Assay system for monitoring the effects of genetically engineered cells to alter function of a syncytium

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Technology description

Summary

Problem or Unmet Need:
Cardiac arrhythmias encapsulate a large group of conditions marked by abnormal electrical activity in the heart. The four general groups of cardiac arrhythmias are: premature atrial complexes (PACs)/ premature ventricular complexes (PVCs), leading to extra heart beats; bradycardias, which make the heart rhythm too slow; tachycardias, which make the heart beat faster; and disorders that affect the bundle branches, referred to as bundle branch block (BBB).
Current treatment of cardiac arrhythmias relies heavily on pharmacology, ablation, or electronic devices. Anti-arrhythmic drugs tend to have side effects that include evoking new arrhythmias. Catheter ablation is effective in curing inborn wiring errors such as accessory tracts, but is mostly ineffective towards more complex cases such as atrial fibrillation (AF) or ventricular tachycardia (VT). Lastly, electronic devices can be effective, but costly. In addition, there are many complications that can arise in implementing electronic devices, including pulmonary collapse, hemorrhage, and bacterial infection. Considering all these shortcomings, there is a need for biological alternatives, or at least adjuvants, to current treatments. A major difficulty in the field lies in the inability to bridge the gap between conceptual innovation and actual translation into new treatments.
This technology details the design and application of a chamber system for use in assaying the efficacy of genetically engineered human adult mesenchymal stem cells (MSCs), or other cells capable of electrically coupling to heart cells or other syncytial cells, to modulate rhythm and/or contractility of the coupled cells. The system can be used to determine how effective a specific gene construct is in modulating basal rhythm/contractility, as well as the cells' responsiveness to agonists or other pharmacologic agents. Besides being a new tool for basic research, this technology provides the basis for a high-throughput, cell-based bioassay for cardiac pacemaker rate regulation by engineered MSCs that are intended for use in cell-based therapy. It provides an additional, quality control assessment of engineered MSCs prior to in vivo implantation for cell-based therapy of cardiac rhythm disorders, likely leading to a decrease in cost for development of new therapies by eliminating the need to delve into animal systems for treatments that later turn out to be ineffective. It is also a step towards developing new biological treatments for cardiac arrhythmias that were previously difficult to attain.

Application area

-- Basic research tool in determining:
- The efficacy of genetically engineered human MSCs.
- The efficiency of a gene construct in modulating rhythm and/or contractility of MSC coupled cells.
- The coupled cells' responsiveness to agonists or pharmacologic agents.
-- High-throughput bioassay for cell-based therapy on cardiac arrhythmias.

Advantages

-- A novel high-throughput method for screening engineered MSCs to optimize genetic engineering and for quality control.
-- Increased quality control will decrease the need to enter into premature in vivo implantation, thereby also decreasing costs associated with cell-based therapy development.

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