

Cell polarity and morphogenesis: new technologies and new findings

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Talks at the Cell Polarity and Morphogenesis Minisymposium featured new technologies, new results, and new ways of thinking about cell polarity and morphogenesis. These talks illustrated ways in which researchers are taking advantage of the tools and strategies of cell biology to understand how cells adhere, polarize, move, and differentiate in multicellular systems.

Cell polarity in vivo

PAR proteins play conserved roles in cell polarization in diverse animal systems. **Daniel Dickinson** (Bob Goldstein laboratory, University of North Carolina at Chapel Hill) developed a method for analyzing biochemical interactions in single cells and used it to show that PAR proteins transiently form oligomeric complexes in *Caenorhabditis elegans* zygotes. Formation of these complexes appears to be important for allowing PAR proteins to move with a transient polarized cortical flow.

Adam Paré (Jennifer Zallen laboratory, Sloan Kettering Institute) addressed how cell polarity is orchestrated in the *Drosophila* embryo. He showed that three transmembrane receptors in the Toll receptor family are expressed in partially overlapping stripes, giving each stripe of cells a unique “Toll code” that orients cell polarity and cell movements that produce the elongated head-to-tail body axis (Paré *et al.*, 2014).

Cell interactions and migration

David Doobin (Richard Vallee laboratory, Columbia University) showed that NDE1, a microcephaly disease protein and dynein reg-

ulator, regulates neural development through multiple roles in cell cycle progression (Doobin *et al.*, 2016). These studies can reveal how viruses such as the Zika virus exert their effects on the brain. He showed that when the Zika virus replicates in brain slice preparations, this causes apoptosis in nearby wild-type cells, possibly as a mechanism to contain the virus and prevent it from spreading throughout the brain.

Cell competition occurs in diverse animal systems, with cells inducing the elimination of other cells. **Eugenia Piddini** (Gurdon Institute) reported that three stress-signaling pathways play important roles in cell competition and identified a molecular signature common to multiple cells that are induced to die. These results suggest that a common mechanism is activated in cells that lose cell competition events by various genetic means.

Cells in multicellular animals are sometimes connected by intercellular bridges, but how such bridges are maintained is not well understood. **Kathryn Rehai** (Amy Maddox laboratory, University of North Carolina at Chapel Hill) identified new regulators of intercellular bridges in *C. elegans* and showed that they inhibit myosin II accumulation in order to stabilize bridges between cells. Together with previous work in *Drosophila* (Ong *et al.*, 2010), these findings suggest that myosin regulation is a common mechanism for stabilizing intercellular bridges and preventing ring closure.

Tatiana Omelchenko (Kathryn Anderson laboratory, Sloan Kettering Institute) used live imaging of whole-mouse embryos to study the dynamics of mesodermal cell migration. She identified the guanine nucleotide exchange factor β -Pix (Omelchenko *et al.*, 2014) as an essential regulator of directional migration in these cells and showed that mutant cells produce less precisely oriented protrusions and migrate less directionally in vivo and in vitro.

Mechanical forces from proteins to cells to tissues

In animal development, cell behavior is regulated by forces generated within cells, such as during apical constriction and rosette formation, but much less is known about how cell behaviors respond to extrinsic forces generated outside the cell (Vijayraghavan and Davidson, 2016). **Deepthi Vijayraghavan** (Lance Davidson laboratory, University of Pittsburgh) reported that the extrinsic forces that cells experience during neurulation can modify cell behavior in the *Xenopus* neural plate when pieces of epithelia are transplanted to new positions or when explanted tissues are grown under mechanically strained conditions.

Justin Crest (David Bilder laboratory, University of California, Berkeley) showed through atomic force microscopy and experimentally induced swelling that the extracellular matrix can provide an instructive force that shapes growing tissues. He reported that the extracellular matrix casing around the *Drosophila* egg chambers is less stiff at the poles than in the middle, which may allow eggs to elongate instead of undergoing uniform spherical growth.

Certain cells divide in specific orientations dictated by neighboring cells (Werts and Goldstein, 2011), but by mechanisms that are largely unexplored. **Martijn Gloerich** (Stanford University, now at the Medical Center Utrecht) showed that E-cadherin can act as a cue for orienting mitotic spindles. Contact with E-cadherin-coated walls oriented divisions of cultured epithelial cells (Gloerich *et al.*, 2017).

DOI:10.1091/mbc.E16-11-0797

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MBcC is pleased to publish this summary of the Minisymposium “Cell Polarity and Morphogenesis” held at the 2016 ASCB Annual Meeting, San Francisco, CA, December 6, 2016.

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Gloerich showed that LGN, a well-known regulator of spindle positioning, can associate with E-cadherin adhesions that are under tension, suggesting a mechanism by which tensile forces can recruit specific proteins to adherens junctions to control cell division orientation.

The nanoscale architecture of these junctions was elucidated in spectacular detail by **Cristina Bertocchi** (Pakorn Kanchanawong laboratory, Mechanobiology Institute, Singapore), who used super-resolution microscopy to unravel the spatial organization of the interface between cadherins and actin. The results revealed how vinculin, a central component in cadherin mechanotransduction, integrates mechanical and biochemical signals at junctions (Bertocchi *et al.*, 2017).

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