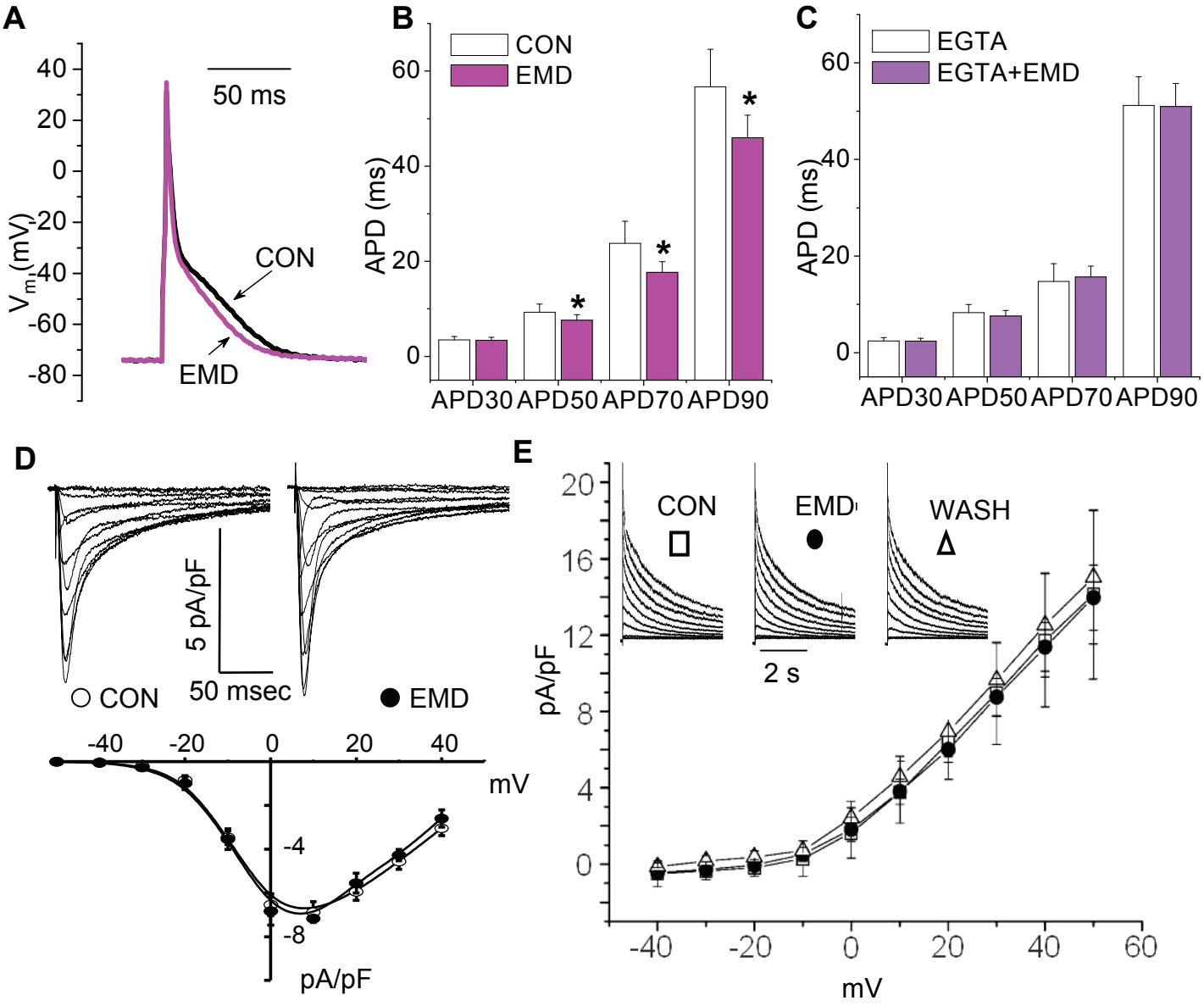
Supplemental Figure 1



Supplemental Figure 1 Effect of EMD (3 µM) on ventricular action potential, L-type Ca^{2+} currents and outward K^+-currents

(A) Membrane potential recording using the perforated patch technique from a mouse ventricular myocyte paced at 4 Hz at baseline (CON) and in presence of EMD).

(B) Mean APD90, APD70, APD50 and APD30 before and after application of EMD. *p<0.05 by paired t-test. N=7 myocytes

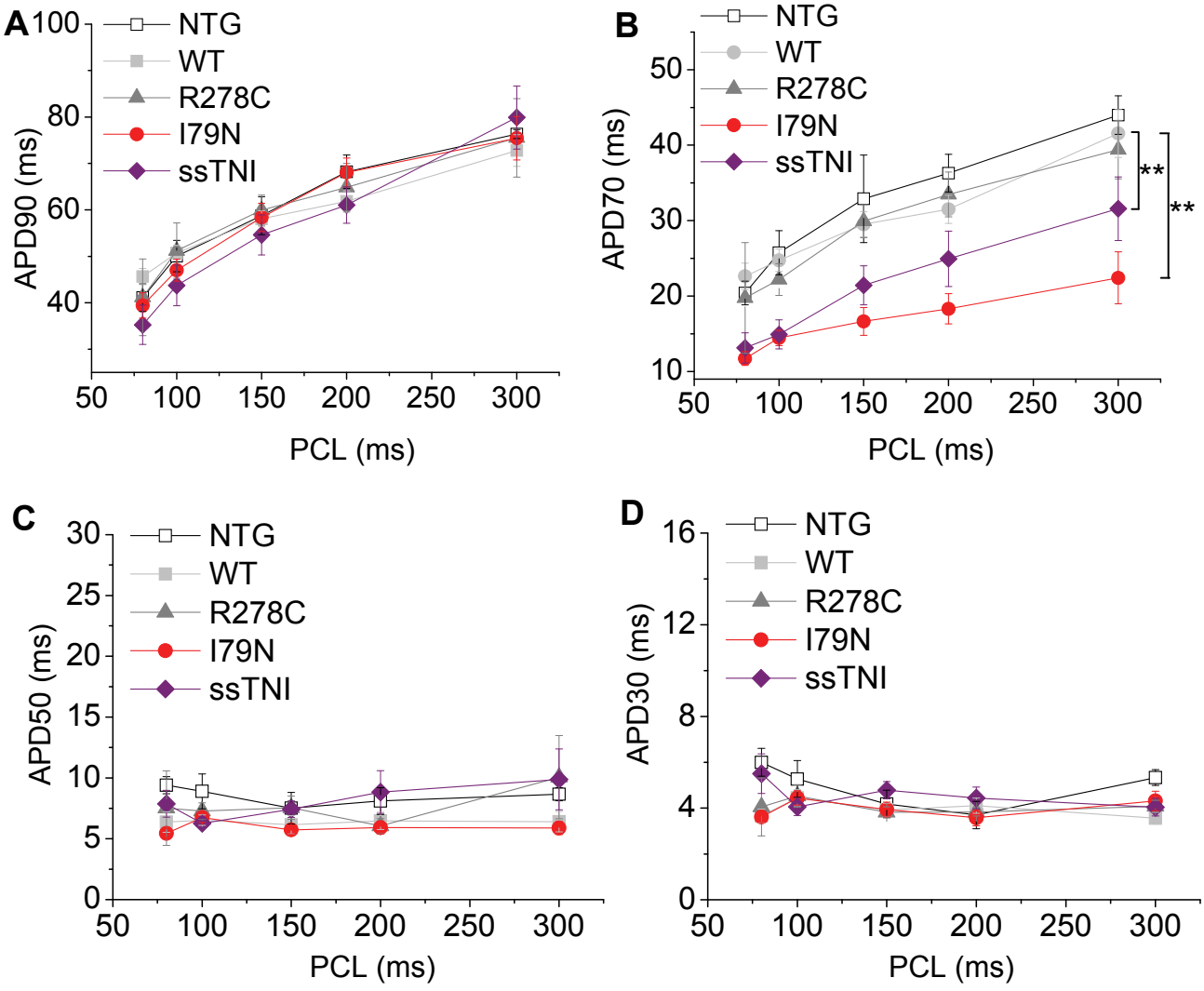
(C) Strong cytosolic buffering with EGTA (14 mM) that prevents myofilament activation and myocyte contraction completely abolishes the effect of EMD on mean APD90, APD70, APD50 and APD30. N=12 myocytes

(D) L-type Ca^{2+} currents recorded in response to step-wise membrane depolarizations. EMD has no significant effect. N=8 myocytes

(E) Voltage-gated outward K^+ currents recorded in response to step-wise membrane depolarizations. EMD has no significant effect. N=9 myocytes

All current and voltage clamp studies were carried out with experimental solutions and voltage protocols as described in: Knollmann, B.C., Kirchhof, P., Sirenko, S.G., Degen, H., Greene, A.E., Schober, T., Mackow, J.C., Fabritz, L., Potter, J.D., and Morad, M. 2003. Familial hypertrophic cardiomyopathy-linked mutant troponin T causes stress-induced ventricular tachycardia and Ca2+-dependent action potential remodeling. Circ Res 92:428-436.

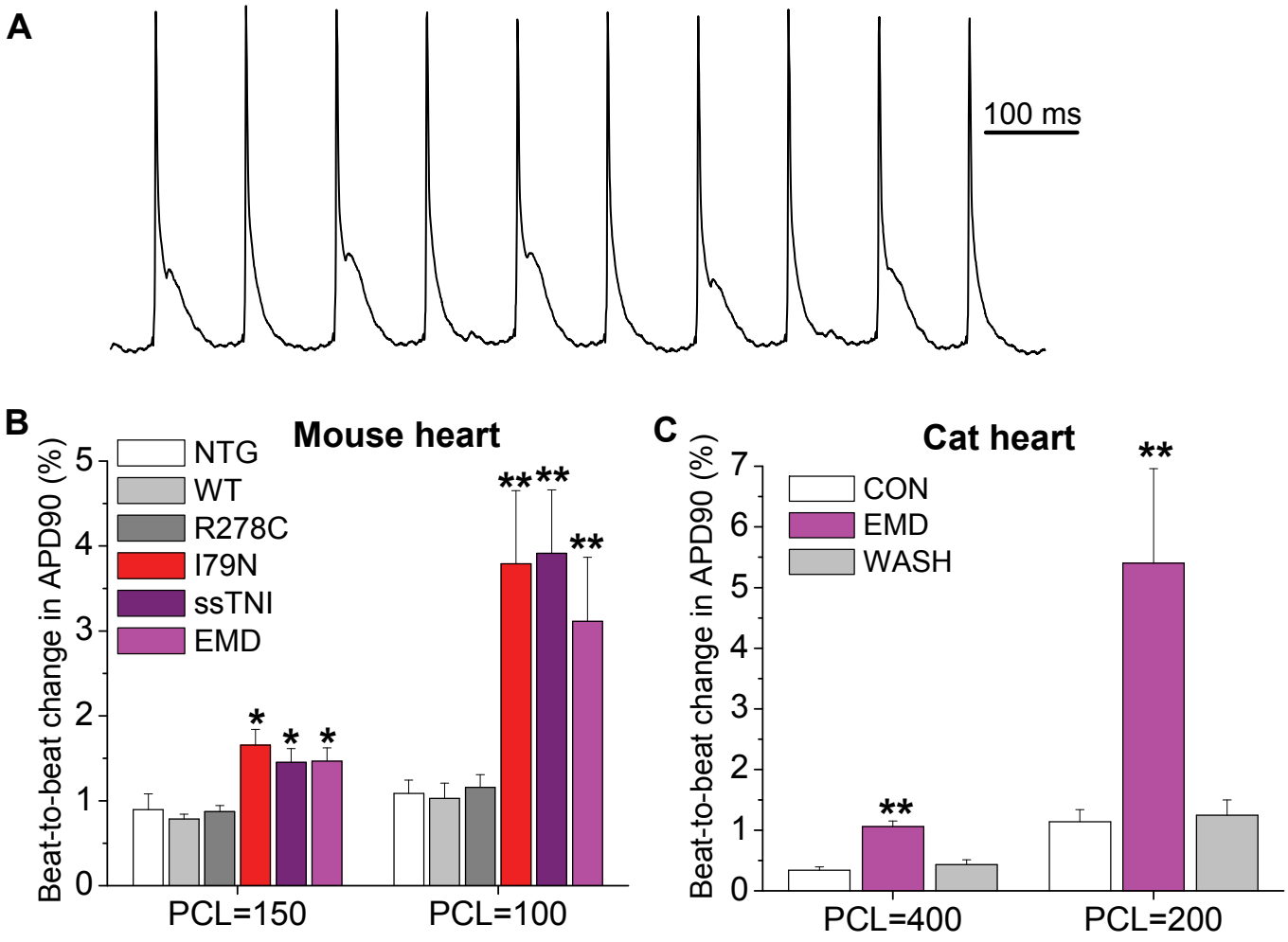
Supplemental Figure 2



Supplemental Figure 2 Ca^{2+} sensitized transgenic hearts exhibit APD70 shortening at all pacing rates.

(A-D) Average AP durations meaured at 90% (APD90, panel **A**), 70% (APD70, panel **B**) 50% (APD50, panel **C**), and 30% repolarization (APD30, panel **D**) plotted as function of pacing cycle length (PCL). Note that Ca^{2+} sensitized transgenic hearts (I79N and ssTNI) exhibited significantly shortened APD70 at all pacing rates. APD90, APD50 and APD30 were not significantly different from NTG or WT hearts. NTG n=6 hearts, WT n=12, R278C n=6, I79N n=11, ssTNI n=6. **p<0.01 by 2-way ANOVA with repeated measures compared to WT or NTG.

Supplemental Figure 3



Supplemental Figure 3 Beat-to-beat APD instability is significantly increased in Ca^{2+}-sensitized mouse and cat hearts.

(A) Example of a prominent APD alternans in an I79N heart. Pacing cycle length (PCL) = 100 ms. **(B-C)** Average beat-to-beat instability in APD90 of mouse (**B**) and cat (**C**) hearts at two different pacing rates. APD instability increased with faster pacing predominantly in the Ca^{2+} sensitized hearts. To quantify APD instability, the absolute difference in the APD90 between two consecutive beat was measured and expressed as % of APD90. For each heart and each pacing rate, 7-10 consecutive beats were analyzed and averaged. N = 6-7 mouse hearts per group, n = 7-9 recordings from 4 cat hearts per group, *p<0.05, **p<0.01 compared to NTG and WT for mouse hearts and compared to CON and WASH for cat hearts by Mann-Whitney Test.