Ofer Binah Lab: Cardiac and Stem Cells Physiology

My Lab is located on the 12th Floor, at the Ruth & Bruce Rappaport Faculty of Medicine of the Technion, Haifa, Israel. During recent years my lab is focused on three major research topics:

(1) We are investigating the functional properties of induced Pluripotent Stem Cell-derived cardiomyocytes (iPSC-CMs). Under this topic we explore the mechanisms underlying the spontaneous firing (pacemaker) of iPSC-CMs as well as the development of the intracellular calcium handling machinery, contraction and responsiveness to autonomic regulation.

(2) We are investigating the pathophysiology (for example, heart failure, arrhythmias) of inherited cardiac diseases by means of the patients' iPSC-CMs, which carry the mutation and present key clinical features of the patient (Figure 1). In order to generate iPSCs, we reprogram fibroblasts derived from skin biopsies or keratinocytes derived from hair (Figure 2).

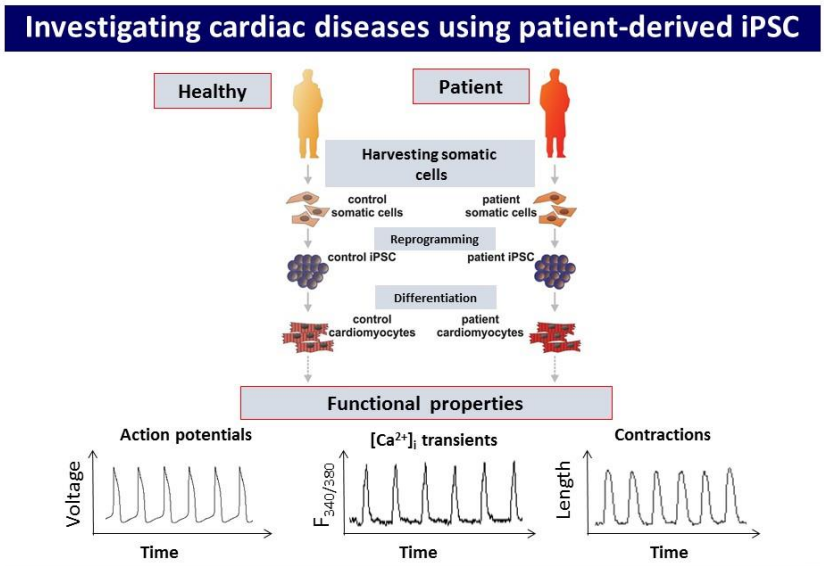

Figure 1: Investigating inherited cardiac diseases by patient's induced Pluripotent Stem Cell-derived cardiomyocytes (iPSC-CMs).

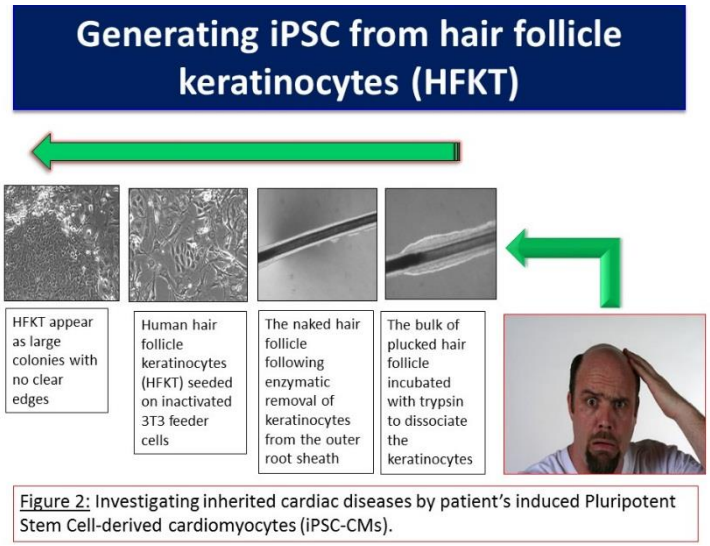

Figure 2: Investigating inherited cardiac diseases by patient's induced Pluripotent Stem Cell-derived cardiomyocytes (iPSC-CMs).

(3) We are investigating the pathophysiological mechanism underlying the lethal inherited cardiac disease – Duchenne Muscular Dystrophy (DMD), aiming at discovering new therapies for this devastating disease (Figure 3). To accomplish this goal we are using DMD patient-derived diseased iPSC-CMs as well as the *mdx* mouse model of DMD.

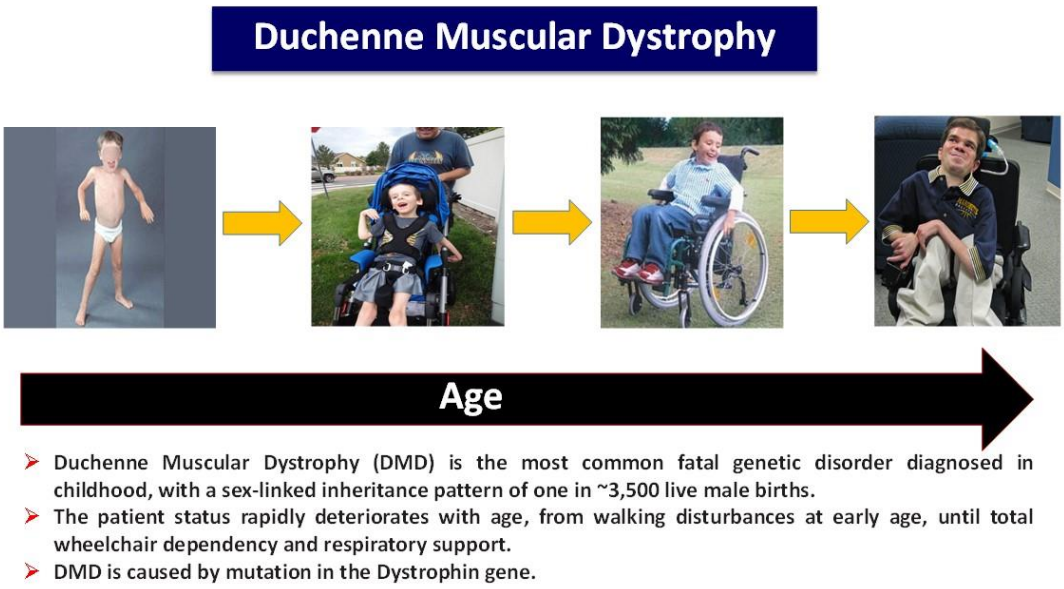

Figure 3: The major clinical hallmarks of Duchenne Muscular Dystrophy.

Available positions in my Lab

I will be happy to mentor excellent, enthusiastic and highly motivated students who seek cutting-edge stem cell research! Positions are open for post-docs, M.Sc and Ph.D students. **Qualified students will be entitled to a full fellowship**.

If you wish to be a part of my Lab exciting research, please call (04-8295262) or send your Curriculum Vitae (CV) to Ofer Binah at: binah@technion.ac.il.

Selected recent publications (graduate students and post-docs are marked in bold letters)

1) **Novak** A, Shtrichman R, **Germanguz** I, Segev H, **Zeevi-Levin N**, Fishman B, **Mandel** Y, **Barad** L, **Domev** H, Kotton DN, Mostoslavsky I, Binah O, Itskovitz-Eldor J. Enhanced reprogramming and cardiac differentiation of human keratinocytes derived from plucked hair follicles, using a single excisable lentivirus. Cellular Reprogramming. 2010;12:665-78.

2) **Ertracht O**, Liani E, **Bachner N**, Bar-Am O, Ovcharenko E, Awad H, Barac Y, Frolov L, Amit T, Abassi Z, Adam D, Youdim M, Binah O. The cardioprotective efficacy of TVP1022 in a rat model of myocardial infarction: Involvement of the glycogen synthase kinase 3β pathway and the mitochondrial permeability transition pore. Br J Pharmacol. 2011;163:755-69.

3) **Germanguz I**, **Sedan O**, **Zeevi-Levin N**, Shtrichman R, Barak E, Ziskind A, **Eliyahu S**, **Meiry G**, Amit M, Itskovitz-Eldor J, Binah O. Molecular characterization and functional properties of cardiomyocytes derived from human inducible pluripotent stem cells. J Mol Cell Med. 2011;15:38-51.

4) Gherghiceanu M, **Barad L**, **Novak A**, Reiter I, Itskovitz-Eldor J, Binah O, Popescu LM. Cardiomyocytes derived from human embryonic and induced pluripotent stem cells: comparative ultrastructure. J Cell Mol Med. 2011;15:2539-51.

5) **Novak A**, **Barad L**, **Zeevi-Levin N**, **Schick R**, Shtrichman R, Lorber A, Itskovitz-Eldor J, Binah O. Cardiomyocytes generated from CPVTD307H patients are arrhythmogenic in response to β-adrenergic stimulation. J Cell Mol Med. 2012;16:468-82.

6) **Mandel Y**, A Weissman A, **Novak A**, **Meiry G**, Goldberg S, Lorber A, Rosen MR, Itskovitz-Eldor J, Binah O. Human embryonic and induced pluripotent stem cells-derived cardiomyocytes exhibit beat rate variability and power-law behavior. Circulation. 2012;125:883-93.

7) Binah O, Weissman A, Itskovitz-Eldor J, Rosen MR. Integrating beat rate variability from single cells to hearts. Heart Rhythm. 2013:10:928-32.

8) **Weisbrod D**, Peretz A, Ziskind A, Menaker N, Oz S, **Barad L**, **Eliyahu S**, Itskovitz-Eldor J, Dascal N, Khananshvili D, Binah O, Attali B. SK4 Ca^{2+} activated K^{+} channel is a critical player in cardiac pacemaker derived from human embryonic stem cells. Proc Natl Acad Sci U S A. 2013;110:E1685-94.

9) **Ben-Ari M**, **Schick R**, **Barad L**, **Novak A**, **Ben-Ari E**, Lorber A, Itskovitz-Eldor J, Rosen R, Weissman A, Binah O. From beat rate variability in induced pluripotent stem cell-derived pacemaker cells to heart rate variability in human subjects. Hear Rhythm. 2014;11:1808-18.

10) **Novak A**, **Barad L**, Lorber A, Gherghiceanu M, Reiter I, **Eisen B**, Eldor L, Itskovitz-Eldor J, Eldar M, Arad M, Binah O. Functional abnormalities in iPSC-derived cardiomyocytes generated from CPVT1 and CPVT2 patients carrying ryanodine or calsequestrin mutations.J Cell Mol Med. 2015;19:2006-18.

11) **Malka A**, Meerkin D, **Barac YD**, Malits E, Bachner-Hinenzon N, Carasso S, **Ertracht O**, Angel I, Shofti R, Youdim M, Abassi Z, Binah O. TVP1022: A Novel Cardioprotective Drug Attenuates Left Ventricular Remodeling After Ischemia/Reperfusion in Pigs. J Cardiovasc Pharmacol. 2015;66:214-22.

12) **Ben-Ari M**, **Naor S**, **Zeevi-Levin N**, **Schick R**, **Ben Jehuda R**, Reiter I, **Raveh A**, **Grijnevitch I**, Barak O, Rosen MR, Weissman A, Binah O. Developmental changes in electrophysiological

characteristics of human induced pluripotent cells-derived cardiomyocytes. Heart Rhythm, Heart Rhythm. 2016 Sep 14. pii: S1547-5271(16)30745-7.

13) **Hallas T**, **Eisen B**, **Shemer Y**, **Naor S**, **Revital S**, **Benaim B**, Reiter I, Lorber A, Vlodavsky E, Katz Y, Õunap K, Rodenburg R, Mandel H, Gherghiceanu M, Binah. Investigating the cardiac pathological features of SCO2-mediated hypertrophic cardiomyopathy using the patients' induced Pluripotent Stem Cell–derived cardiomyocytes. Submitted to Cardiovasc Res.