Non-integrating, transient optogenetic modification of human iPSC-derived cardiomyocytes using ChR2 and GCaMP6f mRNAs

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Abstract:

Monolayers of human iPSC-derived cardiomyocytes (hiPSCM) reveal spontaneous rhythmic beating which can be monitored either by means of microelectrode array recording of extracellular field potentials or by kinetic fluorescent plate readers using calcium- or voltage-sensitive dyes. Furthermore, the beat rate determines the duration of the field potentials (FPD) as well as the calcium transient (CTD) in a reverse use- dependent manner. However, to understand drug mediated frequency changes, hiPSCM require a frequency correction of the FPD/CTD according to experimentally determined restitution curves or, preferably, cells can be paced by electrical means to beat at a constant rate. To address this experimental limitation, we present a novel lipid-based transfection method which allows for a highly efficient and non-integrating optogenetic modification of hiPSCM using channelrhodopsin 2 and GCaMP6f (calcium sensor) mRNA. First, channel rhodopsin 2 mRNA was transfected into hiPSCMs which were then cultured and measured on Axion Maestro microelectrode arrays and CardioExcyte NSP96 plates. The channel rhodopsin 2 enabled the cells to be paced by optical stimulation (blue light) at defined rates for more than 2 weeks using the new Lumos light delivery system for the Axion Maestro or the CE96 optical stimulation system currently under development for CardioExcyte, respectively. Importantly, cells followed pacing frequencies from 1.5 Hz up to 5 Hz (higher frequencies were not tested).