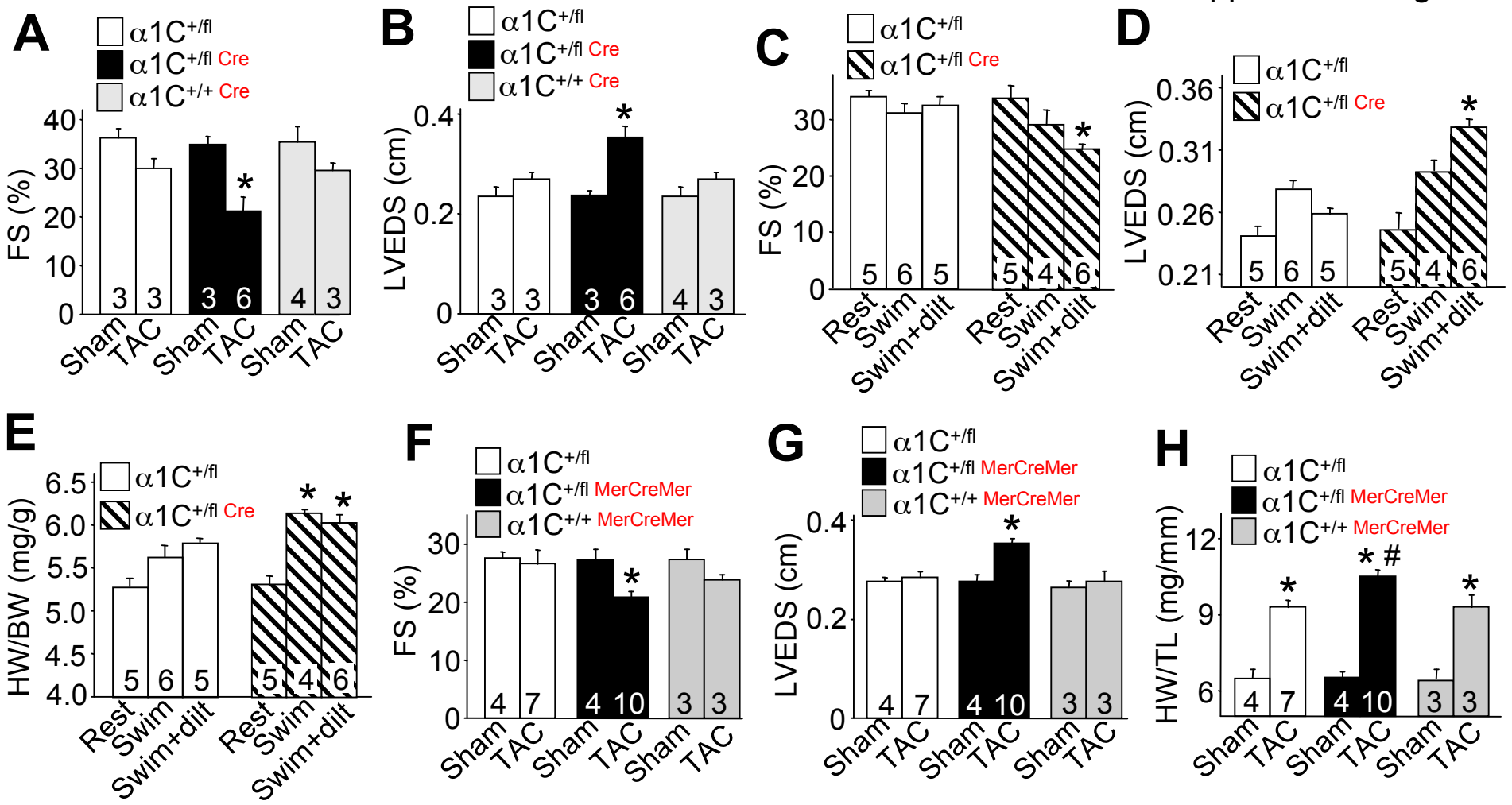

Figure S1. Mice with conditional deletion of a single α1C allele exhibit enhanced responsiveness to pressure overload and swimming. (A and B) Echocardiographic assessment of fractional shortening (FS) percentage and left ventricular chamber dimensions at systole (LVEDS) in $\alpha1C^{+/fl}$, $\alpha1C^{+/+\ Cre}$ control mice and $\alpha1C^{+/fl}$ mice containing the α-MHC-Cre transgene after 2 weeks of pressure overload stimulation. (C, D and E) Echocardiographic assessment of FS, LVEDS and heart-weight to body weight in $\alpha1C^{+/fl}$ control mice and $\alpha1C^{+/fl}$ mice containing the α-MHC-Cre transgene after 21 days of swimming. (F and G) Echocardiographic assessment of FS and LVEDS in 2 control groups and $\alpha1C^{+/fl}$ mice containing the α-MHC-MerCreMer transgene given tamoxifen for 5 days, rested for 4 weeks, then subjected to 2 weeks of pressure overload stimulation. (H) Heart weight to tibia length quantitation in the mice shown in F. *P<0.05 compared to $\alpha1C^{+/fl}$ Sham mice. #P<0.05 compared to $\alpha1C^{+/fl}$ TAC mice. Number of animals used in each genotype shown in the graphs.

Supplemental Figure 2

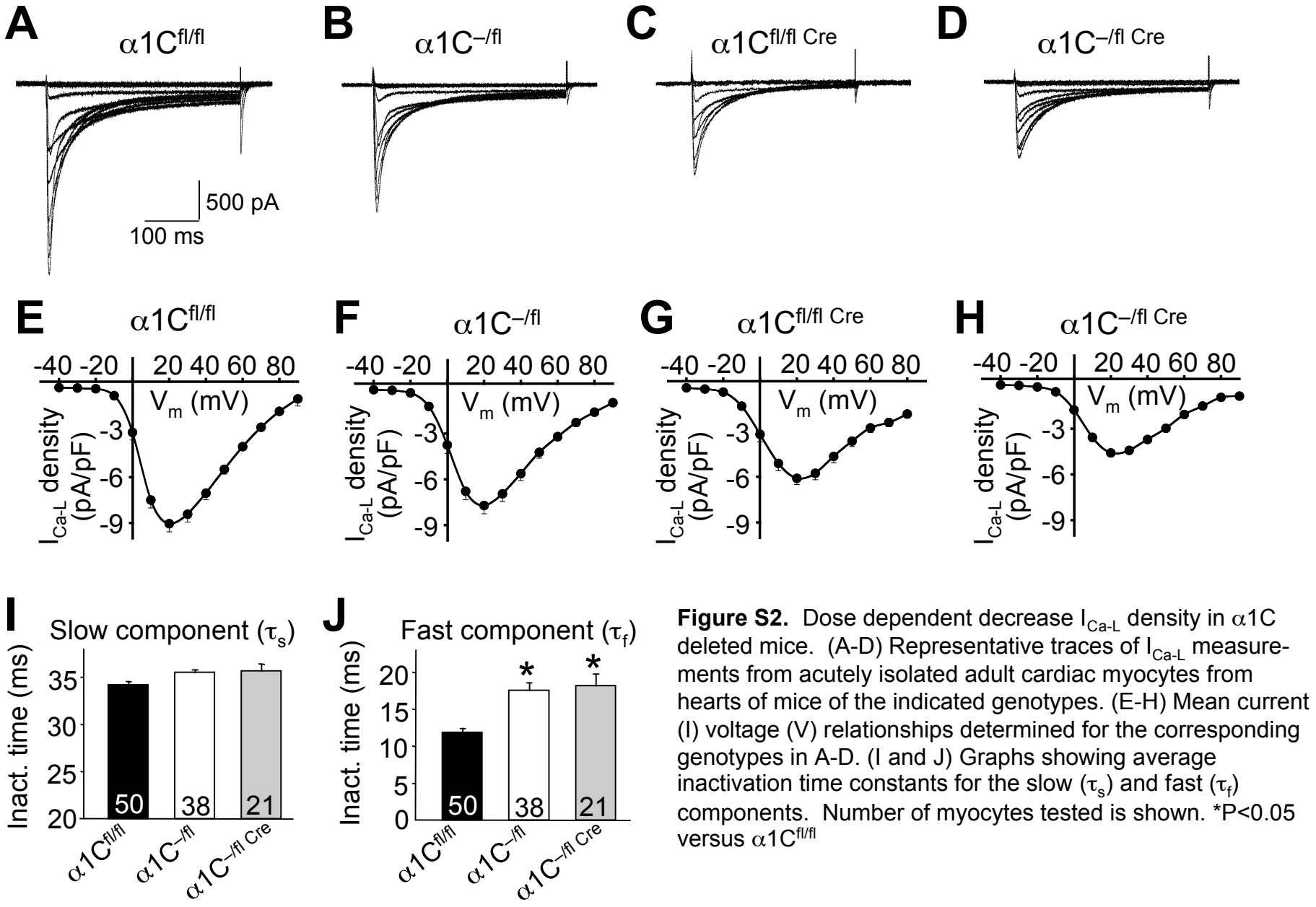

Figure S2. Dose dependent decrease $I_{Ca\text{-}L}$ density in α1C deleted mice. (A-D) Representative traces of $I_{Ca\text{-}L}$ measurements from acutely isolated adult cardiac myocytes from hearts of mice of the indicated genotypes. (E-H) Mean current (I) voltage (V) relationships determined for the corresponding genotypes in A-D. (I and J) Graphs showing average inactivation time constants for the slow (τ_s) and fast (τ_f) components. Number of myocytes tested is shown. *P<0.05 versus $\alpha1C^{fl/fl}$

Supplemental Figure 3

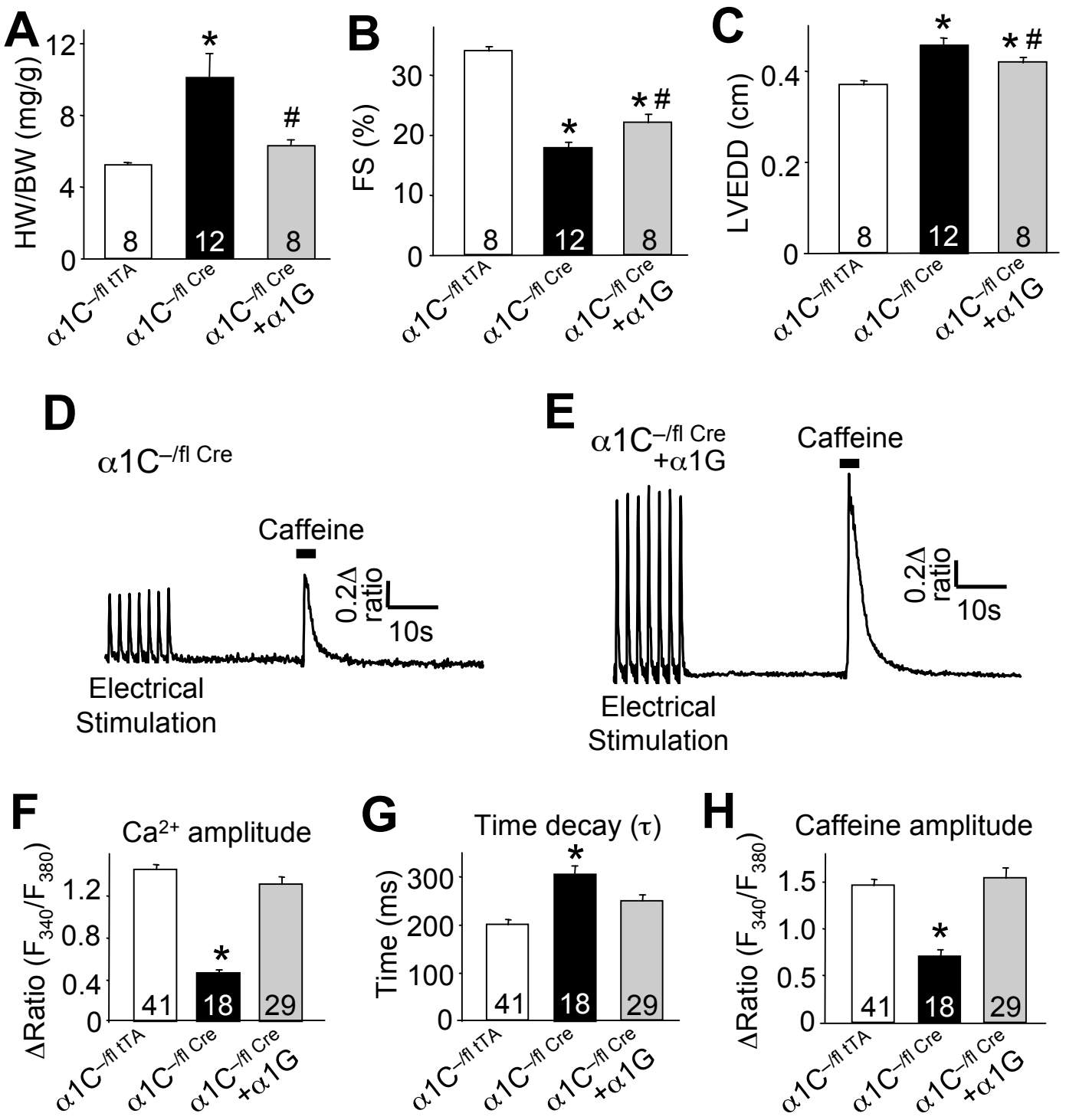

Figure S3. α1G can partially rescue the α1C deleted phenotype in the heart. (A) HW/BW as a measure of cardiac hypertrophy (B) FS%, (C) and LVEDD measured using echocardiographic analysis of control, $\alpha1C^{-/fl\ Cre}$ and $\alpha1C^{-/fl\ Cre}$ mice that also contain the α1G/tTA transgenes. (D and E) Representative traces of the Fura-2 F_{340}/F_{380} fluorescence ratio recorded in $\alpha1C^{-/fl\ Cre}$ and $\alpha1C^{-/fl\ Cre}$ mice that also contain the α1G/tTA transgenes. (F) Mean average amplitude of Ca^{2+} transients, (G) decay time constant, (H) and maximal response to 10 mM caffeine in myocytes from hearts of the the indicated mouse genotypes.

Supplemental Figure 4

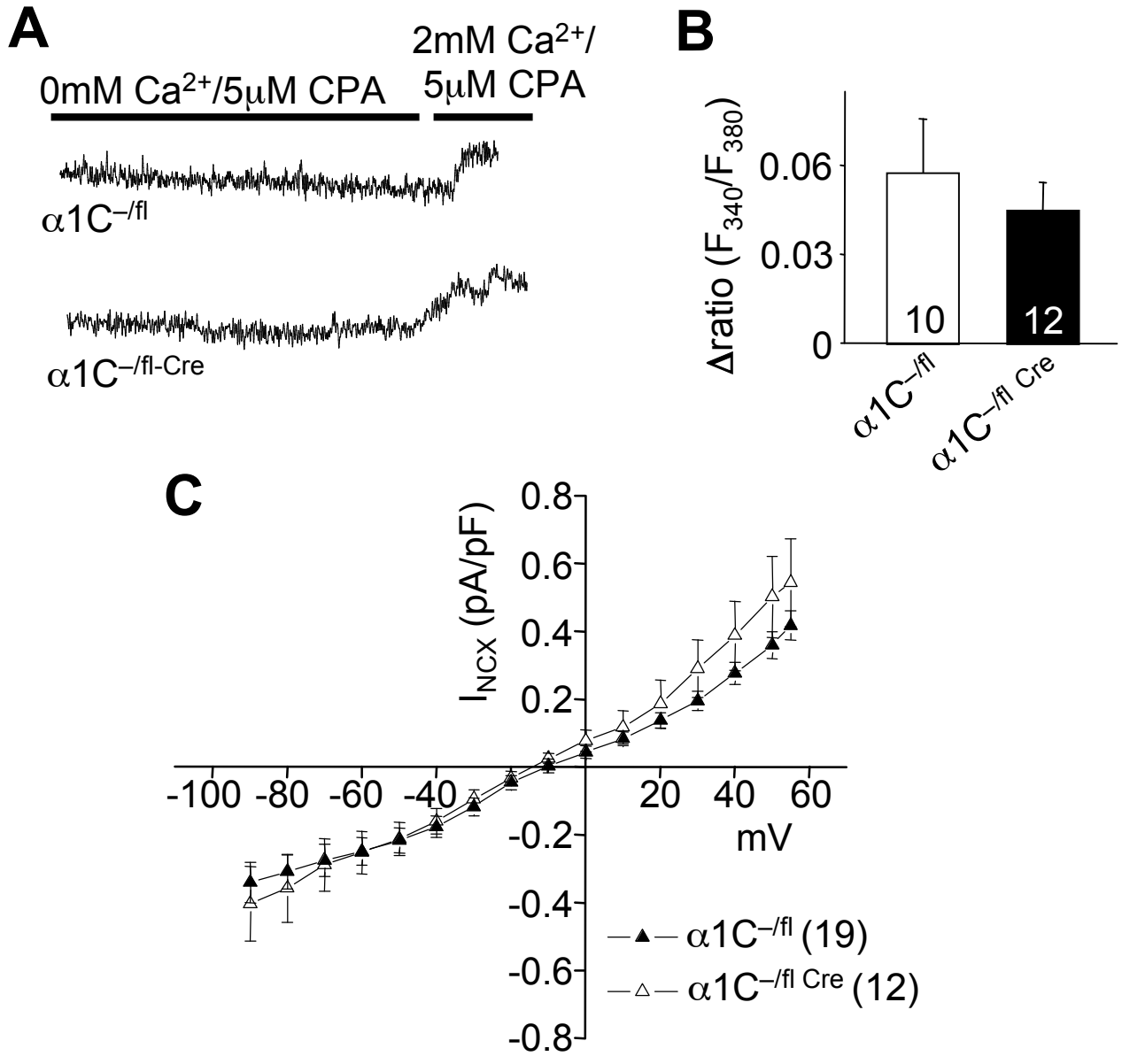

Figure S4. Deletion of α1C does not potentiate store-operated Ca^{2+} entry or NCX activity. (A) Representative traces of fluorescence ratio (F_{340}/F_{380}) recordings to assess store operated Ca^{2+} entry across the sarcolemma in $\alpha1C^{-/fl}$ and $\alpha1C^{-/fl\ Cre}$ myocytes. (B) Maximal average change in amplitude of fluorescence following Ca^{2+} reintroduction in the store operated Ca^{2+} measurements. (C) Current-voltage relationships of I_{NCX} density in myocytes isolated from hearts of $\alpha1C^{-/fl}$ and $\alpha1C^{-/fl\ Cre}$ mice. Total number of myocytes used in the experiments is shown (minimum of 3 mice).

Supplemental Figure 5

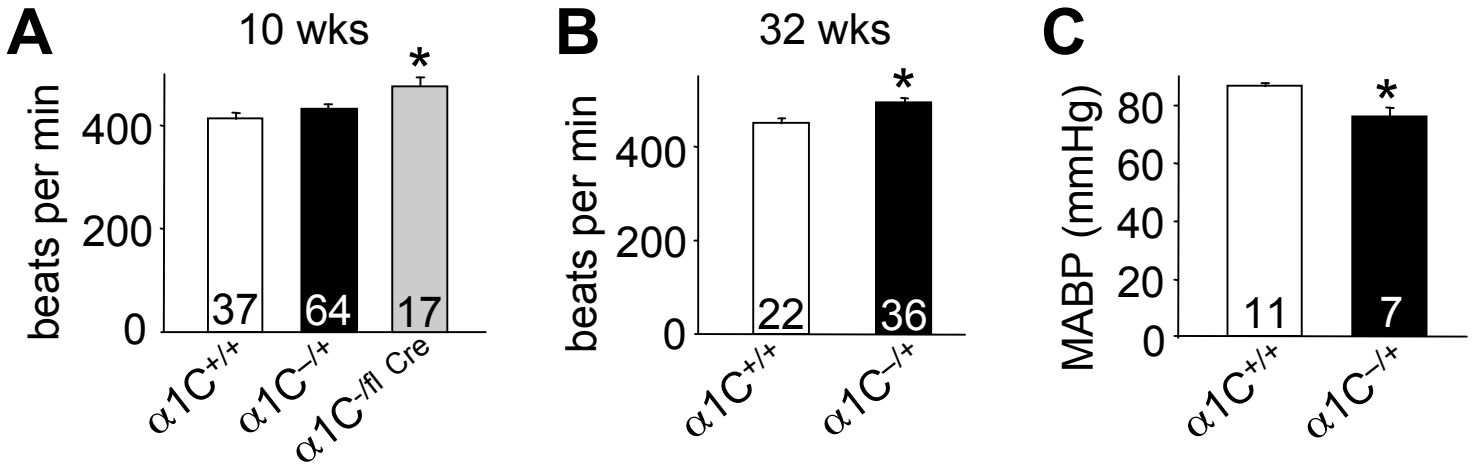

Figure S5. Decrease in α1C leads to a modest increase in heart rate and decreased mean arterial blood pressure. (A) Heart rate calculated from R-R intervals in echocardiographic measurements in mice at 10 (B) and 32 wks. (C) Mean arterial blood pressure (MABP) in the indicated genotypes.
*P<0.05 versus α1C$^{+/+}$

Supplemental Figure 6

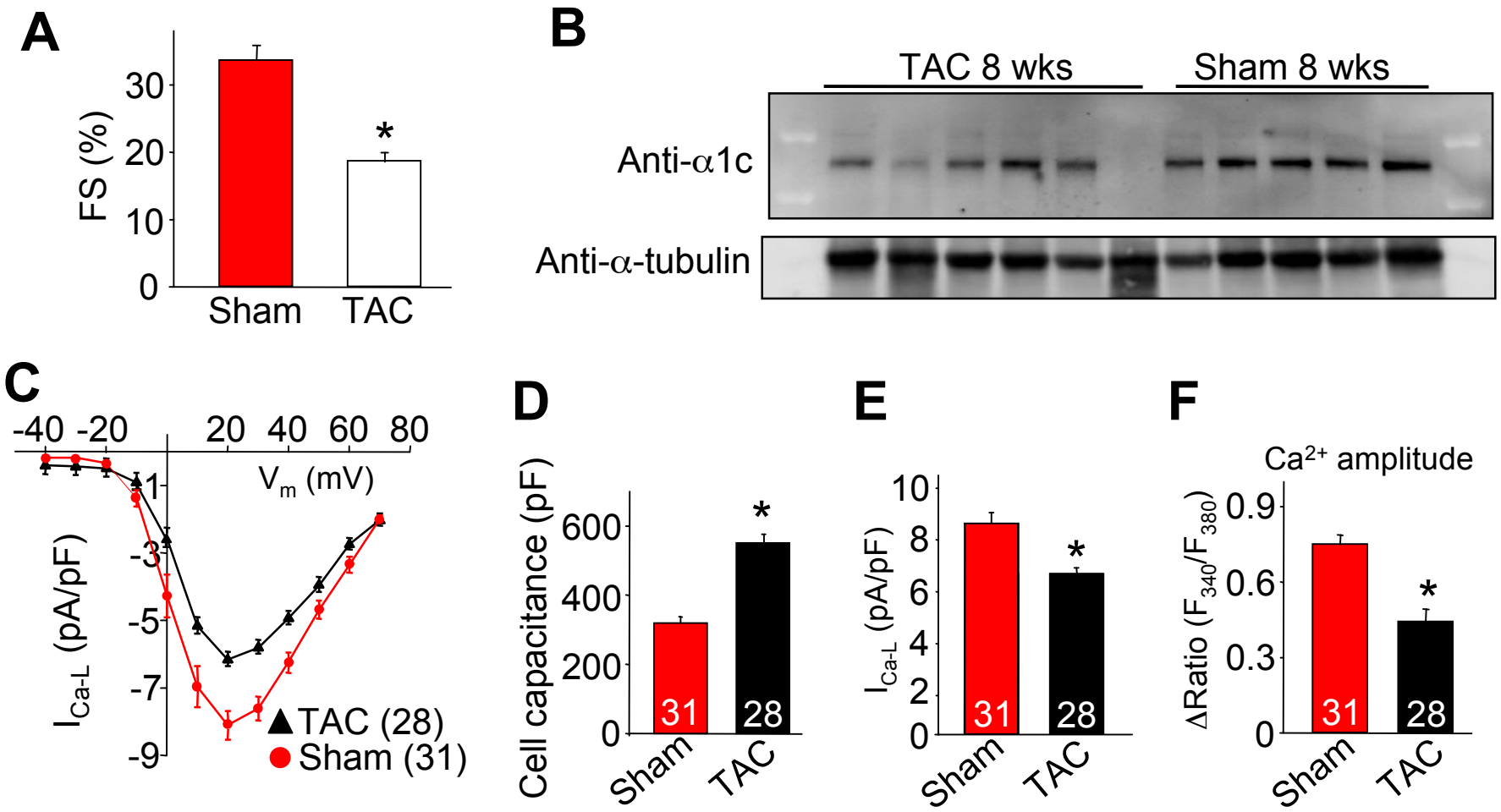

Figure S6. Cardiac dysfunction and remodeling is associated with decreased $I_{Ca\text{-}L}$ density in a mouse model of heart failure. (A) Echocardiographic assessment of FS (%) in wildtype mice subjected to 8 weeks of pressure overload by transverse aortic constriction (TAC). *P<0.05 compared with sham. (B) Western blot analysis of α1C expression or α-tubulin (control) from the hearts of mice described in A. (C) Voltage dependence of $I_{Ca\text{-}L}$ density measured in adult cardiomyocytes isolated from sham-operated and TAC mice. (D and E) Cell capacitance and maximal amplitude of $I_{Ca\text{-}L}$ density recorded in whole-cell patch clamp experiments in myocytes isolated from Sham operated and TAC hearts. (F) Maximal amplitude of electrically evoked Ca^{2+} transients recorded in myocytes isolated from the indicated genotypes. *P<0.05 compared to Sham. Number of myocytes used in the analysis is shown in the panels.