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ELECTROMECHANICAL MEMORY OF CARDIOMYOCYTES

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Myocarditis is an inflammatory condition of the heart muscle that frequently leads to chronic heart failure months or years after acute inflammation is resolved. According to American Heart Association, among 15 per 100 000 are found annually which make the problem is on top of discussion. There are several ways of inflammation treatment, but still it requires more investigation work.

We propose the concept of electromechanical memory as a promising way to encode mechanical stress and explain reasons of changes in contractile myocardium.

Our aim was lying down in establishment of electromechanical memory as a distinct mechanism explaining persistent myocardial dysfunction following resolved myocarditis.

In recent years a lot of studies are concentrated on electrical remodeling for analysis of ion channels damages, the problem of action potential prolongation, and disruption of gap junctions in contractile myocardium. This model helps to investigate presence of arrhythmias and abnormalities in electrocardiogram (ECG). Stimulus such as mechanical stress and inflammation result in changes of contractile myocardium sarcomere structure, that in turn can activate altered pathways of proteins work. However, the question of impaired relaxation is hard to investigate using only ECG data. The electrical modelling model cannot fully explain persistent mechanical dysfunction of contractile myocardium in patient after inflammatory process ends. So, there is the need to find new ways to analyze continuous myocardial stiffness and impaired contractility.

Persistent dysfunction without active inflammation is found in patients after myocarditis. Electrical remodeling cannot explain the reasons of consequences of myocarditis such as diastolic dysfunction, increased heart stiffness, impaired contractility, and persisted failure. However, the concept of electromechanical memory describes the prior mechanical stress within a cardiomyocyte structure and signaling machinery during inflammation that continues even after it resolves.

Based on electromechanical memory model we can explain three proposed mechanisms leading to heart dysfunction.

Firstly, titin modification as a result of unfolding hidden parts of its structure. According to this mechanism, under oxidative stress titim modifies its cryptic cysteines. It results in decreased elasticity of cardiomyocyte, and stretching and relaxing of contractile cells become impossible.

Secondly, mechanotransudction of YAP/TAX changes the ability of force sensitivity. Under normal conditions there is “off” position of YAP so hypertrophy of heart is not found. But during inflammation the tendency to myofibroblast differentiation is increased, and the size of cells becomes bigger. Moreover, YAP is stuck at “on” position, and it leads to thickened heart which loose its ability to contract normally.

Thirdly, physical force activates hidden titin kinase which turns in Ca^{2+} overload. As a result, it increases arrhythmia risks and altered resting membrane potential that in turn leads to sustaining electrical, metabolic, and functional effects.

These three mechanism together are making the electromechanical memory model the most useful concept of investigating consequences of heart inflammation. Even if there are still unstudied problems such as temporal window or cell-type specificity, electromechanical memory concept can be used for further analysis for deep understanding of how mechanical (physical) history of heart work can become molecular memory.

In conclusion, we advise the usage of electromechanical model as a framework for further researches to find o way of reversing inflammation consequences.