Program/Abstract # 57
Wnt/β-catenin signaling regulates morphogenesis of the zebrafish lateral line
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Analysis of the developing lateral line serves as a tractable model of morphogenesis. The lateral line develops from a primordium that migrates from the head to the tail tip periodically depositing proprioceptive sensory organs. While much has been learned about the regulation of primordium migration, little is known about mechanisms underlying periodic deposition of sensory organs. A cell signaling feedback network within the primordium stably subdivides the tissue into two distinct domains. Wnt signaling induces and localizes Fgf signaling to the trailing portion of the primordium, which in turn restricts Wnt signaling to the leading region. This compartmentalization is not only important for primordium migration but is also crucial for generating periodicity of sensory organ deposition. Although lateral line and somite segmentation superficially resemble each other, we show that unlike somitogenesis, periodicity of sensory organ distribution depends crucially on the rate of cell proliferation. Wnt dependent cell proliferation in the leading region causes the tissue to continuously lengthen, displacing sensory organs toward the trailing edge. Upon reaching a Wnt signaling deficient region, cells slow down and deposit. The segmentation mechanism underlying periodic sensory organ formation relies on two continuous processes, stable compartmentalization and steady proliferation, with no input from molecular oscillators. Our work also demonstrates that the feedback mechanisms between Wnt and Fgf signaling coordinates primordium migration, sensory organ formation and deposition, thus orchestrating morphogenesis of the lateral line sensory system.

doi:10.1016/j.ydbio.2010.05.091

Program/Abstract # 58
Structure–function analyses of the Tre1 G protein-coupled receptor involved in primordial germ cell development of Drosophila
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Function of the Tre1 G protein-coupled receptor is required for the proper migration and programmed cell death of Drosophila primordial germ cells during early development. We have established that deletion of the 8 amino acids, RYILACH, located at the junction of the third transmembrane domain and second intracellular loop of this receptor, results in a severe loss-of-function phenotype in which the germ cells fail to migrate to the gonads. The critical amino acid in this region is the arginine, which is conserved in 96% of rhodopsin family G protein-coupled receptors. Currently, additional analyses of this region of Tre1 are being performed to determine how amino acid substitutions in this region affect the structure and function of the protein.

doi:10.1016/j.ydbio.2010.05.092

Program/Abstract # 59
Endoderm morphogenesis and its effect on heart precursor cell migration in the ascidian Ciona intestinalis
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How do embryonic cells find their precise place in the developing embryo? Do neighboring tissues play an instrumental or a passive role in this decision? Do the migrating cells themselves shape their environment? To answer these questions, we chose to study the interactions between the migrating heart precursor cells and their neighboring tissues in the ascidian Ciona intestinalis. Two bilateral sets of heart precursors migrate anteriorly and meet at the ventral midline of the trunk. During their migration, the heart precursors are in contact with the epidermis ventrally and the endoderm dorsally, which also undergoes dramatic morphogenetic changes. Interestingly, the heart precursors stop and anchor on precise endoderm regions. We blocked the activity of the Zn-finger GATA transcription factor specifically in the endoderm and observed that heart precursors migrated anteriorly but failed to reach the midline. Time series analysis of fixed embryos showed that in these mutants the posterior endodermal cells are mispositioned blocking the proper extension of the endodermal strand. This led to misfolding of the endoderm in the trunk such that the two lateral sheets of endoderm epithelia failed to meet in the middle. Interestingly, the heart precursors retained their attachment to endodermal regions suggesting that their inability to meet in the middle is due to the malformed endoderm. We are currently investigating whether heart precursors stop in response to specific endodermal cell-surface landmarks or in response to the contour of the overall endodermal landscape on which they are migrating.

doi:10.1016/j.ydbio.2010.05.093

Program/Abstract # 60
A novel Slit–Robo–miR-218 signaling axis regulates VEGF-mediated heart tube formation in zebrafish
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During vertebrate heart morphogenesis, bilateral groups of myocardial and endocardial cells migrate toward the midline to form the heart tube. Despite the investigation of several mutations affecting this process, the midline-derived cues guiding cardiac cell migration are still unknown. Here, we take a more targeted approach to this question by analyzing the role of known guidance molecules expressed at the midline, including Slits and their Robo receptors. Although primarily known as repulsive axon guidance cues, studies in Drosophila have indicated a role for Slit/Robo signaling in heart development. Using in vivo live cell imaging in zebrafish, we found that multiple Slit/Robo signaling components regulate cardiac cell migration. Slit2 appears to slow endocardial motility and increase cell–cell adhesion as cells approach the midline. We also found that the micro-RNA miR-218, which is intronically-encoded in Slit2 and Slit3 and suppresses Robo1 and Robo2 expression, promotes cardiac cell migration toward the midline. Surprisingly, we found that Robo1 also had pro-migratory functions in part by potentiating VEGF-signaling, revealing a previously unappreciated role for VEGF during heart tube formation. Together these findings reveal a novel signaling network composed of Slit/Robo, miR-218, and VEGF that functions to control vertebrate cardiac cell migration.

doi:10.1016/j.ydbio.2010.05.094

Program/Abstract # 60
Genetic analysis of mammalian Hippo signaling
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