РАЗДЕЛ III

БИОФИЗИКА

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OPTICAL CONTROL OF INTERCELLULAR CALCIUM DYNAMICS IN INDUCED PLURIPOTENT STEM CELL-DERIVED CARDIOMYOCYTES WITH HYPERTROPHIC CARDIOMYOPATHY*

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Abstract

Since the treatment of hypertrophic cardiomyopathy (HCM) is symptomatic and given the lack of early diagnostic methods [1], the development of targeted therapies and diagnostic tools that can detect early alterations in excitation abnormalities in HCM patients is important to improve the condition of the patients and stop the progression of the disease. Implementing patient-specific induced pluripotent stem cells-derived cardiomyocytes has an advantage as it allows testing specific therapeutic interventions for a specific case. Moreover, the combination of experimental and computational approaches to explore additional parameters and mechanisms involved in HCM, will help uncover new therapeutic targets and strategies.

Hypertrophic cardiomyopathy is one of the most common inherited cardiovascular diseases affecting one in 500 people globally [2]. It is mainly caused by mutations encoding sarcomere-associated proteins [3]. The most common treatment options for HCM are those that aim to relieve the symptoms and the risk of sudden cardiac death [4]. However, there is still no efficient treatment for HCM and a better understanding of the pathogenicity of this disease will help to improve early diagnostic and therapeutic methods. Using induced pluripotent stem cells-derived cardiomyocytes model is of great importance that enables us to study HCM features . In this study, two iPSC lines, including a control cell line (m34Sk3) and patient-derived cell line (HCM-11f3), were differentiated into cardiomyocytes. Optical mapping was conducted at different timepoints of the differentiation process to measure calcium and voltage changes. Computational modeling approach was also applied to investigate the changes in calcium dynamics. Results showed differences in HCM features like calcium concentration before the 30th day of the differentiation process in the diseased cell line. In order to use the experimentally measured action potential as input data for modeling, removing the noise using activation map seemed to be efficient for our data. Computational modeling results showed the main parameters that may affect the differences in calcium dynamics between healthy and diseased cell lines.

This study will help to develop a more detailed understanding and description of the calcium disturbance mechanisms in hypertrophic cardiomyopathy. Moreover it will develop a better understanding of the arrhythmia occurrence and further improve the diagnostics and the therapeutics methods of HCM and arrhythmia.

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