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Abstract

Mathematical Modeling of the Role of Electrophysiological Coupling in Mesenchymal Stem Cell Enhancement of Cardiomyocyte Function

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Human mesenchymal stem cell delivery has exhibited potential in clinical myocardial infarction therapies; however, the large-scale application of this method is limited by the fact that researchers do not fully understand the mechanisms by which mesenchymal stem cells enhance cardiomyocyte function. Mathematical modeling is a powerful tool that can predict how mesenchymal stem cells interact with cardiomyocytes. Therefore, to better understand the electrical role of mesenchymal stem cells, three novel electrophysiology models were developed. The consequences of electrical interactions between cardiomyocytes and mesenchymal stem cells were predicted by coupling the ten Tusscher cardiomyocyte model to the three novel models developed in this study. Significant electrophysiological consequences were evident when the ten Tusscher model was coupled to each of the mesenchymal stem cell models in ratios of 9:1, 4:1, and 1:1, respectively. These effects include decreases in action potential duration and plateau height, and corresponding variations in ionic current. Furthermore, there was a decrease in conduction velocity and maximum upstroke velocity. These consequences correspond to established *in vitro* electrical effects, and show mesenchymal stem cells are capable of predisposing re-entrant arrhythmias. A sensitivity analysis on the mesenchymal stem cell inputs shows the robustness of the results. Overall, this model provides promising insight into the electrical interactions between the two cells types, and can be used in future studies to optimize conditions for mesenchymal stem cell therapy.