HUMAN-INDUCED PLURIPOTENT STEM CELL-DERIVED ATRIAL CARDIOMYOCYTES: A MODEL FOR ATRIAL FIBRILLATION RESEARCH AND THERAPY

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Introduction: Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting over 33 million individuals worldwide. Despite extensive research, current AF treatment options are limited by high recurrence rates, adverse effects, and variability in pathophysiology. Human-induced pluripotent stem cell-derived atrial cardiomyocytes (hiPSC-aCMs) offer a promising in vitro model for studying AF, drug screening, and personalized therapy.
Materials and Methods: The differentiation of hiPSCs into atrial cardiomyocytes involves the manipulation of signaling pathways such as Wnt, retinoic acid, and bone morphogenetic proteins. Techniques including electrical stimulation, metabolic modifications, and three-dimensional (3D) tissue engineering have been employed to enhance hiPSC-aCM maturation. Additionally, CRISPR/Cas9 gene editing and electrophysiological assessments have been utilized to refine AF models and investigate patient-specific mutations.
Results: Studies have demonstrated that hiPSC-aCMs recapitulate key electrophysiological and structural characteristics of atrial cardiomyocytes. Patient-specific hiPSC-aCMs have been used to model familial AF and investigate the impact of ion channel mutations. Furthermore, pharmacological assessments using atrial-selective drugs, such as IKur and If channel inhibitors, have validated hiPSC-aCMs as a robust platform for drug screening. In disease modeling, optogenetic pacing has been used to induce AF-like remodeling, revealing novel insights into AF pathophysiology.
Conclusions: The development of hiPSC-aCMs represents a significant advancement in AF research, providing a scalable and patient-specific model for studying disease mechanisms, drug efficacy, and toxicity. Despite the challenges of achieving full cellular maturation, continued optimization of culture conditions and gene-editing technologies holds promise for refining AF models. Ultimately, hiPSC-aCMs offer a transformative approach to personalized medicine, enabling the development of targeted therapies and regenerative strategies for AF treatment.
Keywords: Atrial fibrillation, human-induced pluripotent stem cells, atrial cardiomyocytes, disease modeling, pharmacological testing, personalized medicine.