Seminar/Talk

Design Principles of Heart Morphogenesis: Forms, Forces and Fate

Rashmi Priya
Max Planck Institute for Heart and Lung Research

Host: Ani Kicheva

Embryogenesis entails generation of diverse cell fates and emergence of complex morphogenetic patterns. A key question remains as to how morphogenesis and mechanics contribute to cell fate decisions in a complex and growing organ. During cardiac development, the myocardial wall transforms from a monolayer to an intricate topological structure consisting of two distinct types of cardiomyocytes (CMs): outer compact and inner trabecular layer CMs. This process of cardiac trabeculation is crucial for cardiac function as aberrations lead to congenital cardiomyopathies and embryonic lethality. Yet, the mechanisms underlying the emergence and specification of trabecular CMs remain unknown. Using the zebrafish heart in combination with high-resolution quantitative microscopy, in vivo measurements of tension/subcellular dynamics, genetic mosaic tools and embryological interventions, I now report that contractility couples morphogenesis and cell fate to ensure robust self-organization of CMs into compact versus trabecular layer. Proliferation induced crowding triggers symmetry breaking by generating local differences in cellular contractility. These effects lead to stochastic delamination of CMs from the outer compact layer to seed the inner trabecular layer. By manipulating contractility at the single cell-level, I show that reducing contractility abrogates delamination while inducing contractility Augments delamination, and strikingly, inducing contractility is sufficient to drive delamination even in the absence of critical trabeculation signals like Nrg/Erbb2 or blood- flow. Further, using controlled perturbations to decouple mechanical cues from biochemical signaling, I find that mechanical cues drive CM fate specification. Inducing tension heterogeneity (and thereby CM delamination) by manipulation of cell density or contractility is sufficient to generate differential Notch activity as well as apicobasal polarity. Overall, this study reveals how form and function emerge as a collective product of individual cell behaviors, and argues for a system-level approach integrating mechanics with regulatory circuits for a cogent understanding of multicellular organization in vivo. As part of my future research plans, I will also discuss strategies to decode the principles of self-organization across length scales underlying the emergence of complex topological orders during organogenesis.

Monday, February 24, 2020 09:00am - 10:00am
Mondi Seminar Room 2, Central Building

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