1550786

**Healthy And Heart Failure Patient-Generated Induced Pluripotent Stem Cells Derived Cardiomyocytes**

*Zwi, L; Huber, I; Caspi, O; Arbel, G; Gepstein, A; Gepstein, L*
*Technion - Israel Institute of Technology, Haifa, Israel*

The groundbreaking induced pluripotent stem cells (iPSC) technology allows the reprogramming of adult somatic cells, yielding pluripotent cells with characteristics similar to those of embryonic stem cells. This technology holds great promise for the emerging disciplines of personalized and regenerative medicine, because of the potential to derive patient-specific in vitro models and the ability to elude the immune system. The aim of the current study was to establish and characterize human iPSC derived cardiomyoctyes (hiPSC-CMs) from healthy and heart-failure patients. Healthy and heart-failure patients derived iPSC lines were achieved by retroviral reprogramming of dermal fibroblasts, using three reprogramming factors (Oct4, Sox2, and Klf4) and VPA without the oncogene c-Myc. Cardiomyocytes (CMs) differentiation of all iPSC lines was induced using the embryoid body (EB) differentiation system. Gene expression studies demonstrated that the CMs differentiation process was characterized by an initial increase in mesoderm and cardiomesoderm markers, followed by expression of cardiac specific transcription factors and finally by cardiac-specific structural genes and ion channels. hiPSC-CMs were stained positively for cardiac specific genes. Electrophysiological multielectrode array recordings of hiPSC-CMs established the development of a functional syncytium with stable pacemaker activity, action potential propagation, and responsiveness to adrenergic and muscarinic stimuli. Our study shows that hiPSC from healthy and heart failure patients are capable of differentiating into CMs presenting cardiac-specific molecular, structural, and functional properties. Their ability to respond to adrenergic and muscarinic stimuli introduces them as potential in vitro tissue models for personalized patient-specific drug screening. Most importantly, these cells demonstrate a functional syncytium crucial for the development of cell replacement strategies for myocardial repair.