

Experimental Molecular and Stem Cells Therapies in Cardiac Electrophysiology

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ABSTRACT: One of the most exciting fields in cardiovascular research today involves the use of stem cells, cell and gene therapies, and tissue engineering for the treatment of a variety of cardiovascular disorders. Here, we focus on the possible applications of these emerging strategies in the field of cardiac electrophysiology. Initially, the elegant cell and gene therapy approaches proposed for the treatment of bradyarrhythmias will be described. These gene therapy approaches mainly focused on the generation of biological pacemakers either by altering the neurohumoral control of existing pacemaking cells (by overexpressing the β -adrenergic receptor) or by converting quiescent cardiomyocytes into pacemaking cells by shifting the balance between diastolic repolarization and depolarization currents. An alternative approach explores the possibility of grafting pacemaking cells, which we either derived directly during the differentiation of human embryonic stem cells or engineered from mesenchymal stem cells, into the myocardium as a cell therapy strategy for biological pacemaking. We then describe the possible applications of similar strategies for the treatment of common tachyarrhythmias by overexpression of different ion channels, connexins, or their modifiers either directly in host cardiomyocytes or *ex-vivo* in cells that will be eventually transplanted into the heart. Next, the electrophysiological implications of cardiac stem cell therapy for heart failure are discussed, as well as the possible *in vitro* applications of stem cell technology for electrophysiological studies and drug screening. Finally, we address the obstacles, challenges, and the avenues required to make these novel strategies a clinical reality.

KEYWORDS: Cardiac electrophysiology, stem cells, cell therapy, gene therapy, tissue engineering, human embryonic stem cells, heart failure, ion channels, arrhythmias

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