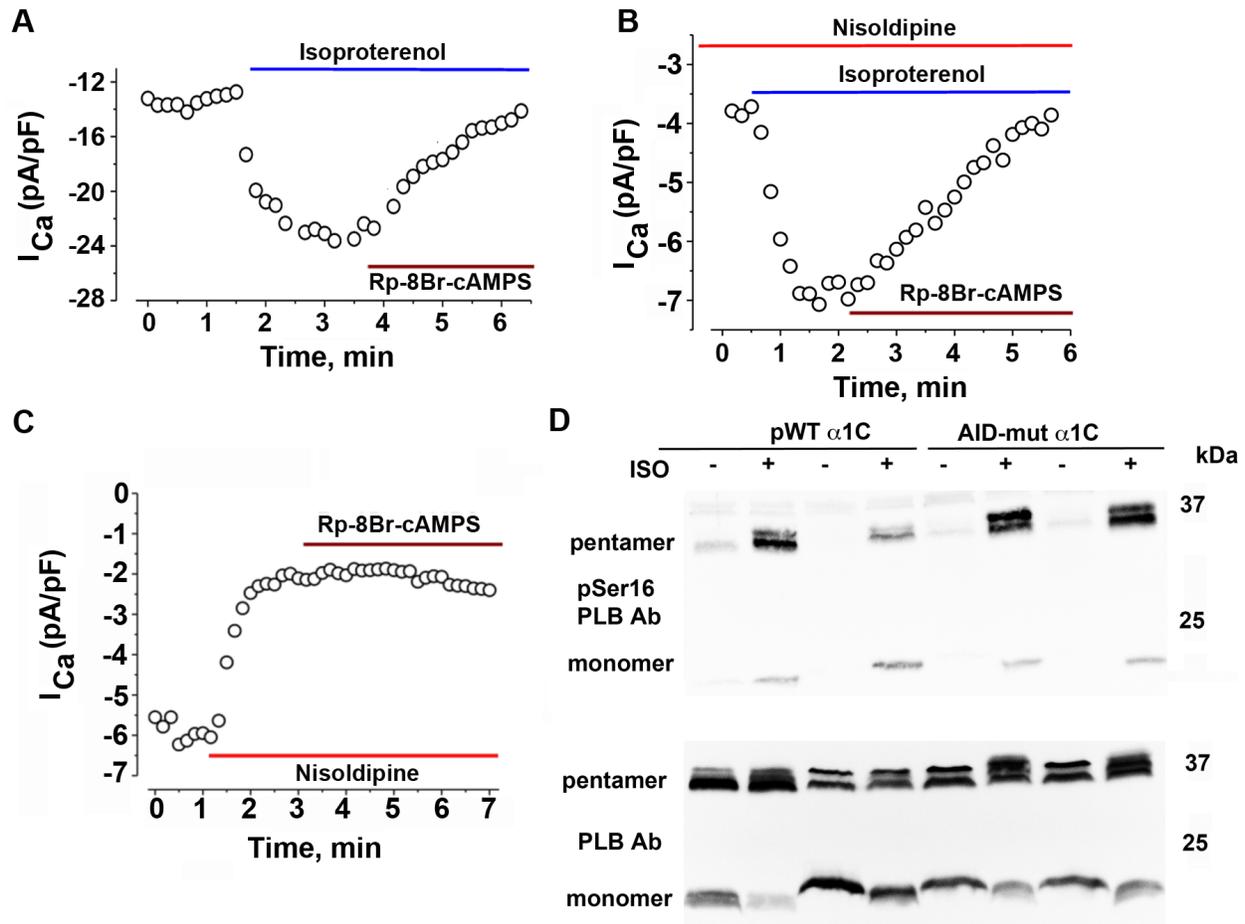


Supplemental Figure 1. Expression of AID-mutant α_{1C} in tsA-201 cells. (A) Anti- β antibody immunoblot (upper) and anti-FLAG antibody (lower) of anti-FLAG antibody immunoprecipitation of homogenates of tsA-201 cells transfected with β_{2b} and either FLAG tagged WT α_{1C} or FLAG-tagged AID-mutant α_{1C} . Representative of 3 experiments. (B) Graph of whole cell Ca^{2+} current density of tsA-201 cells transfected with either WT α_{1C} or AID-mutant α_{1C} , in absence and presence of β_{2b} subunit. Mean \pm SEM. Data obtained from 3 transfections. ** $P < 0.01$, *** $P < 0.001$ by one-way ANOVA and Dunnett's multiple comparisons. (C) Graph of whole cell Ca^{2+} current density of tsA-201 cells transfected with β_{2b} and WT α_{1C} , and either DHP-resistant pWT α_{1C} or DHP-resistant AID-mutant α_{1C} (WT: pWT α_{1C} /AID-mutant α_{1C} in 1:1 ratio). Cells exposed to 300 nM nisoldipine (red circles).



Supplemental Figure 2. β -adrenergic regulation of phospholamban is normal in AID-mutant transgenic hearts (A-C) Representative diary plot of current amplitude (pA/pF) at +10 mV of cardiomyocyte isolated from non-transgenic (NTG), pWT α_{1C} and AID-mutant α_{1C} transgenic mice, in the absence and presence of nisoldipine, isoproterenol and Rp-8Br-cAMPS as shown. Representative of 10 non-transgenic cardiomyocytes, 4 pWT α_{1C} cardiomyocytes and 4 AID-mutant α_{1C} cardiomyocytes. (D) Cardiomyocytes were isolated from pWT and AID-mutant α_{1C} mice. Cells were exposed to 200 nM isoproterenol. Protein extracts were size-fractionated on SDS-PAGE, transferred to nitrocellulose and blotted with anti-pSer16 phospho-specific antibody (upper blot), and anti-PLB antibody (lower blot). Representative of three similar experiments.

	Residue # (human)	Sequence	Mutant TG
NT HOOK	28	RPS	RPA
	58	KAKT	KAKA
	143	KFYS	KFYA
	150	KSGGNS	KSGGNA
	164/65	RKST	RKAA
	195	KPS	KPA
	215	KKT	KKA
	263	RIS	RIA
	268	RVT	RVA
	277	KRS	KRA
	293	RSNT	RSNA
	296	RSS	RSA
	334	KTS	KTAA
	345/346	KISS	KIAA
GK CT	360	RGKS	RGKA
	410	KAT	KAA
	460	RSAS	
	474	KSS	
	478/479/480/481	RSSSS	
	489/491	HRSGT	
	496 (PKG site)	RGLSR	
	500	RQET	
	511	RDS	
	540	RDET	
	543/544	HGSS	
	551/555	RESRHRS	
	572	KQRS	
	576	RHKS	

NOT
REQUIRED

Supplemental Figure 3. Putative PKA phosphorylation sites in human β_{2b} subunit. Residues in red, which are predicted phosphorylation sites, in the N-terminal (NT), Hook and GK domains of β_{2b} were mutated to Ala. Residues in the C-terminal (CT) variable region were not mutated to Ala because deletion of the C-terminal region did not alter β -adrenergic regulation of Cav1.2.