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Supplemental information

Optical modulation of excitation-contraction coupling in human-induced pluripotent stem cell-derived cardiomyocytes

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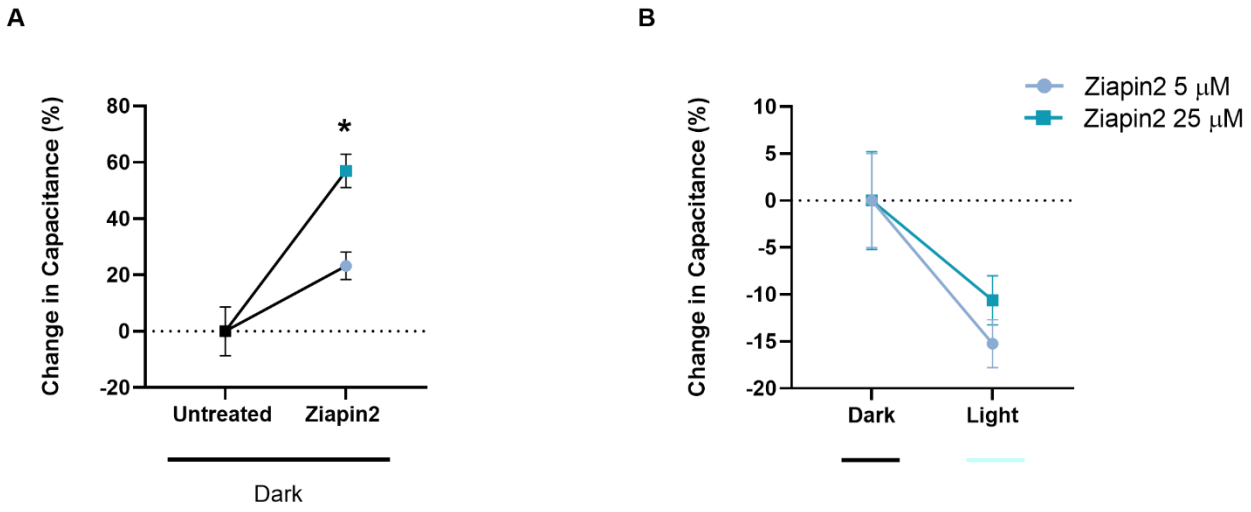

Figure S1. Ziapin2-mediated modulation of membrane capacitance. Evaluation of capacitance changes in hiPSC-CMs upon Ziapin2 membrane partitioning (**panel A**) and photoisomerization (**panel B**). Ziapin2 5μM represented with light blue dots while 25 μM in teal squares. Light power density, 80 mW/mm^2. The experiments were carried out at room temperature (24°C). n = 15 and 20 for untreated and Ziapin2-loaded cells respectively from three independent differentiations. Data are represented as mean ± SEM.

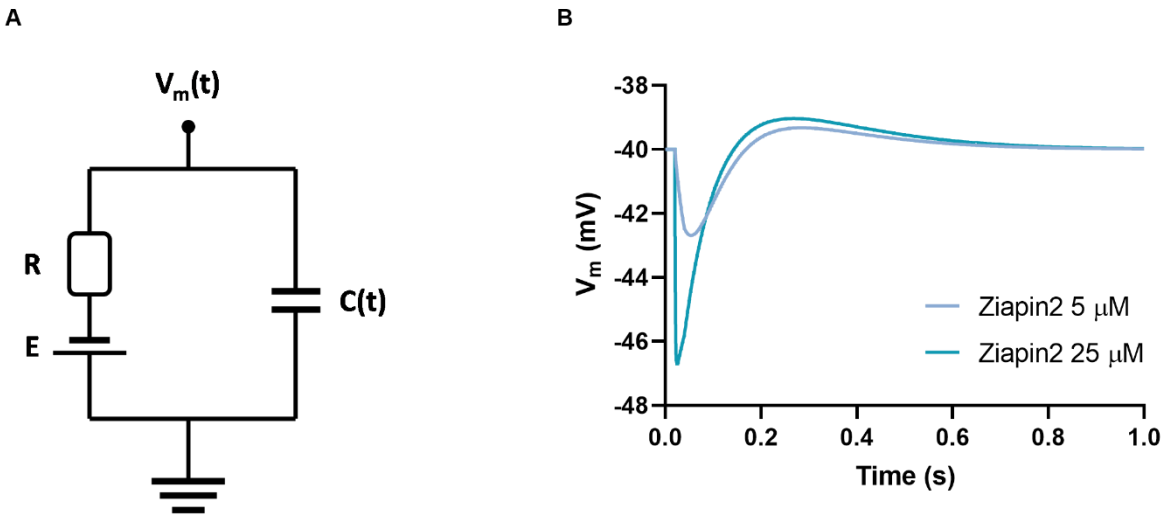

Figure S2. Simulation of membrane voltage. Simulated equivalent circuit (**panel A**) and capacitance-induced membrane potential variation (**panel B**). This simulation, performed as previously described,[46] mimics the effect of a 20 ms light pulse on Ziapin2 photoisomerization (a capacitance variation) and subsequent membrane potential modulation. To reproduce the observed effect, only the photoisomerization characteristic time has been reduced (t_{hyp} = 35 ms for 5 mM and t_{hyp} = 1 ms for 25 mM). This could be consistent with the localization of Ziapin2 in membrane domains more prone to favour isomerization.

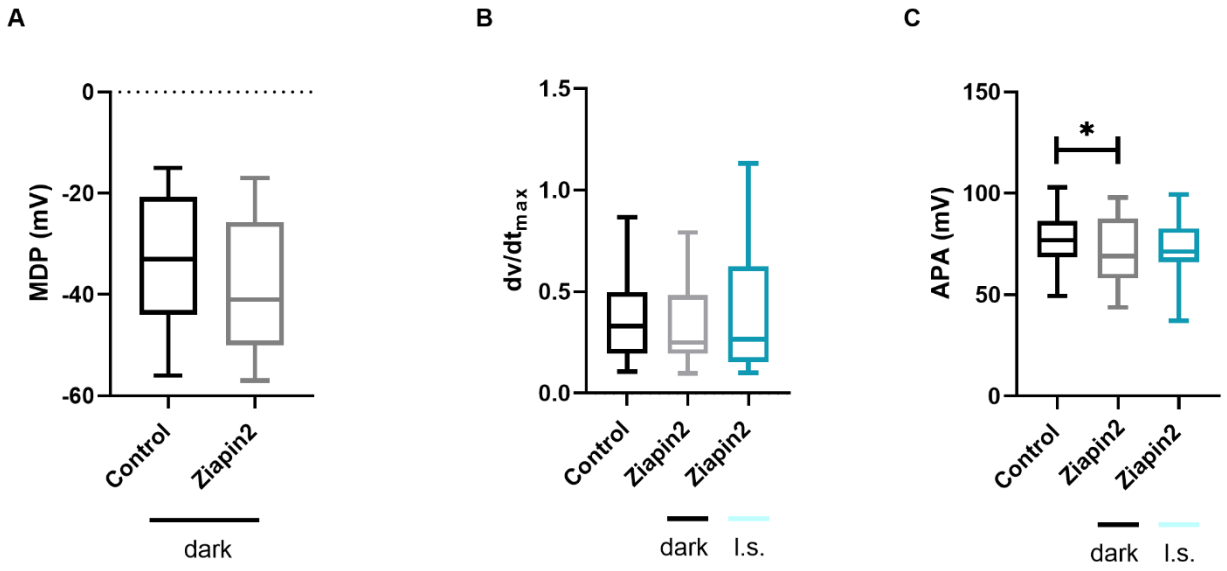

Figure S3. AP parameters in hiPSC-CMs exposed to Ziapin2. Comparison of the maximum diastolic potential (MDP, **panel A**), maximal rate of rise (dv/dt_{max}, **panel B**) and AP amplitude (APA, **panel C**) between spontaneous and light-evoked APs in 25µM Ziapin2 loaded hiPSC-CMs (n > 40 for each condition from three independent differentiations). Data are presented as box and whiskers plot (min to max). Light power density, 80 mW/mm^2. The experiments were carried out at room temperature (24°C). * $p < 0.05$.

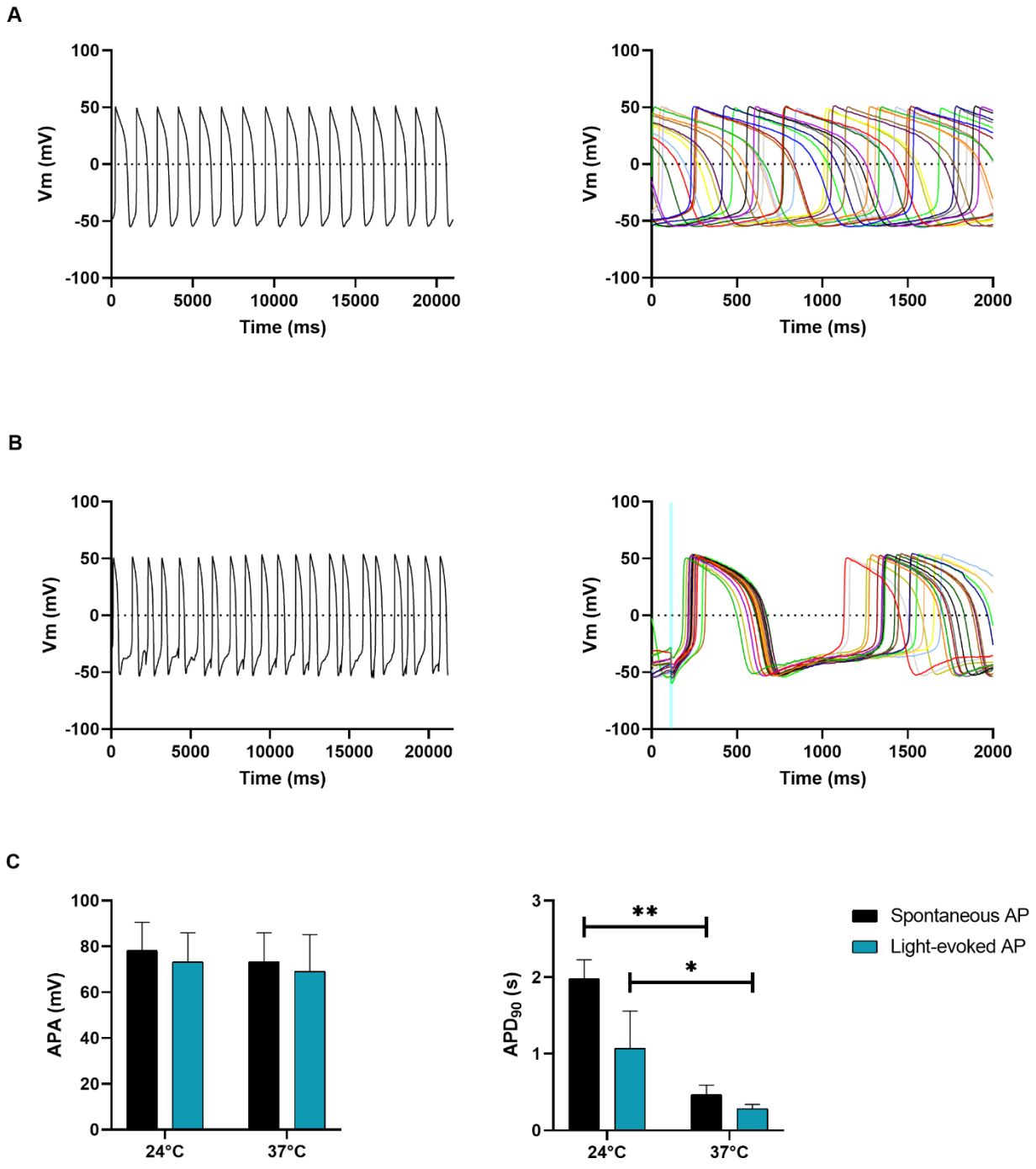

Figure S4. Light-induced Vm modulation in Ziapin2 loaded hiPSC-CMs at 37°C. A) Representative trace of spontaneous APs (left) and their distribution over a 2 second timescale (right). **B)** Representative trace of light-evoked APs (left) and their distribution over a 2 second timescale (right). The APs were generated in response to a light train stimulation (20 ms cycle length; 0.5 Hz stimulation frequency, represented as cyan shaded areas). Light power density, 80 mW/mm^2. The experiments were carried out at 37°C. **C)** Comparison between spontaneous and light-evoked AP parameters (i.e., AP amplitude, APA and AP duration at 90% of repolarization, APD_{90}) recorded either at room temperature or at 37°C ($5<n<30$, data are shown as mean ± SEM). * $p < 0.05$, ** $p < 0.01$.

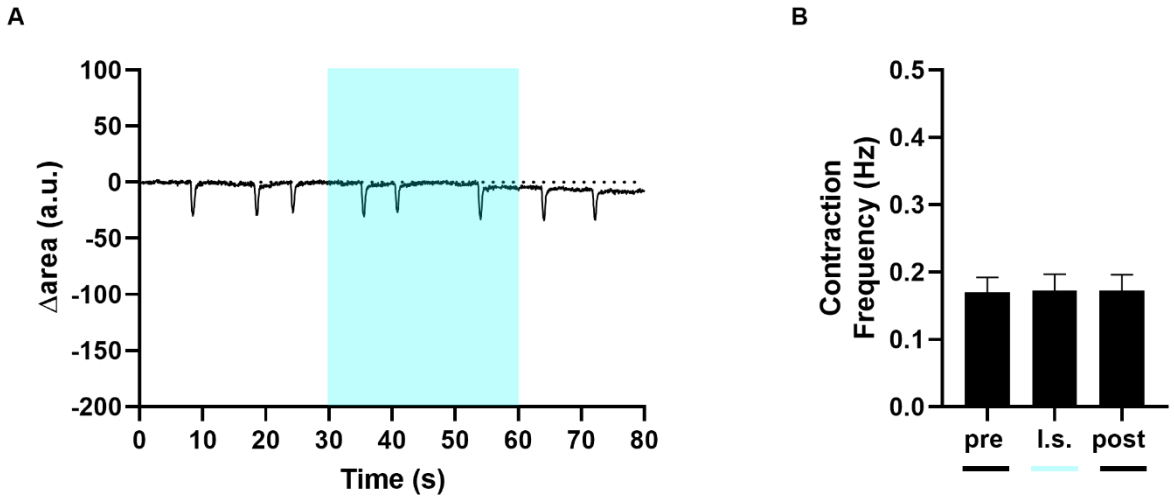

Figure S5. Light-induced contraction rate modulation in hiPSC-CMs incubated with vehicle. A) Representative trace of the contraction behaviour of DMSO-treated hiPSC-CMs. **B)** Contraction frequency before (pre), during (l.s.), and after (post) 1 Hz pulsed light stimulation at light power density = 30 mW/mm^2 (n = 25 from three independent differentiations, data are shown as mean ± SEM). The experiments were carried out at room temperature (24°C).