CDB SEMINAR

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Monday, May 14, 2018
13:30~15:00 Auditorium C1F

Modelling cardiac chamber development in iPS cells and mice

Summary

Central to heart patterning during development is the division of the forming heart tube into chamber and non-chamber myocardium. The pumping chambers (ventricles) develop a luminal sponge-like network of cardiomyocytes (CMs) called trabeculae, which drive chamber growth and constitute the force-generating and conduction components of the early heart. Trabeculae also contribute to ventricular septation, papillary muscles, conduction tracts, and wall thickening through a process called compaction. Thus, trabeculation is critical to many aspects of heart morphogenesis and has likely provided a flexible evolutionary template for heart evolution. In animal models, defective trabeculation leads to embryonic lethality, while in humans, defective chamber growth and trabeculation can lead to severe congenital conditions including hypoplastic left heart (HLH) and non-compaction cardiomyopathy. I will touch on two studies. In the first, we are modelling the genetic and network basis of HLH in human IPS cells. Here, we hypothesize that HLH occurs at the intersection of hemodynamic changes brought about by defects in valves and outflow vessels, and a fundamental deficit in ventricular myocyte growth and function. In a second study, we have developed an entirely new model of cardiac trabeculation in which we propose that antagonistic interactions between the NOTCH and NEUREGULIN (NRG) signaling pathways control endocardial and myocardial behaviors, and the dynamic synthesis and degradation of cardiac extracellular matrix to define the basic segmental units of chamber sub-structure.

Host:
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