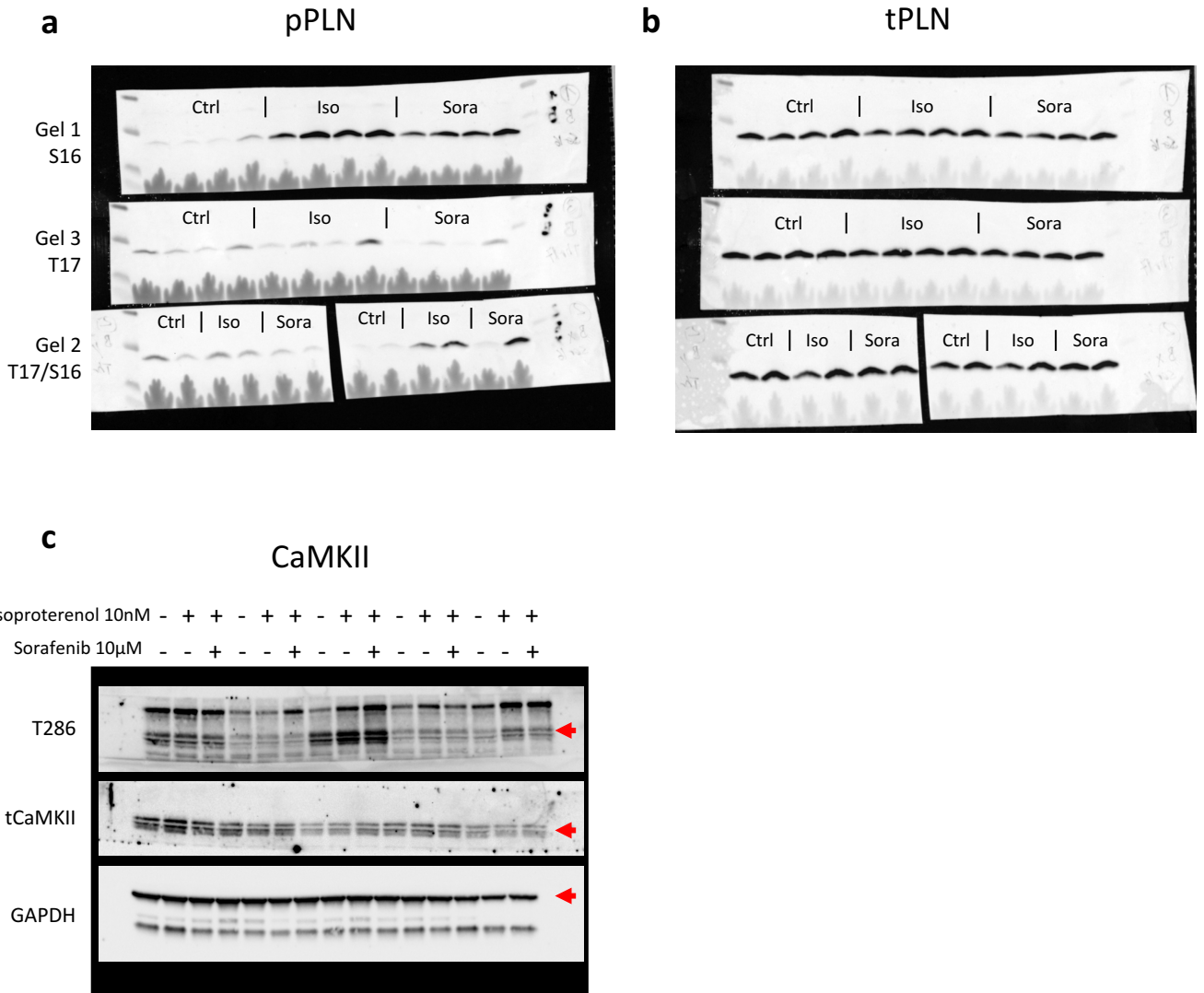
**Fig. S2. CaMKII phosphorylation at threonine 286 is not acutely affected by sorafenib.** Summary data (above) and original blots (below). n=5 hearts per group. For complete western blots see Supplementary Figure S4.

## Supplementary Figure S3



**Fig. S3. Phosphorylation and expression of PLB, RyR, NCX, SERCA2a, PP1 $\alpha$ , and troponin I in dependence of sorafenib (10 $\mu$ M) and/or isoproterenol (10nM).** Adult murine cardiomyocytes were freshly isolated, pre-treated with sorafenib for 5 minutes and exposed to 10 minutes of isoproterenol; fold-changes are provided, n=4-6 hearts.

## Supplementary Figure S4



**Fig. S4. Uncropped Western Blots.** pPLN S16 and T17 (a), tPLN (b), pCaMKII T286, tCaMKII, and GAPDH (c).