CURRENT RESEARCH AND SCHOLARLY INTERESTS
The overarching goal of the research in my lab is to understand how signal transduction pathways regulate morphogenesis - the emergence of spatial organization - during development. Development requires that cells differentiate to acquire the necessary complement of cell fates, and that they adopt the structure required to carry out their functions. In multicellular organisms, signal transduction is essential to these processes, yet while our understanding of how signals regulate gene expression is relatively advanced, our understanding of how signals direct the acquisition of specific shapes and forms is less advanced.

Our major project is to investigate a pathway that controls the polarity of epithelial cells within the plane of the epithelium. Epithelia delimit compartments of differing composition, and are necessarily specialized on their apical and basal surfaces. In addition, many epithelial cells are overtly polarized along an axis orthogonal to the apical-basal axis, in a direction defined by the organization of the tissue or organ [referred to as planar cell polarity (PCP)]. In effect, therefore, cells acquire a global “knowledge” of which way is which, much as a compass tells us direction on the earth’s surface. Some examples include the specialized hair cells of the mammalian cochlea, that display a spectacularly polarized organization of kinocilia and stereocilia on their apical surfaces, the dynamic ciliated cells of the tracheal
and reproductive tract epithelia, and cells in the gastrulating vertebrate embryo that display polarized migration and intercalation behaviors. In each case, PCP is critical to the function of these cells and tissues, and errors in the signaling system controlling PCP lead to human diseases and developmental defects, including congenital deafness, neural tube closure defects and cardiac outflow tract anomalies. The primary goal of my work on PCP has been to elucidate, at molecular and cell biological levels, the nature of the signals that induce subcellular asymmetry, and how cells then respond to this molecular asymmetry to orient their cytoskeletons.

We employ two principal model systems in our work. Because of the availability of remarkably powerful genetic, molecular and cell biological tools, we use the fruitfly, Drosophila melanogaster, as our primary model for investigating the fundamental mechanisms of PCP signaling. Importantly, flies have proven to be a remarkably well-conserved model for the molecular mechanisms of signaling events that direct vertebrate development. More recently, we have taken advantage of our experience in studying these mechanisms to extend our work to vertebrates, using primarily the mouse. To date, our work on vertebrates, along with the work of others, indicates a substantial conservation, but also reveals numerous differences and variations deserving of further study.

Teaching

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)

Publications

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