BDR SEMINAR via Zoom

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Wednesday, October 8, 2025

9:30-10:30

Meeting URL will be announced on the event day by e-mail.

※This seminar is open only for BDR Members

From Epigenome to Organoids: Leveraging Cell Cycle Dynamics to Unlock Cardiac Maturation Competency and Regeneration

Summary

The human heart undergoes a remarkable developmental transition from proliferative fetal cells to highly specialized adult tissues, a process that remains challenging to recapitulate in vitro. Human iPSC-derived cardiomyocytes (hiPSC-CMs) and cardiac organoid models often stall in fetal-like states, limiting their utility for modeling, therapy, and regeneration. Our work addresses these developmental bottlenecks by uncovering the regulatory principles that govern both embryonic maturation competency and postnatal regenerative potential.

We show that the epicardium, a key developmental tissue contributing to heart development and regeneration, undergoes a transition to quiescence regulated by mTOR signaling, which supports cues that drive the reconstruction of postnatal tissues both in a cell-autonomous manner and through paracrine signaling. In parallel, we reveal that hiPSC-CMs accumulate aberrant DNA methylation marks that block maturation. Through transient partial reprogramming, these epigenetic abnormalities can be reset without loss of cardiac identity, restoring the capacity of cardiomyocytes to advance toward adult-like metabolic, structural, and functional states.

By integrating developmental pathway modulation, cell cycle dynamics, epigenetic editing, and organoid engineering, we demonstrate how fetal programs can be rebalanced to achieve mature and regenerative human heart tissues. This seminar will outline a roadmap for aligning in vitro differentiation with in vivo developmental trajectories to enable biologically relevant cardiac maturation and regeneration.