Supplemental Material

Ca^{2+} signaling in human induced pluripotent stem cell-derived cardiomyocytes (iPS-CM) from normal and catecholaminergic polymorphic ventricular tachycardia (CPVT)-afflicted subjects.

by

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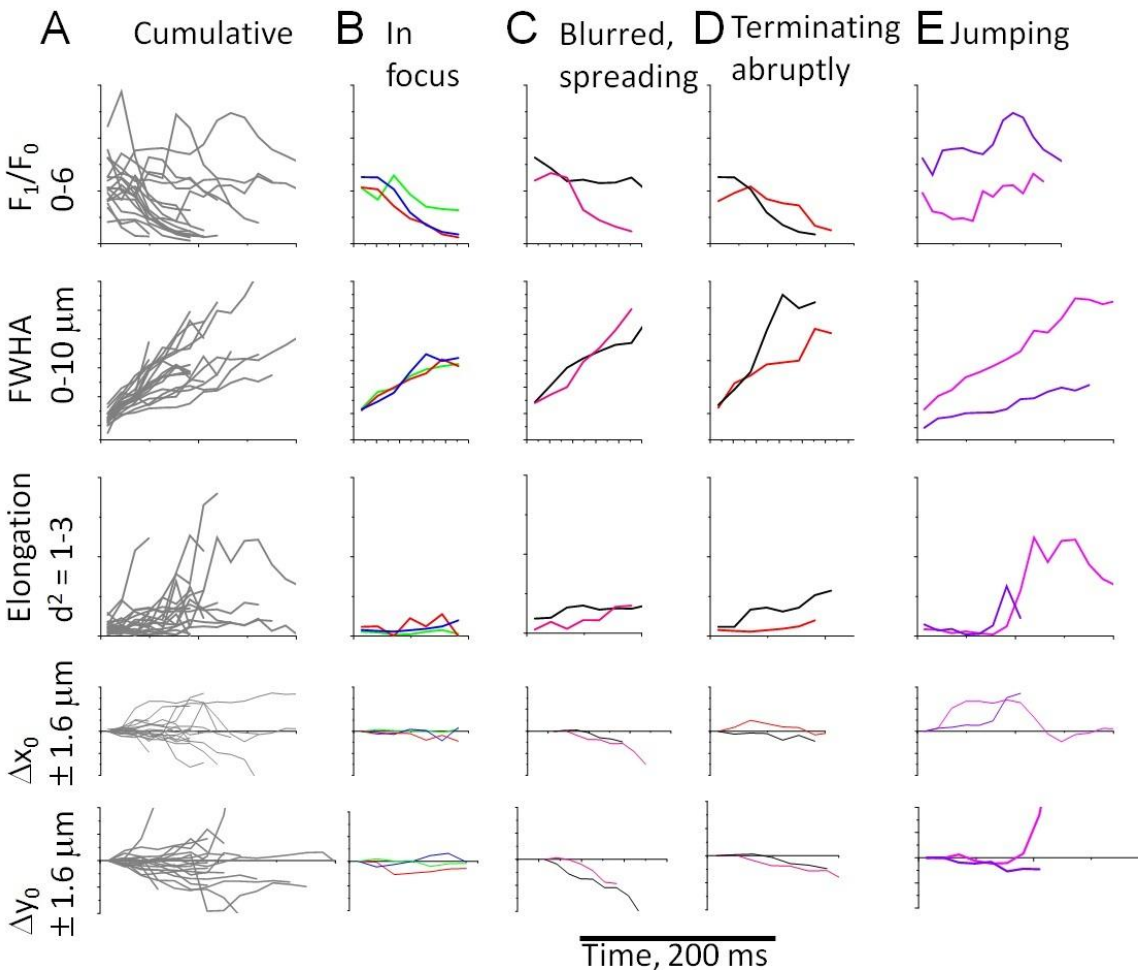
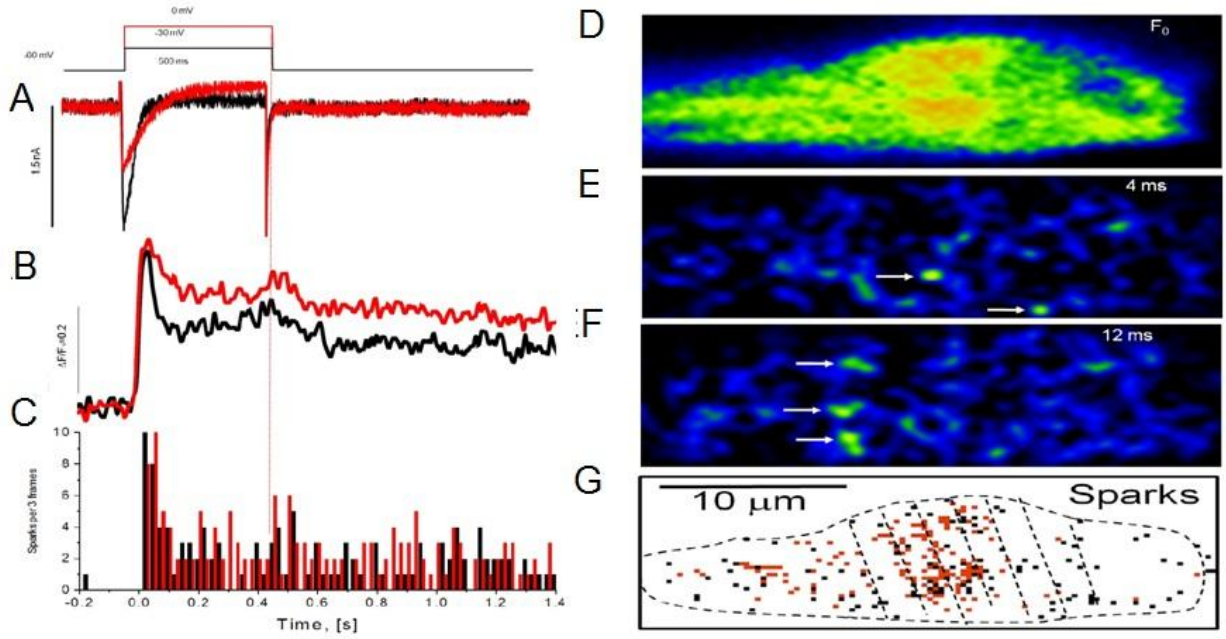
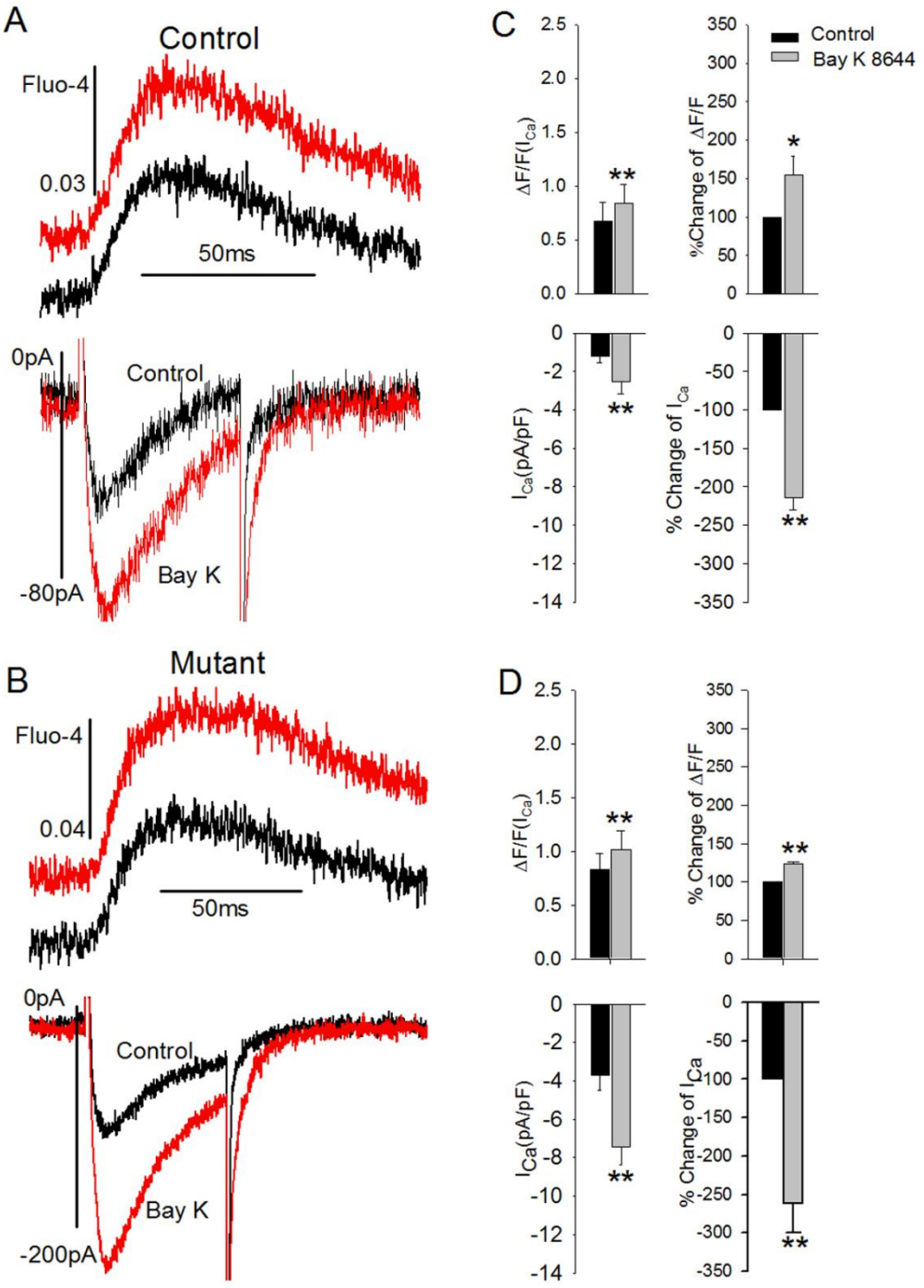


Supplemental Figure 1. Unitary properties of Ca^{2+} sparks. From top to bottom each panel illustrates the time course of local Ca^{2+} releases in terms of their amplitude (F_1/F_0), full-width-at-half-amplitude (FWHA), "elliptical elongation" (d^2), and shifts in location (Δx_0 and Δy_0). A: Distribution of measurements. The individual traces are interpreted as follows: B: Three ordinary Ca^{2+} sparks (red, blue, and green) with a well-defined center of release within the evanescent

field of illumination. C: Diffuse Ca^{2+} releases suggesting Ca^{2+} release outside the evanescent field or asymmetric spread. D: Abrupt termination of long-lasting Ca^{2+} sparks. E: Local Ca^{2+} releases with rapidly shifting centers.



Supplemental Figure 2. Sarcomeric Ca^{2+} release in voltage-clamped elongated iPS-CM. A subset of iPS-CM were elongated and showed some indication of sarcomeric striping as found in adult ventricular cardiomyocytes [2]. A: Membrane currents measured with depolarizing pulses from -60 mV to -30 mV (black) and 0 mV (red). B: Cellular transients of Ca^{2+}-dependent Fluo-4 fluorescence ($\Delta F/F_0$). C: Frequency of Ca^{2+}-sparks binned per 3 frames of 4.17 ms. D: Average fluorescence intensity (F_0). E & F Sample frames showing Ca^{2+} sparks 4 (E) and 12 ms (F) after depolarization from -60 to 0 mV (arrows). G: Distribution of Ca^{2+} sparks. The dashed lines suggest the presence of a faint sarcomeric pattern. Confocal measurement at 240 Hz.



Supplemental Figure 3. Effects of the Ca^{2+} channel agonist Bay K8644 on I_{Ca} and Ca_i-transients in control and mutant iPS-CM. A and B: representative I_{Ca} traces and the corresponding Ca^{2+} fluorescence in control (a and b) and mutant (c and d) iPS-CM before and after exposure to Bay K. The voltage-clamped cells were depolarized to 0 mV from a holding potential of -40 mV. C and D: Average values of peak I_{Ca} and fluorescence in each group before and after Bay K.