Optogenetical Modulation of Anion Channelrhodopsins (GtACR1) on Myocardial Electromechanical Properties: A Computational Study

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Aims: Over the past decade, optogenetic tools have been proposed as powerful means to modulate cardiac physiological and pathological activities. Cation non-selective Channelrhodopsin (ChR) has been extensively corroborated that it can depolarize the membrane potential in cardiomyocytes (CMs) and elicit action potentials (APs). By contrast, Guillardia theta Anion Channelrhodopsin (GtACR1) shows efficient photoinhibition and is used for silencing CM activity. Accordingly, we designed a computational study to assess the effects of GtACR1 on electromechanical characteristics of CM.

Methods: Mathematical modeling was done using a combination of a module of excitation-contraction coupling in the CM and a module of GtACR1 photocurrent kinetics. We simulated light sensitization of GtACR1. To analyze consistency of electrophysiological and mechanical effects, we varied light pulse timing (1–80 ms) and intensity (0.001–10 mW/mm^2).

Results: The simulation results showed that optically paced CM displayed a slower AP onset than that of electrically paced CM, and both prolonged light pulses and enhanced light intensity inhibit CM activation and contraction.

Conclusion: Our findings suggest that GtACR1 plays an important role of optogenetical modulation on CM electromechanical properties. It should be considered in future pathological cardiac mathematical modeling.