Supplementary Figures and Tables:

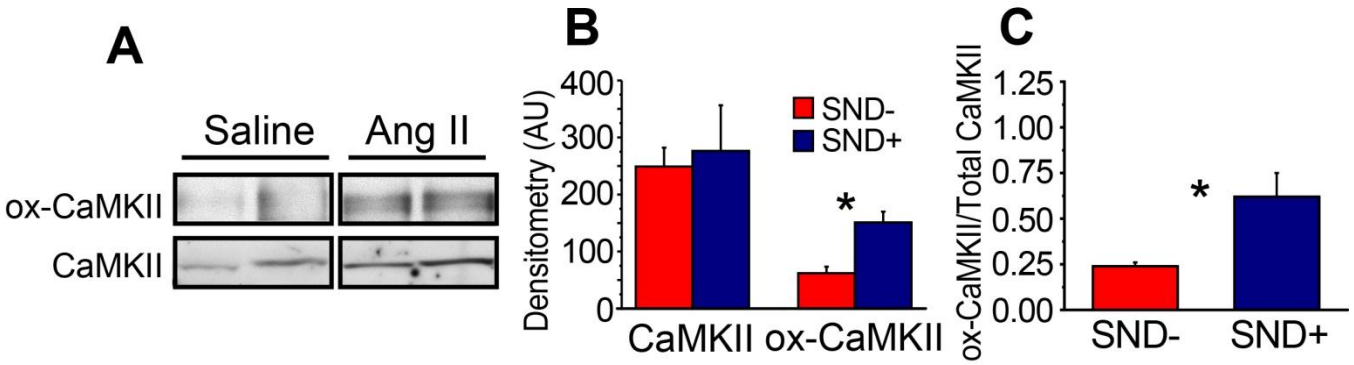

Figure 1: Ox-CaMKII is increased in heart failure dogs with SND (A) Exemplar immunoblots showing ox-CaMKII and total CaMKII from right atrial tissue obtained from dogs with pacing induced heart failure and SND (SND+) and control (SND-) dogs. The lanes were run on the same gel but were noncontiguous. (B) Summary data for ox-CaMKII and total CaMKII in SND- (n=3) and SND+ (n=3) dogs (**P*=0.02) (C) Increased ox-CaMKII normalized to total CaMKII in dog samples shown in panel B (**P*=0.049).

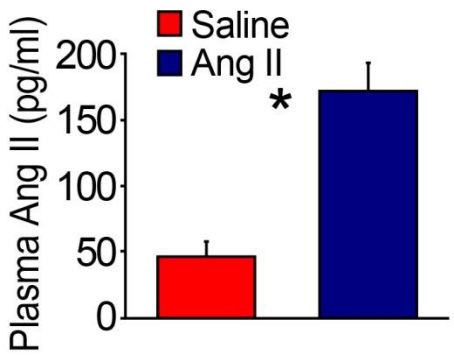

Figure 2: Plasma Ang II levels are increased in Ang II infused mice compared to WT mice. Ang II infusion (3 mg/kg/day) caused a significant (*P*=0.001) increase in plasma Ang II levels compared to saline infusion (n=5-7 mice/group).

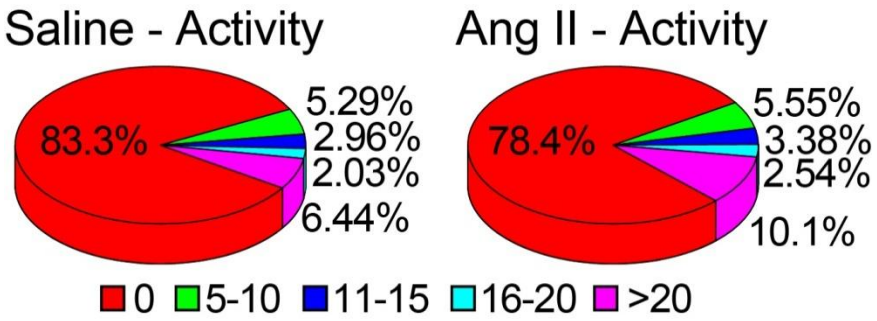

Figure 3: Ang II and Saline treated mice had similar activity levels at the end of 3 weeks. Pie chart shows the percentage of time spent at each level of activity (n=5/group). These data are from experiments shown in Figure 2B.

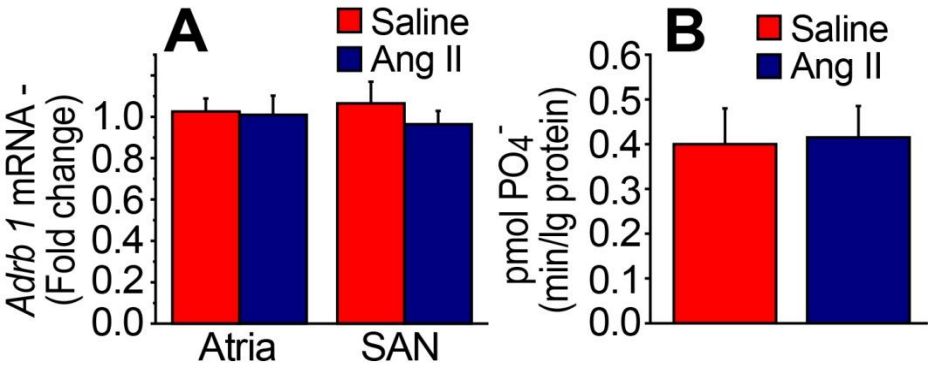

Figure 4: Ang II induced sinus bradycardia was independent of β_1–adrenergic receptor expression or activity: q-RT-PCR of *Adrb1* from SAN and atrial tissue of Ang II and saline treated mice do not show significant differences (*P*=0.86 for atria and *P*=0.40 for SAN, n=5-8/group). PKA activity measured from AngII and saline treated WT mice do not show a significant difference (*P*=0.9, n=4/group).

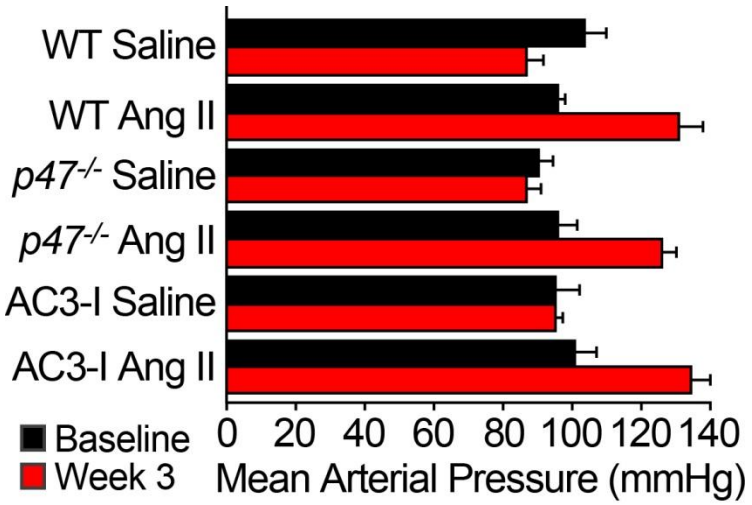

Figure 5: WT, AC3I and *p47*$^{-/-}$ mice had equivalent Ang II induced increases in BP. BP change from baseline to 3 weeks post-infusion of Ang II or saline in each genotype. Final BP was not different (n=5-6/group) compared between saline treatment in all genotypes (p-0.15) and AngII treatment in all genotypes (p-0.91). Comparison between before pump implantation and 3 weeks post pump in each treatment group (**P*<0.05). Comparison of BP three weeks post Ang II or saline infusion in each genotype (**P*<0.05).

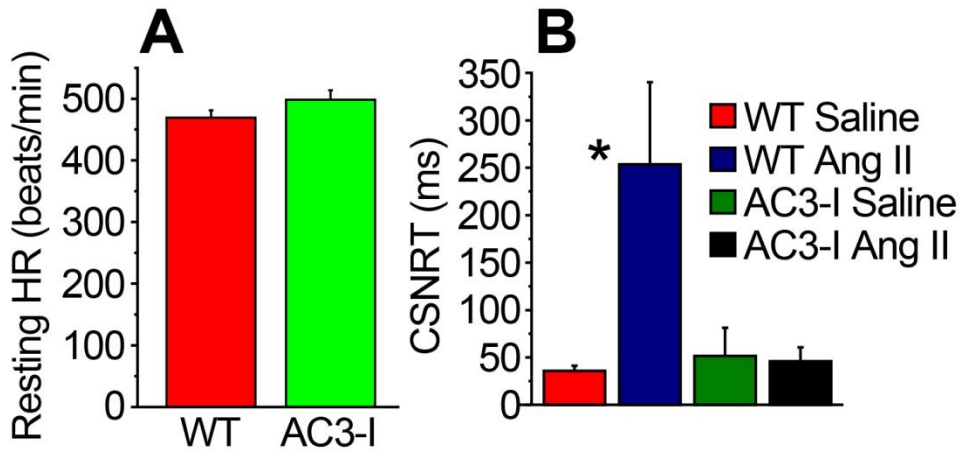

Figure 6: AC3I mice are protected from AngII induced SND: (A) AC3-I mice and WT mice have comparable baseline HRs at rest (n=8-12/group). (B) Summary data showing that hearts isolated from Ang II and saline infused AC3-I mice do not have prolonged CSNRT, in contrast to WT Ang II infused mice (**P*=0.04, n=5/group)

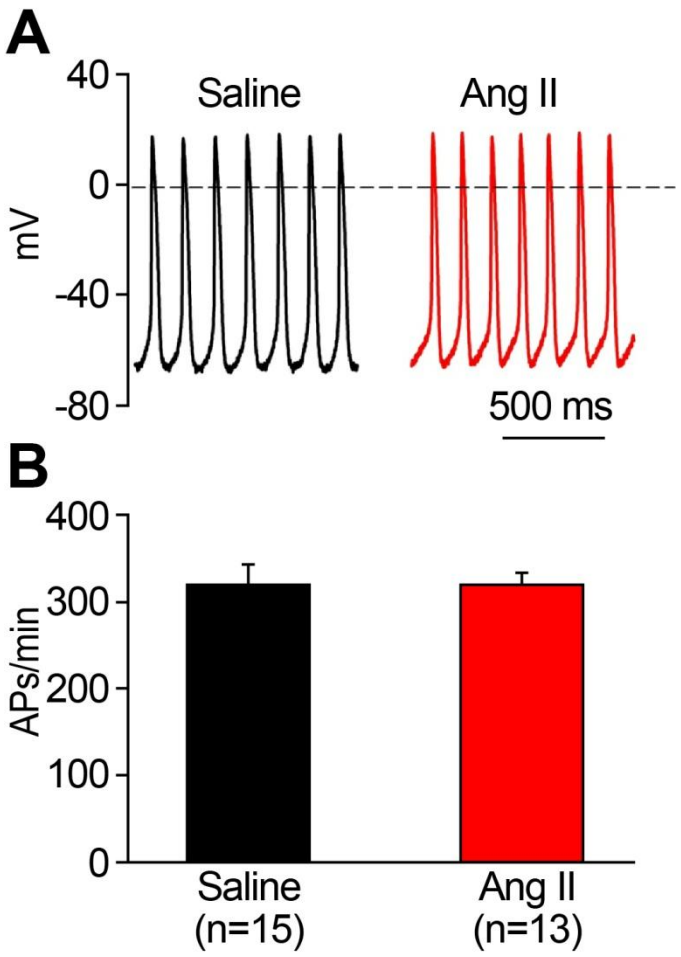

Figure 7: AngII treatment does not affect spontaneous single SAN cell automaticity: (A) Representative samples of single SAN cell action potentials from Ang II and saline treated mice (B) Summary data showing no difference (*P*=0.98) in single SAN cell action potential rates between saline and AngII treated mice.

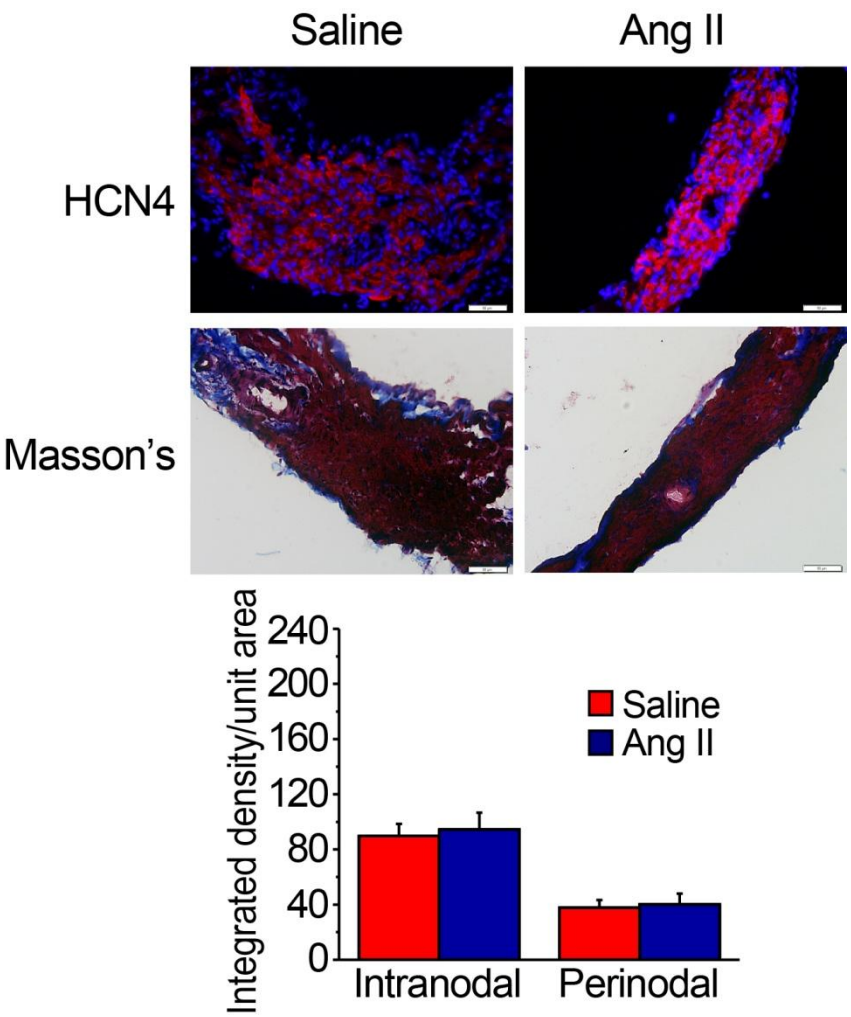

Figure 8: AC3I mice are protected from Ang II induced SAN fibrosis: (A) Representative samples of Masson's trichrome staining showing no increase in SAN fibrosis in AC3-I mice infused with Ang II compared to saline for three weeks. Calibration bars indicate 50μm. (B) Summary data showing no increase fibrosis in the SAN (intranodal, *P*=0.78, n=3-4) and in SAN adjacent tissue (perinodal, *P*=0.8, n=3-4)

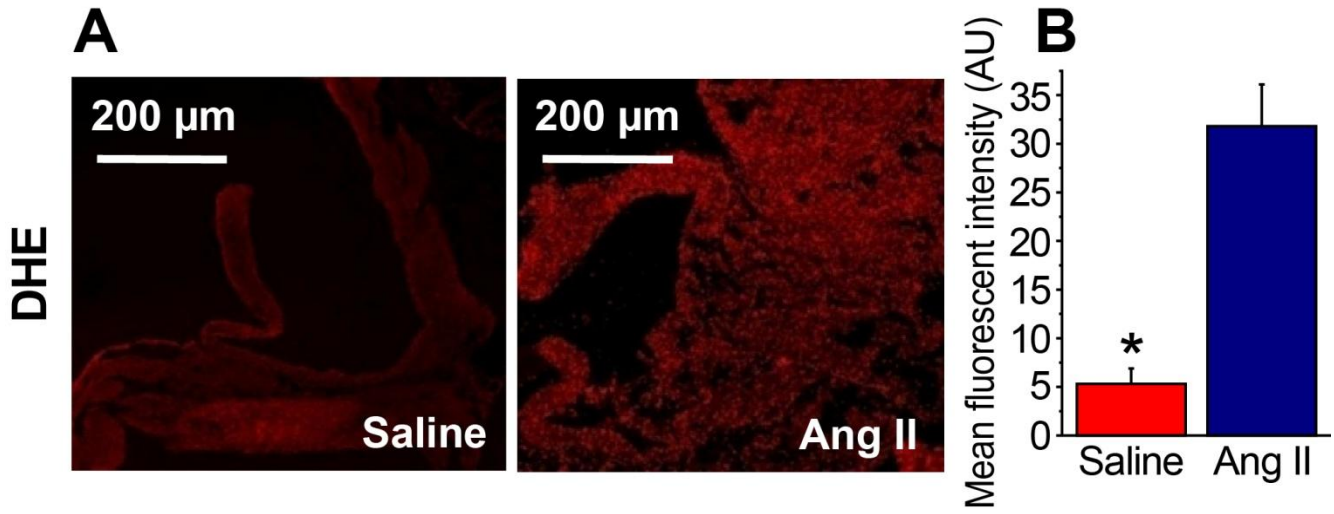

Figure 9: Ang II increases right atrial ROS (A) Ang II infusion for three weeks caused increased right atrial ROS as detected by DHE (red) staining. (B) Summary data showing fluorescent intensity of DHE staining in WT mice treated with saline and Ang II (n=3/group, **P*<0.01)

	Variable	-PM(n=10)	HF-PM (n=6)	HF+PM (n=5)	P
1	Age (Mean±SEM)	66.7±4.02	69.5±5.9	68.4±8.04	NS
2	Males (%)	72	83	80	NS
3	CAD (%)	46	50	20	NS
4	HTN (%)	91	83	80	NS
5	DM (%)	27	33	60	NS
6	Hyperlipidemia (%)	64	100	20	0.02 (HF-PM vs HF+PM)
7	LVEF (Mean±SEM)	52.9±2.7	30.2±2.5	29.2±2.9	<0.01 (-PM vs HF-PM & HF+PM)
8	Atrial Fibrillation	0	0	0	NS
9	ACEI (%)	82	100	80	NS
10	BB (%)	64	83	40	NS
11	Ca^{2+} blockers (%)	36	16	0	NS
12	Statins (%)	46	33	20	NS

Table 1: Patient characteristics for right atrial tissue shown in Figure 1.

	ECHO Parameter	Saline (n=13)	AngII (n=14)	p
1	End diastolic volume(µl)	50.3±4.2	35.4±2.7	<0.01
2	LV Mass (mg)	97.2±4.3	111.7±3.6	0.02
3	Volume/ Mass	0.52±0.03	0.32±0.02	<0.01
4	Stroke volume (µL)	36.8±2.8	28.7±2.3	0.03
5	Cardiac output(mL/min)	18.6±1.16	16.9±1.32	0.3
6	Ejection Fraction	0.75±0.03	0.81±0.02	0.07

Table 2: AngII infusion for three weeks causes significant increase in left ventricular (LV) mass and decrease in end diastolic volume and LV volume/mass ratio compared to saline infusion for three weeks but does not significantly alter other echocardiographic parameters.

Cell Type	Cell model	Radius	Length	Capacitance	$R_{gap,\ longitudinal}$	$R_{gap,transverse}$
Atrial	Courtemanche et al. 1998*	8 μm	100 μm	100 pF	1.5 Ωcm^2	15.0 Ωcm^2
Peripheral SAN	Kurata et al. 2008#	4 μm	70 μm	65 pF	10.0 Ωcm^2	100.0 Ωcm^2
Central SAN	Kurata et al. 2002§	4 μm	70 μm	32 pF	30.0 Ωcm^2	300.0 Ωcm^2
Inexcitable cell	Morita et al. 2009†	8 μm	100 μm	100 pF	4000 Ωcm^2	40000 Ωcm^2

*Courtemanche et al. Am J Physiol. 1998;275:H301-321.
#Kurata et al. Biophys J. 2008;95:951-977 with sodium channel conductance = 1.8523×10^{-6} nS/pF.
§Kurata et al. Am J Physiol Heart Circ Physiol. 2002;283:H2074-2101.
†Morita et al. Am J Physiol Heart Circ Physiol. 2009;297:H1594 with E_f = -40 mV.

Table 3: Regional cell properties for the mathematical SAN model