## **Supplementary Figures**

## Fig. S1



## Figure S1. Ca<sup>2+</sup> transient alternans in intact RyR2-WT hearts.

Langendorff-perfused RyR2-WT hearts were loaded with Rhod-2 AM. Ca<sup>2+</sup> transients were elicited by pacing at 8 Hz, and recorded using line-scanning confocal imaging. Cell boundaries were indicated by black bars. The F/Fo traces depict the average fluorescence signal of the scan area.







Langendorff-perfused RyR2-SOF mutant hearts were loaded with Rhod-2 AM. Hearts were first stimulated at 5 Hz for 30 seconds (S1), followed by a single S2 stimulation. A series of S1S2 stimulations are repeatedly applied with progressively reduced S1S2 interval from 200 to 50 ms. The amplitude of  $Ca^{2+}$  transients was recorded using the line-scan mode. The relationship between S2/S1 ratio of  $Ca^{2+}$  transient amplitude and S1S2 interval is shown. Data shown are mean  $\pm$  SEM (n=3 RyR2-SOF hearts) (\*p<0.05).





**Figure S3.** Ca<sup>2+</sup> **transients in intact RyR2-SOF hearts before carvedilol treatment.** Langendorff-perfused RyR2-SOF mutant hearts were loaded with Rhod-2 AM. Ca<sup>2+</sup> transients were elicited in intact RyR2-SOF hearts by pacing at 5 Hz, and recorded before the application of carvedilol using the line-scan mode. Cell boundaries were indicated by the black bars. The F/Fo traces depict the average fluorescence signal of the scan area.