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Concurrent Session 6: Generation of Asymmetry

Program/Abstract # 39
The role of PCP signaling, fluid flow and cytoskeletal dynamics in orienting motile cilia

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The ability of ciliated epithelia to generate directed flow is critical to diverse biological processes. To achieve this flow, ciliated cells must generate ~100 cilia that are coordinately polarized along a common axis. Here I present a model for how motile cilia in the *Xenopus* larval skin are polarized. In this model, the PCP components Vangl2 and Fz3 provide non-cell autonomous cues to orient ciliated-cells. These cues bias cilia and initiate a weak, but directed flow. This flow initiates a positive feedback loop, such that non-aligned cilia respond to the prevailing flow as well as to intracellular hydrodynamic forces to achieve coordinated polarity. This process indicates that cilia orientation is malleable, yet the mechanisms regulating this remain unexplored. EM studies have revealed a close association between ciliary basal bodies and the cytoskeleton. We address this relationship in detail by analyzing the role of cytoskeletal dynamics in regulating cilia orientation. Specifically, we report the effects of cytoskeleton modulating drugs on the process of generating cilia polarity.

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Program/Abstract # 40
Establishment of left–right asymmetry in zebrafish: Surprising predictions from a modeling approach

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Left–right (LR) axis specification leads to the proper arrangement of asymmetric organs in the body. In vertebrates, the Nodal signaling pathway is asymmetrically expressed and plays an essential role in LR patterning. We have determined that the levels and spatial pattern of the Nodal co-factor, *one-eyed pinhead* (*oep*) are critical for proper asymmetric signaling. Our data suggests that oep expression in the midline acts as a key regulator for the establishment of *nodal* asymmetry. In addition, ectopic expression of *oep* results in loss of *nodal* asymmetry, suggesting that *oep* is not a permissive factor in LR patterning, as was previously believed. We used the profile of *nodal* expression to determine the relationship between the propagation speed of *nodal* and the mRNA turnover rate. Using this data we have constructed a two-dimensional mathematical model of zebrafish LR axis establishment. Our model makes several predictions which we have confirmed through additional testing. Surprisingly, our model along with additional experiments from our group, support the idea that there is a prepattern of asymmetric information in the embryo that is strengthened by activity at Kupffer's vesicle. In mutants where fluid flow is slowed, but not eliminated, proper asymmetric expression occurs correctly more often than expected if fluid flow was the only method of establishing asymmetry. Our model provides clues as to why *pkd2* mutants in zebrafish produce bilateral *nodal* signals, while loss of this gene in mouse is reported to cause an absence of *Nodal*. Our work generating and confirming the model will be presented.

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Program/Abstract # 41
Asymmetry, fate and self-renewal in stomatal development

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Self-renewing populations of cells are integral to the creation and maintenance of tissues and organs. The overarching regulatory issues for these diverse tissues include establishing the populations of self-renewing (stem) cells in discrete locations and ensuring that these cells divide and create new differentiated cells at the appropriate rate and in the appropriate place. Plants have a remarkable ability to maintain these populations; yet, this ability to self-renew does not seem to come at the price of increased susceptibility to cancerous growth. Stomata (epidermal structures that regulate CO_2 and H_2O exchange in plants) are a useful genetic model to understand the mechanism(s) by which dispersed self-renewing populations are established and how their division and differentiation behavior is directed by interaction with neighboring cells. Our current studies address control over the asymmetric divisions that generate stomatal stem-cell populations, focusing on the signals and transcription factors that regulate the frequency and position of the divisions and the downstream factors required to carry out the divisions.

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Program/Abstract # 42
The Par6 complex is required for both early and late orientation of the left–right axis in *Xenopus*

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A three protein signaling complex, composed of Par3, Par6 and atypical protein kinase C (aPKC), is a central part of the mechanism that regulates cell polarity in a wide range of organisms. In *C. elegans*, this complex is responsible for the establishment of the anterior–posterior axis and regulation of asymmetric cell division. Additionally, a recent *in vitro* study of neutrophil-like cells revealed a role for Par6 in an intrinsic chirality that allows single cells to reliably distinguish left from right in culture. Because left–right (LR) asymmetry is fundamentally linked to cellular polarity, we probed the roles of Par6 and aPKC in the orientation