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Red light-absorbing conjugated polymer optically modulates Ca^{2+} dynamics in cardiomyocytes derived from human induced pluripotent stem cells

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1. Introduction

Human induced pluripotent stem cell derived-cardiomyocytes (hiPSC-CMs) are widely recognized as a valuable experimental model to study mechanisms of cardiovascular diseases. They recapitulate *in vitro* the patient-specific genotype, providing a powerful tool for the development of more targeted therapies.

Photo-stimulation by conjugated polymers, used as exogenous light-sensitive actuators, is a novel approach to modulate the cellular activity with high spatial and temporal resolution, permitting lower invasiveness and high selectivity.

Hence, the potential of photo-stimulation to modify the electrophysiological and Ca^{2+} signaling properties of hiPSC-CMs will be extremely relevant for their potential use in cardiovascular disease therapies.

2. Aim:

To investigate the effects of photomodulation, mediated by a red light-absorbing conjugated polymer substrate, on function of hiPSC-CMs.

3. Methods:

hiPSC-CMs were plated on a red light-absorbing conjugated polymers substrate, namely Poly[2,6-(4,4-bis-(2-ethylhexyl)-4H-cyclopenta [2,1-b;3,4-b′]dithiophene)-alt-4,7(2,1,3-benzothiadiazole)] (PCPDTBT), in the form of thin film, which is characterized by a low energy gap and high charge generation efficiency. Glass was used as reference.

Active polymer photoexcitation is provided by a red-light source on restricted spatial regions through an upright fluorescence microscope. Measurements without photoexcitations were used as reference (dark). Fluo4-AM, with a negligible spectral overlap with the PCPDTBT optical absorption, was used to evaluate the spontaneous Ca^{2+} dynamics. Thapsigargin was used to assess the sarcoplasmic reticulum Ca^{2+} re-uptake. The experiments were performed at physiological temperature (37 °C).

4. Results:

The incidence of spontaneous Ca^{2+} transients and hiPSC-CMs having a regular beating was similar between cells plated on PCPDTBT and controls, both in dark and upon illumination.

Red light induced a faster Ca^{2+} transient decay in both groups; however, the red-light modulation was larger in hiPSC-CMs plated on PCPDTBT. Furthermore, at the highest power densities of excitation the red light photo-stimulation mediated by PCPDTBT induced an enhancement of beating frequency.

Under red-light stimulation, PCPDTBT reduced the inhibitory effect of thapsigargin on Ca^{2+} transients; more cells exhibited Ca^{2+} transients after partial SERCA2a block.

5. Conclusions:

Current work aims to elucidate the physiological mechanisms underneath the photo-stimulation mediated by a red light-absorbing conjugated polymer. These results confir the biocompatibility of PCDPTBT for hiPSC-CMs with and without photoexcitation and suggest that the photomodulation mediated by PCDPTBT influences the Ca^{2+} reuptake through an indirect modulation of SERCA2a activity.