ABSTRACT: Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) have become a powerful tool for human disease modeling and therapeutic testing. However, their use remains limited by their heterogeneity. To characterize the source of this heterogeneity, we applied complementary single-cell RNA-seq and bulk RNA-seq technologies over time during hiPSC cardiac differentiation and in the adult heart. Using integrated transcriptomic and splicing analysis, more than half a dozen distinct single-cell populations were observed, several of which were coincident at a single time-point, day 30 of differentiation. To dissect the role of distinct cardiac transcriptional regulators associated with each cell population, we systematically tested the effect of gain and loss of three transcription factors (NR2F2, TBX5, and HEY2), using CRISPR genome editing and ChIP-seq, in conjunction with patch clamp, calcium imaging, and CyTOF analysis. These analyses confirm that the transcription factors NR2F2 and HEY2 mediate opposing roles in the early stages of cardiac differentiation. These new targets, data, and integrative genomics analysis methods provide a powerful platform for understanding in vitro cellular heterogeneity.

BIO: Jared Churko, PhD, joined the University of Arizona Department of Cellular and Molecular Medicine in April 2018, following his position as an instructor within Stanford University's Cardiovascular Institute. His lab is located within the Sarver Heart Center where he studies cardiovascular disease. Specifically, his lab combines systems biology, stem cell biology, cardiac biology, genetic engineering, and bioinformatics to understand the mechanisms leading to heart disease. He is appointed as the director of the University of Arizona iPSC Core funded by BIO5 and the UA Center for Innovation in Brain Science. Human Induced Pluripotent Stem Cells (hiPSC), can be differentiated into many cell types with potential for developing precision patient care.

Please join us on
Monday, October 1st, 2018
12:00-12:50 pm, Keating Bldg., Room 103
Refreshments will be available at 11:50 am

Host: Minkyu Kim, Ph.D.
minkyukim@email.arizona.edu
Persons with a disability may request a reasonable accommodation by contacting the Disability Resource Center at 621-3268 (V/TTY).