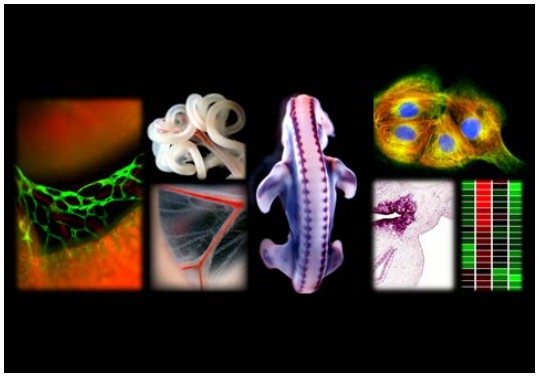
GUEST SPEAKER SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

Transcriptional control and cellular interactions during gut vascular morphogenesis



The Kurpios lab uses a combination of classical chicken embryology and modern mouse genetics to elucidate how basic cellular processes define the shape and function of organs. We are most fascinated by the evolutionarily conserved left-right (LR) organ asymmetry as errors of organ laterality are fundamentally linked to life-threatening birth defects. The chirality of gut rotation serves as a powerful model to study LR asymmetry. A critical aspect of this rotation is initiation of a leftward tilt directed by the conserved Pitx2 transcription factor, the master regulator of LR organ asymmetry. Failure to do so leads to gut malrotation and catastrophic volvulus in pediatric patients. The direction of gut rotation is driven by asymmetric cellular behavior within the dorsal mesentery (DM), a mesodermal structure that suspends the gut tube and whose cellular architecture is downstream of Pitx2 expressed strictly on the DM left side. We performed laser capture microdissection and genome-wide sequencing of the left (Pitx2 positive) and right (Pitx2 negative) DM and have since pioneered this tissue as a highly tractable in vivo model to study organogenesis at the level of cell shape, adhesion, ECM, actin cytoskeleton, and most recently vascular development and chromatin structure. While our initial effort focused on the identification of molecular and cellular targets of Pitx2, our research unexpectedly revealed that vascular development of gut arteries is commensurate with the onset of gut rotation and proceeds strictly on the DM left side dependent on Pitx2. Importantly, we discovered substantial errors in the standard textbook accounts of the origins and remodeling of mesenteric lymphatic vessels, which are among the largest in the body and defects of which cause debilitating intestinal dysfunctions such as inflammatory bowel disease and obesity. Our current research is in the following three areas: 1) Mechanisms underlying asymmetric gut rotation and vascular remodeling; 2) Signaling pathways involving lymphatic development; 3) Chromatin level mechanisms at the Pitx2 locus.

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Host: Dr. Tae-Hee Kim

Date: Monday December 14th, 2015
Time: 4PM
Place: FitzGerald Building
150 College Street
Room 103