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## Molecular characterization and functional properties of induced pluripotent stem cells-derived cardiomyocytes from healthy and diseased individuals. Models for investigating inherited cardiac diseases

In view of the therapeutic potential of cardiomyocytes derived from human induced pluripotent stem cells (iPSC-CM), our overall goal is to investigate their molecular characteristics, functional properties related to the excitation-contraction coupling (e.g., $[Ca^{2+}]i$ handling), pacemaker function and underlying ion currents, the effects of □-adrenergic stimulation, and responsiveness to common modifiers of cardiac function (e.g. If blocker). The iPSC clones we investigate are derived from human dermal fibroblasts or hair keratinocytes, and reprogramming is accomplished by infecting the cells with four human genes: OCT4, Sox2, Klf4 and C-Myc. Our major findings show that iPSC-CM: express cardiac specific RNA and proteins; exhibit regular pacemaker activity; exhibit key features of the excitation contraction coupling machinery; respond to ryanodine and caffeine (though less than adult cardiomyocytes), and express the SR-$Ca^{2+}$ handling proteins ryanodine receptor and calsequestrin; respond to autonomic agonists and antagonists. Hence, our work demonstrates that iPSC-CM exhibit features resembling the adult myocardium, and thus constitute a potential source for cardiac regeneration. Concomitantly, in order to decipher the pathological mechanisms of inherited cardiac arrhythmias and cardiomyopathies, we are investigating iPSC-CM generated from skin biopsies/keratinocytes obtained from patient's catecholaminergic polymorphic ventricular tachycardia (CPVT), laminopathies, WPW and Duchenne muscular dystrophy (DMD). Our research shows that the mutated iPSC-CM feature key clinical phenotype of the disease, thus establishing the foundation for developing novel drug modalities.

### Biography

Ofer Binah works at the Technion – Israel Institute of Technology, Israel. He is a Professor in the Department of Physiology, Biophysics and Systems Biology at the Ruth and Bruce Rappaport Faculty of Medicine. He has published more than 108 articles in reputed journals.

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