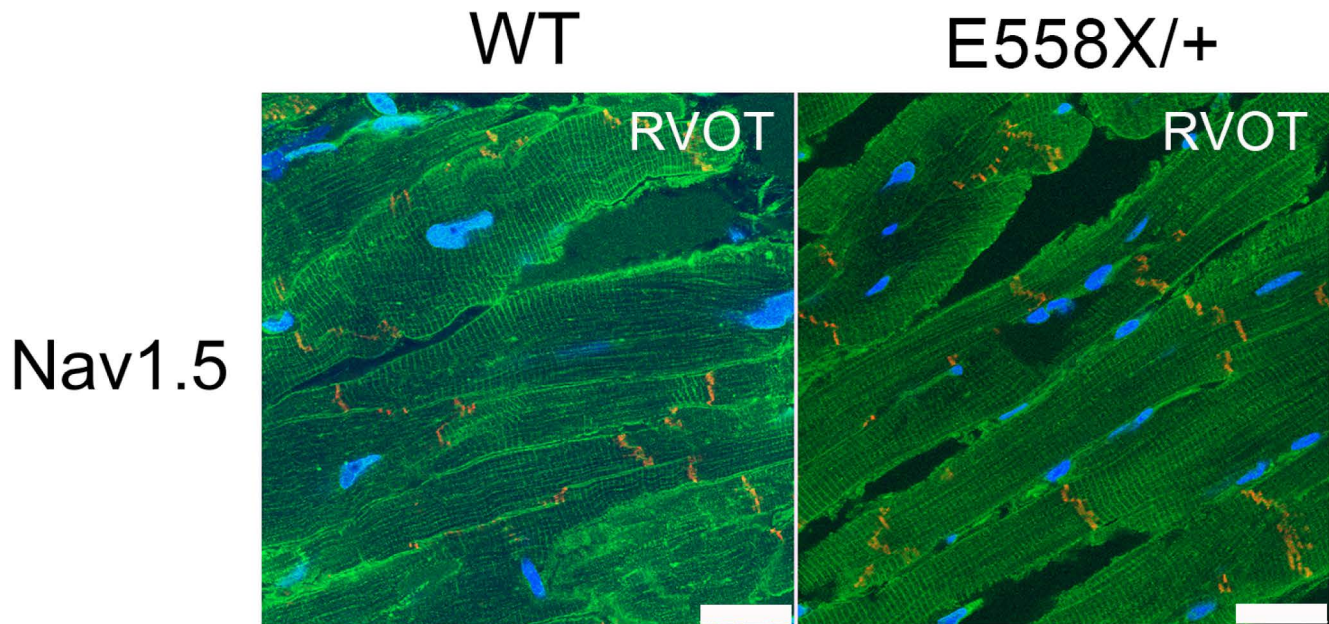
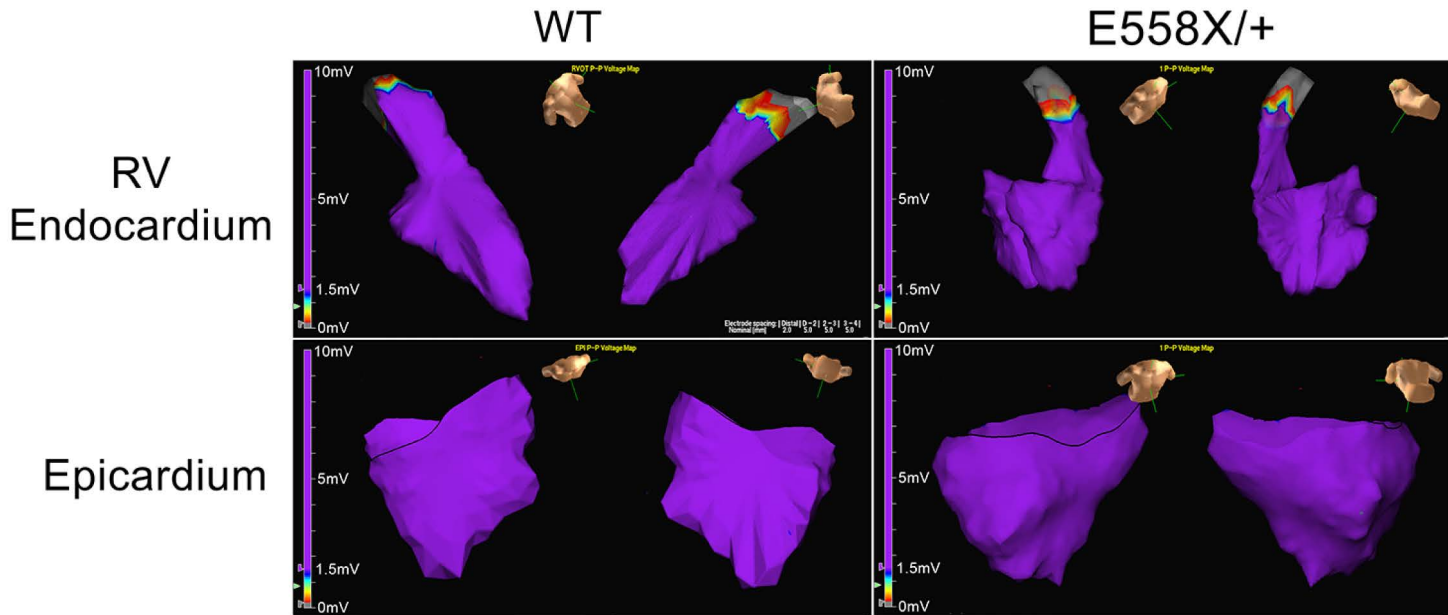


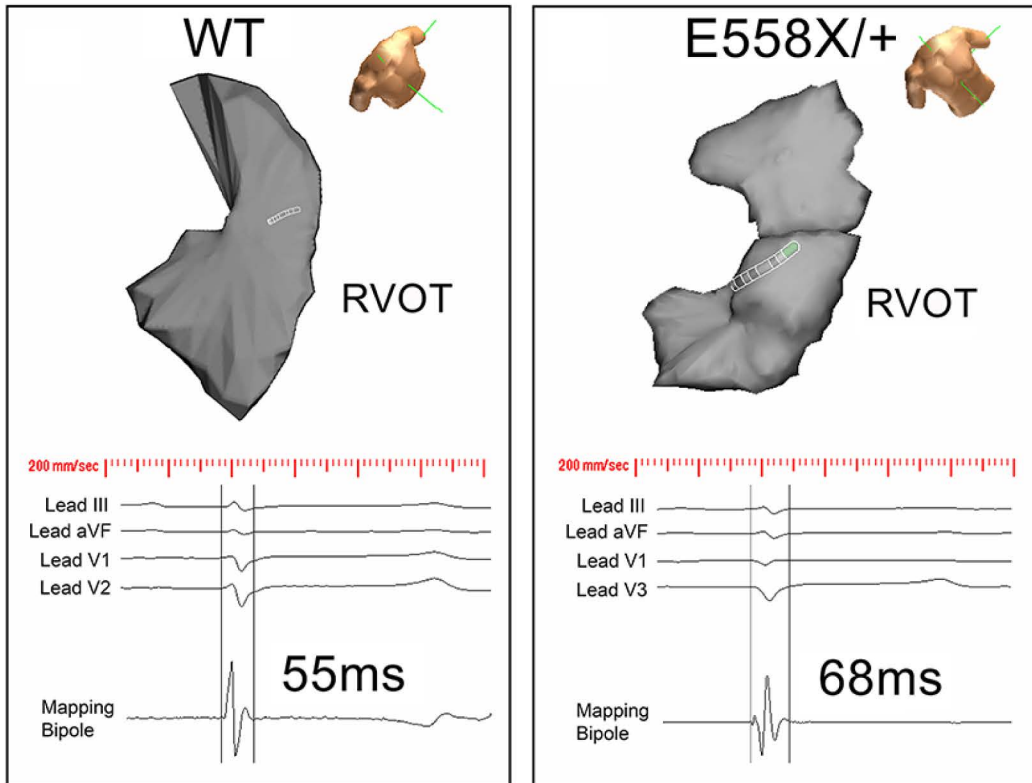
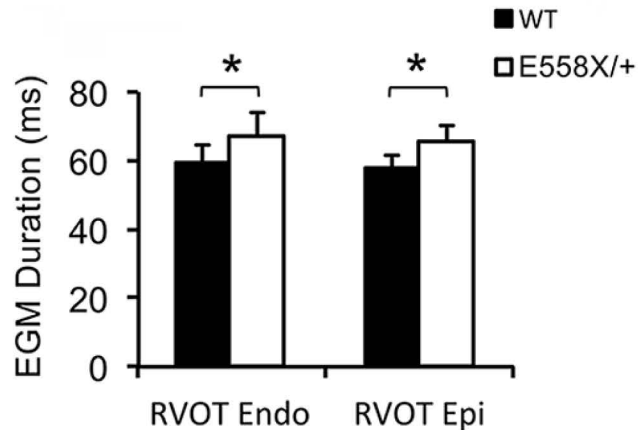
Supplemental Figure 1. 12-lead electrocardiogram of 10 year-old Brugada patient harboring the SCN5A^{E555X/+} mutation.



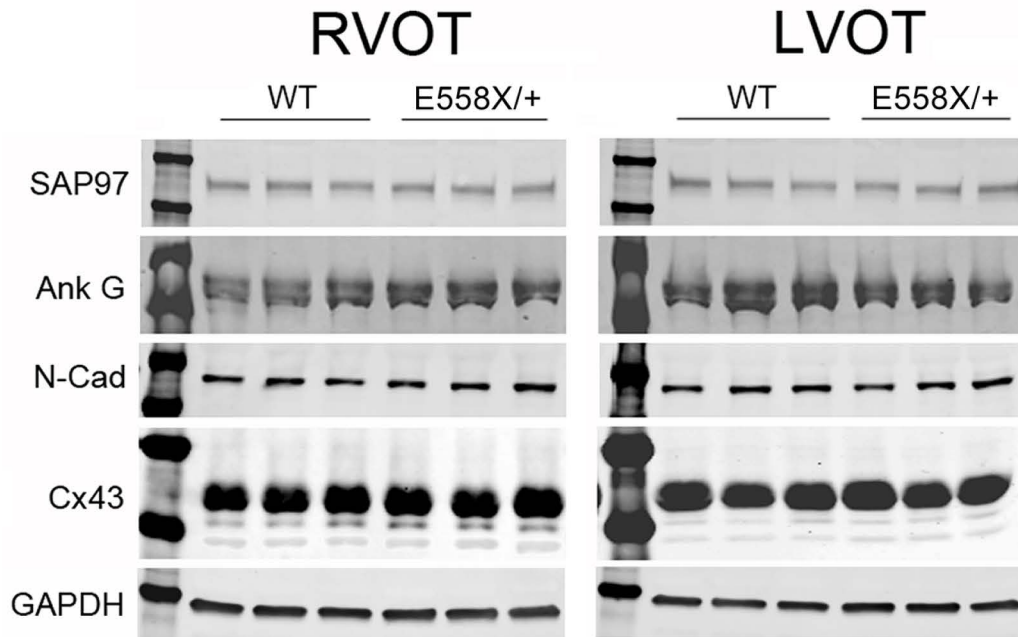
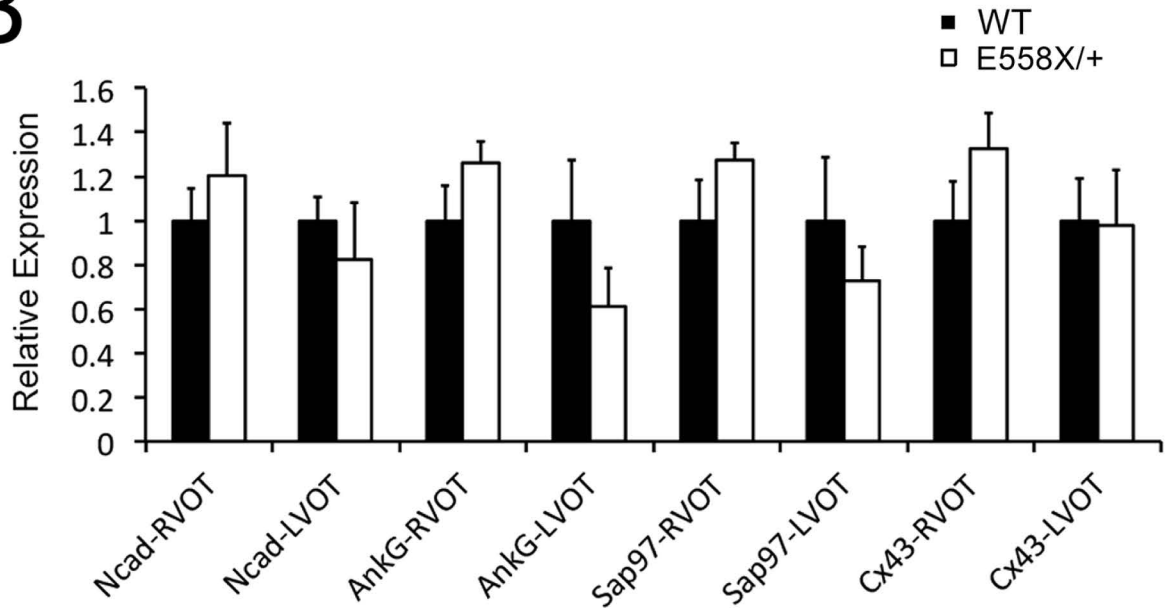
Supplemental Figure 2. Representative immunostaining of $\text{Na}_v1.5$ (green) and N-Cadherin (red) from cryopreserved RVOT sections of WT and $\text{SCN5A}^{\text{E558X/+}}$ hearts. Nuclei were stained with DAPI (blue). Scale bar=25 μm .



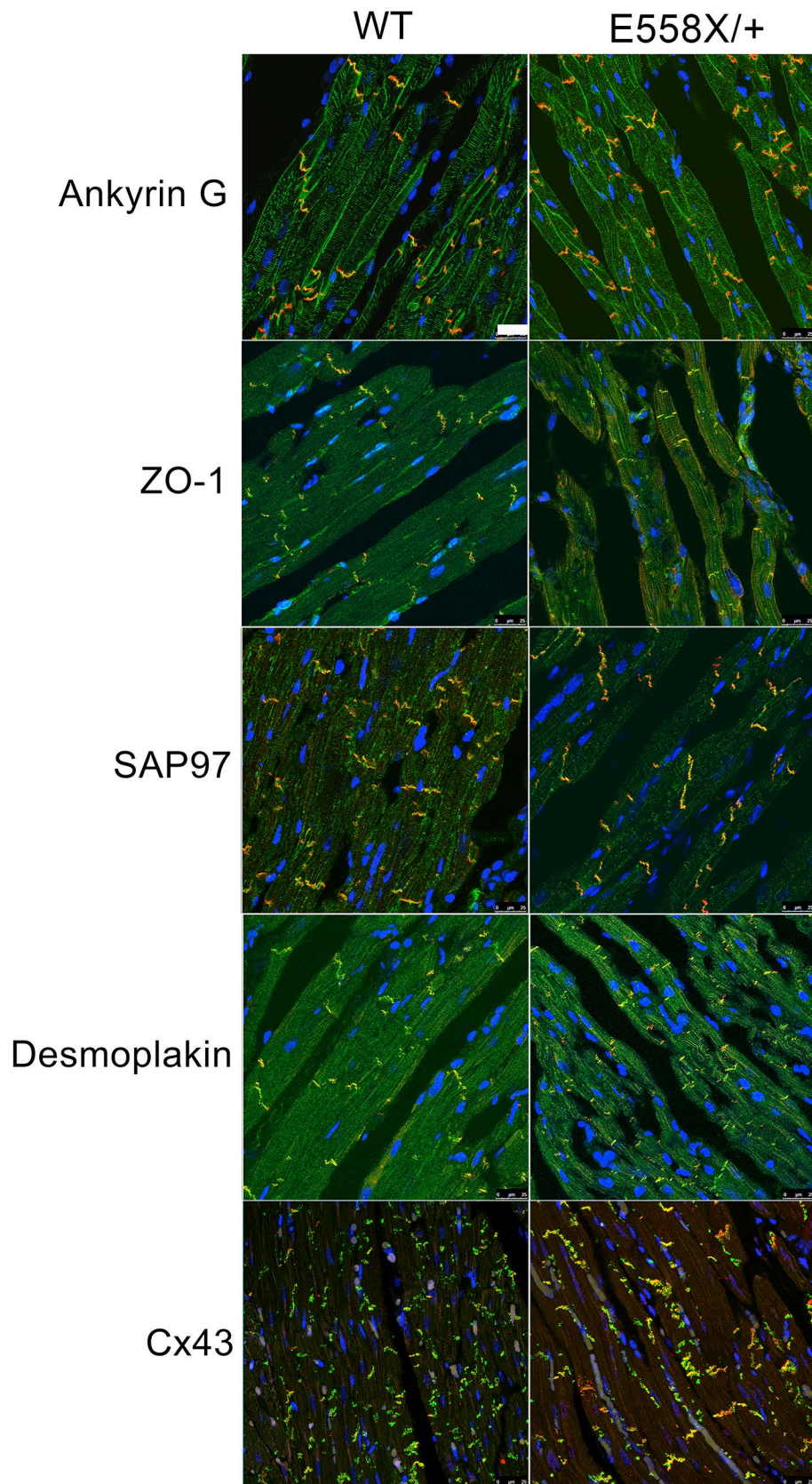
Supplemental Figure 3. Representative RVOT endocardial and epicardial voltage maps of WT and *SCN5A*^{E558X/+} hearts. Low voltage electrograms were defined as bipolar signals below 1.5mV in peak-to-peak amplitude.

A**B**

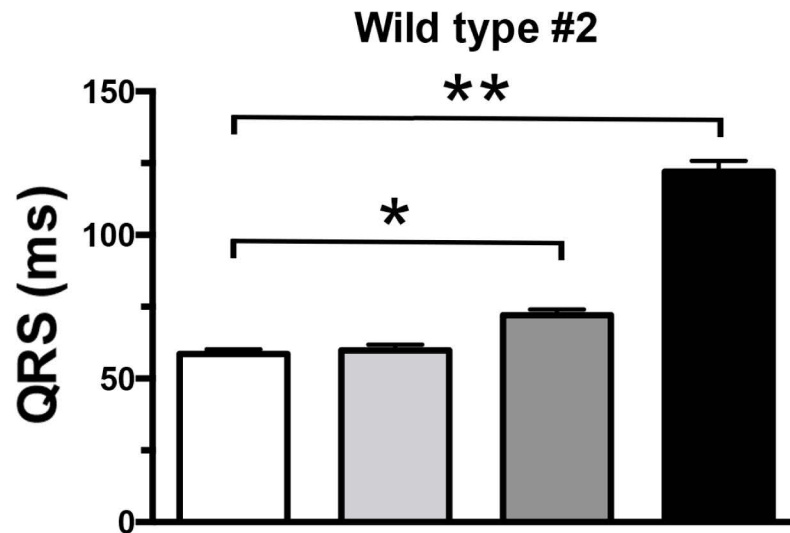
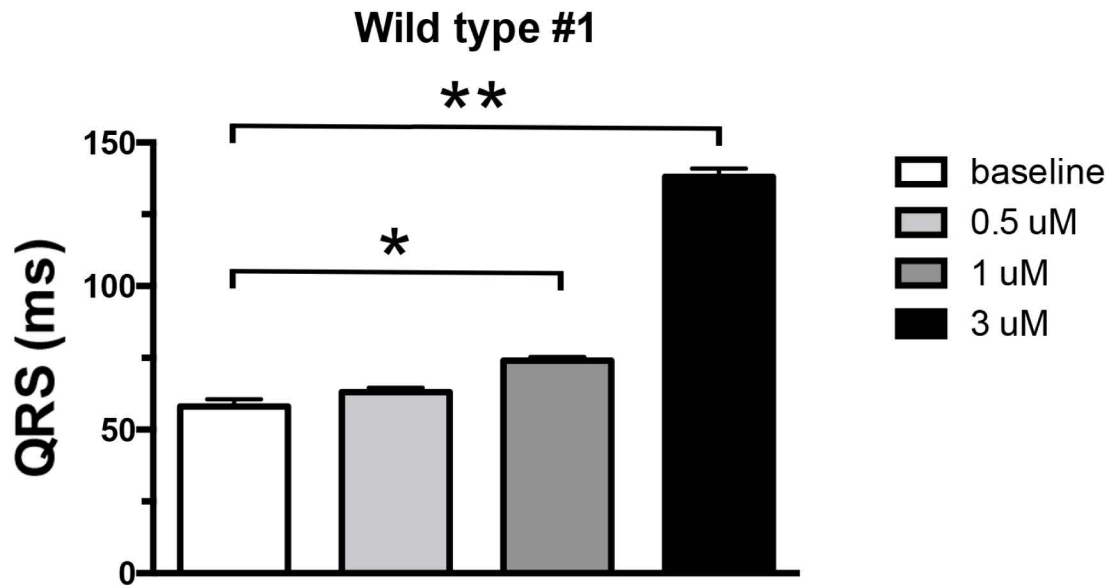
Supplemental Figure 4. A) Representative bipolar electrogram recordings from the RVOT endocardial surface of WT and *SCN5A*^{E558X/+} hearts. B) Average bipolar electrogram (EGM) durations (N=10 recordings from each region) recorded from RVOT endocardial and epicardial surfaces of WT (n=3, age 22±1 months) and mutant (n=3, age 22±1 months) pigs, *p<0.00002.

A**B**

Supplemental Figure 5. A) Western blot analysis of Na_v1.5-associated proteins in WT and *SCN5A*^{E558X/+} RVOT and LVOT. B) Quantitative analysis using densitometry demonstrated no significant difference in protein expression levels of voltage-gated sodium channel associated proteins.



Supplemental Figure 6. Representative staining patterns of $\text{Na}_v1.5$ -associated proteins (green) and N-Cadherin (red) from cryopreserved RVOT sections of WT and $\text{SCN5A}^{\text{E558X/+}}$ hearts. Nuclei were stained with DAPI (blue). Scale bar = 25 μm .



Supplemental Figure 7. Langendorff-perfused WT hearts (n=2, age 19 months) at 39°C (Protocol #1) were challenged with low (0.5µM), intermediate(1µM), and high-doses of flecainide (up to 3µM), which resulted in significant QRS prolongation. (*p=0.01, **p<0.001)

WT v *SCN5A*^{E558X/+} p=N.S. for all values

Genotype	LVEDD (cm)	LVESD (cm)	FS (%)	LVPWd (cm)	LVPWs (cm)	LVSD (cm)	LVSs (cm)	RVOTd (cm)	RVIFd (cm)
Wildtype	4.27±0.21	3.08±0.16	28±0.87	1.07±0.04	1.55±0.06	1.02±0.03	1.58±0.03	2.54±0.04	2.37±0.14
<i>SCN5A</i> ^{E558X/+}	4.36±0.26	3.17±0.24	27±1.52	1.06±0.02	1.56±0.05	1.04±0.03	1.51±0.10	2.52±0.04	2.29±0.14

Supplemental Table 1. Transthoracic echocardiography of WT and *SCN5A*^{E558X/+} pigs.