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

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)
Paola Moreno-Roman

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)

Publications

PUBLICATIONS

- Cyclin-dependent kinase control of motile ciliogenesis ELIFE  
  2018; 7

- Disruption of Core Planar Cell Polarity Signaling Regulates Renal Tubule Morphogenesis but Is Not Cystogenic CURRENT BIOLOGY  
  Kunimoto, K., Bayly, R. D., Vladar, E. K., Vonderfecht, T., Gallagher, A., Axelrod, J. D.  
  2017; 27 (20): 3120-+

- Airway epithelial homeostasis and planar cell polarity signaling depend on multiciliated cell differentiation. JCI insight  
  Vladar, E. K., Nayak, J. V., Milla, C. E., Axelrod, J. D.  
  2016; 1 (13)

- Clustering and negative feedback by endocytosis in planar cell polarity signaling is modulated by ubiquitinylation of prickle. PLoS genetics  
  Cho, B., Pierre-Louis, G., Sagner, A., Eaton, S., Axelrod, J. D.  
  2015; 11 (5)

- Microtubules provide directional information for core PCP function ELIFE  
  2014; 3

- Planar Polarized Protrusions Break the Symmetry of EGFR Signaling during Drosophila Bract Cell Fate Induction DEVELOPMENTAL CELL  
  Peng, Y., Han, C., Axelrod, J. D.  
  2012; 23 (3): 507-518

- Asymmetric homotypic interactions of the atypical cadherin Flamingo mediate intercellular polarity signaling CELL  
  2008; 133 (6): 1093-1105

- FijiWingsPolarity: An open source toolkit for semi-automated detection of cell polarity FLY
Dobens, L. L., Shipman, A., Axelrod, J. D.  
2018; 12 (1): 23–33

- **Wnt Signaling in Chronic Rhinosinusitis with Nasal Polyps** AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY  
Boeske, R., Vladar, E. K., Koenecke, M., Huesing, B., Linke, R., Pries, R., Reiling, N., Axelrod, J. D., Nayak, J. V., Wollenberg, B.  
2017; 56 (5): 575-584

- **Prickle1 mutation causes planar cell polarity and directional cell migration defects associated with cardiac outflow tract anomalies and other structural birth defects** BIOLOGY OPEN  
2016; 5 (3): 323-335

- **Prickle isoforms control the direction of tissue polarity by microtubule independent and dependent mechanisms.** Biology open  
Sharp, K. A., Axelrod, J. D.  
2016; 5 (3): 229-236

- **The Phenotypic Effects of Royal Jelly on Wild-Type D. melanogaster Are Strain-Specific.** PloS one  
2016; 11 (8)

- **Observing planar cell polarity in multiciliated mouse airway epithelial cells.** Methods in cell biology  
Vladar, E. K., Lee, Y. L., Stearns, T., Axelrod, J. D.  
2015; 127: 37-54

- **Coordinating cell polarity: heading in the right direction?** DEVELOPMENT  
Axelrod, J. D., Bergmann, D. C.  
2014; 141 (17): 3298-3302

- **prickle modulates microtubule polarity and axonal transport to ameliorate seizures in flies.** Proceedings of the National Academy of Sciences of the United States of America  
2014; 111 (30): 11187-11192

- **Prickle/spiny-legs isoforms control the polarity of the apical microtubule network in planar cell polarity.** Development  
Olofsson, J., Sharp, K. A., Matis, M., Cho, B., Axelrod, J. D.  
2014; 141 (14): 2866-2874

- **Methods for studying planar cell polarity** METHODS  
Olofsson, J., Axelrod, J. D.  
2014; 68 (1): 97-104

- **Myb promotes centriole amplification and later steps of the multiciliogenesis program** DEVELOPMENT  
2013; 140 (20): 4277-4286

- **Regulation of PCP by the Fat signaling pathway** GENES & DEVELOPMENT  
Matis, M., Axelrod, J. D.  
2013; 27 (20): 2207-2220

- **Absolute requirement of cholesterol binding for Hedgehog gradient formation in Drosophila.** Biology open  
Ducuing, A., Mollereau, B., Axelrod, J. D., Vincent, S.  
2013; 2 (6): 596-604

- **Microtubules Enable the Planar Cell Polarity of Airway Cilia** CURRENT BIOLOGY  
Vladar, E. K., Bayly, R. D., Sangoram, A. M., Scott, M. P., Axelrod, J. D.  
2012; 22 (23): 2203-2212

- **Remodeling a Tissue: Subtraction Adds Insight** SCIENCE SIGNALING  
Axelrod, J. D.  
2012; 5 (252)
• A Mathematical Model to Study the Dynamics of Epithelial Cellular Networks *IEEE-ACM TRANSACTIONS ON COMPUTATIONAL BIOLOGY AND BIOINFORMATICS*
  Abate, A., Vincent, S., Dobbe, R., Silletti, A., Master, N., Axelrod, J. D., Tomlin, C. J.
  2012; 9 (6): 1607-1620

• A universal analysis tool for the detection of asymmetric signal distribution in microscopic images *DEVELOPMENTAL DYNAMICS*
  Matis, M., Axelrod, J. D., Galic, M.
  2012; 241 (8): 1301-1309

• Nuclear localization of Prickle2 is required to establish cell polarity during early mouse embryogenesis *DEVELOPMENTAL BIOLOGY*
  2012; 364 (2): 138-148

• Multicilin promotes centriole assembly and ciliogenesis during multiciliate cell differentiation *NATURE CELL BIOLOGY*
  Stubbs, J. L., Vlader, E. K., Axelrod, J. D., Kintner, C.
  2012; 14 (2): 140-147

• Asymmetric Protein Localization in Planar Cell Polarity: Mechanisms, Puzzles, and Challenges *PLANAR CELL POLARITY DURING DEVELOPMENT*
  Peng, Y., Axelrod, J. D.
  2012; 101: 33-53

• Modeling the control of planar cell polarity *WILEY INTERDISCIPLINARY REVIEWS-SYSTEMS BIOLOGY AND MEDICINE*
  Axelrod, J. D., Tomlin, C. J.
  2011; 3 (5): 588-605

• Pointing in the right direction: new developments in the field of planar cell polarity *NATURE REVIEWS GENETICS*
  Bayly, R., Axelrod, J. D.
  2011; 12 (6): 385-391

• Versatile spectral methods for point set matching *PATTERN RECOGNITION LETTERS*
  Silletti, A., Abate, A., Axelrod, J. D., Tomlin, C. J.
  2011; 32 (5): 731-739

• Mutations in Prickle Orthologs Cause Seizures in Flies, Mice, and Humans *AMERICAN JOURNAL OF HUMAN GENETICS*
  2011; 88 (2): 138-149

• STED Super-resolution Microscopy in Drosophila Tissue and in Mammalian Cells *Conference on Reporters, Markers, Dyes, Nanoparticles, and Molecular Probes for Biomedical Applications III*
  Lau, L., Lee, Y. L., Matis, M., Axelrod, J., Stearns, T., Moerner, W. E.
  SPIE-INT SOC OPTICAL ENGINEERING.2011

• Delivering the Lateral Inhibition Punchline: It's All About the Timing *SCIENCE SIGNALING*
  Axelrod, J. D.
  2010; 3 (145)

• Planar Cell Polarity Enables Posterior Localization of Nodal Cilia and Left-Right Axis Determination during Mouse and Xenopus Embryogenesis *PLOS ONE*
  Antic, D., Stubbs, J. L., Suyama, K., Kintner, C., Scott, M. P., Axelrod, J. D.
  2010; 5 (2)

• Studies of epithelial PCP. *Seminars in cell & developmental biology*
  Axelrod, J. D.
  2009; 20 (8): 956-?

• Progress and challenges in understanding planar cell polarity signaling *SEMINARS IN CELL & DEVELOPMENTAL BIOLOGY*
  Axelrod, J. D.
  2009; 20 (8): 964-971

* Planar Cell Polarity Signaling: The Developing Cell's Compass *COLD SPRING HARBOR PERSPECTIVES IN BIOLOGY*
Vladar, E. K., Antic, D., Axelrod, J. D.
2009; 1 (3)

- Bone morphogenetic protein 2 induces pulmonary angiogenesis via Wnt-beta-catenin and Wnt-RhoA-Rac1 pathways JOURNAL OF CELL BIOLOGY
Perez, V. A., Alastalo, T., Wu, J. C., Axelrod, J. D., Cooke, J. P., Amieva, M., Rabinovitch, M.
2009; 184 (1): 83-99

- Cell packing influences planar cell polarity signaling PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA
Ma, D., Amonlirdviman, K., Raffard, R. L., Abate, A., Tomlin, C. J., Axelrod, J. D.
2008; 105 (48): 18800-18805

- A Homozygous Mutation in Human PRICKLE1 Causes an Autosomal-Recessive Progressive Myoclonus Epilepsy-Ataxia Syndrome AMERICAN JOURNAL OF HUMAN GENETICS
2008; 83 (5): 572-581

- Dishevelled links basal body docking and orientation in ciliated epithelial cells TRENDS IN CELL BIOLOGY
Vladar, E. K., Axelrod, J. D.
2008; 18 (11): 517-520

- Bad hair days for mouse PCP mutants NATURE CELL BIOLOGY
Axelrod, J. D.
2008; 10 (11): 1251-1253

- Hedgehog and Wingless stabilize but do not induce cell fate during Drosophila dorsal embryonic epidermal patterning DEVELOPMENT
Vincent, S., Perrimon, N., Axelrod, J. D.
2008; 135 (16): 2767-2775

- Basal bodies, kinocilia and planar cell polarity NATURE GENETICS
Axelrod, J. D.
2008; 40 (1): 10-11

- An adjoint-based parameter identification algorithm applied to planar cell polarity signaling IEEE TRANSACTIONS ON AUTOMATIC CONTROL
Raffard, R. L., Amonlirdviman, K., Axelrod, J. D., Tomlin, C. J.
2008: 109-121

- An adjoint-based parameter identification algorithm applied to planar cell polarity signaling IEEE TRANSACTIONS ON CIRCUITS AND SYSTEMS I-REGULAR PAPERS
Raffard, R. L., Amonlirdviman, K., Axelrod, J. D., Tomlin, C. J.
2008: 109-121

- Biology by numbers: mathematical modelling in developmental biology NATURE REVIEWS GENETICS
Tomlin, C. J., Axelrod, J. D.
2007; 8 (5): 331-340

- Asymmetric distribution of Prickle-like 2 reveals an early underlying polarization of vestibular sensory epithelia in the inner ear JOURNAL OF NEUROSCIENCE
Deans, M. R., Antic, D., Suyama, K., Scott, M. P., Axelrod, J. D., Goodrich, L. V.
2007; 27 (12): 3139-3147

- The Drosophila casein kinase I epsilon/delta Discs overgrown promotes cell survival via activation of DIAP1 expression DEVELOPMENTAL BIOLOGY
Guo, J., Li, H., Rogulja, A., Axelrod, J. D., Cadigan, K. M.
2007; 303 (1): 16-28

- Cell shape in proliferating epithelia: A multifaceted problem CELL
Axelrod, J. D.
2006; 126 (4): 643-645

* A WNTer wonderland in Snowbird DEVELOPMENT

Page 5 of 7
• Automatic parameter identification via the adjoint method, with application to understanding planar cell polarity 45th IEEE Conference on Decision and Control
  Raffard, R., Amonlirdviman, K., Axelrod, J. D., Tomlin, C. J.
  IEEE. 2006: 13–18

• Understanding biology by reverse engineering the control PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA
  Tomlin, C. J., Axelrod, J. D.
  2005; 102 (12): 4219–4220

• D-2 dopamine receptors colocalize regulator of G-protein signaling 9-2 (RGS9-2) via the RGS9 DEP domain, and RGS9 knock-out mice develop dyskinesias associated with dopamine pathways JOURNAL OF NEUROSCIENCE
  2005; 25 (8): 2157–2165

• Mathematical modeling of planar cell polarity to understand domineering nonautonomy SCIENCE
  Amonlirdviman, K., Khare, N. A., Tree, D. R., Chen, W. S., Axelrod, J. D., Tomlin, C. J.
  2005; 307 (5708): 423–426

• A second canon: Functions and mechanisms of beta-catenin-independent wnt signaling DEVELOPMENTAL CELL
  Veeman, M. T., Axelrod, J. D., Moon, R. T.
  2003; 5 (3): 367–377

• Fidelity in planar cell polarity signalling NATURE
  Ma, D., Yang, C. H., McNeill, H., Simon, M. A., Axelrod, J. D.
  2003; 421 (6922): 543–547

• A three-tiered mechanism for regulation of planar cell polarity SEMINARS IN CELL & DEVELOPMENTAL BIOLOGY
  Tree, D. R., Ma, D. L., Axelrod, J. D.
  2002; 13 (3): 217–224

• Prickle mediates feedback amplification to generate asymmetric planar cell polarity signaling CELL
  2002; 109 (3): 371–381

• Regulation of Frizzled by fat-like cadherins during planar polarity signaling in the Drosophila compound eye CELL
  Yang, C. H., Axelrod, J. D., Simon, M. A.
  2002; 108 (5): 675–688

• Coupling planar cell polarity signaling to morphogenesis. TheScientificWorldJournal
  Axelrod, J. D., McNeill, H.
  2002; 2: 434–454

• Strabismus comes into focus NATURE CELL BIOLOGY
  Axelrod, J. D.
  2002; 4 (1): E6–E8

• Unipolar membrane association of dishevelled mediates frizzled planar cell polarity signaling GENES & DEVELOPMENT
  Axelrod, J. D.
  2001; 15 (10): 1182–1187

• Drosophila Rho-associated kinase (Drok) links frizzled-mediated planar cell polarity signaling to the actin cytoskeleton CELL
  2001; 105 (1): 81–91

• naked cuticle targets dishevelled to antagonize Wnt signal transduction GENES & DEVELOPMENT
• Frizzled signaling and the developmental control of cell polarity  *TRENDS IN GENETICS*
  Shulman, J. M., Perrimon, N., Axelrod, J. D.
  1998; 14 (11): 452-458

• Differential recruitment of Dishevelled provides signaling specificity in the planar cell polarity and Wingless signaling pathways  *GENES & DEVELOPMENT*
  Axelrod, J. D., Miller, J. R., Shulman, J. M., MOON, R. T., Perrimon, N.
  1998; 12 (16): 2610-2622

• Wingless refines its own expression domain on the Drosophila wing margin  *NATURE*
  Rulifson, E. J., Micchelli, C. A., Axelrod, J. D., Perrimon, N., Blair, S. S.
  1996; 384 (6604): 72-74

• Conservation of dishevelled structure and function between flies and mice: Isolation and characterization of Dvl2  *MECHANISMS OF DEVELOPMENT*
  Klingensmith, J., Yang, Y., Axelrod, J. D., Beier, D. R., Perrimon, N., Sussman, D. J.
  1996; 58 (1-2): 15-26

• The wingless signaling pathway is directly involved in Drosophila heart development  *DEVELOPMENTAL BIOLOGY*
  Park, M. Y., Wu, X. S., GOLDEN, K., Axelrod, J. D., Bodmer, R.
  1996; 177 (1): 104-116

• Interaction between wingless and notch signaling pathways mediated by dishevelled  *SCIENCE*
  Axelrod, J. D., Matsuno, K., ARTAVANISTSAKONAS, S., Perrimon, N.
  1996; 271 (5257): 1826-1832

• THE COLLECTION AND EVALUATION OF PERIPHERAL-BLOOD PROGENITOR CELLS SUFFICIENT FOR REPETITIVE CYCLES OF HIGH-DOSE CHEMOTHERAPY SUPPORT  *TRANSFUSION*
  1995; 35 (10): 837-844

• GAL4 DISRUPTS A REPRESSION NUCLEOSOME DURING ACTIVATION OF GAL1 TRANSCRIPTION INVIVO  *GENES & DEVELOPMENT*
  Axelrod, J. D., Reagan, M. S., Majors, J.
  1993; 7 (5): 857-869

• PROLINE-INDEPENDENT BINDING OF PUT3 TRANSCRIPTIONAL ACTIVATOR PROTEIN DETECTED BY FOOTPRINTING INVIVO  *MOLECULAR AND CELLULAR BIOLOGY*
  Axelrod, J. D., Majors, J., Brandriss, M. C.
  1991; 11 (1): 564-567

• AN IMPROVED METHOD FOR PHOTOFOOTPRINTING YEAST GENES INVIVO USING T7 POLYMERASE  *NUCLEIC ACIDS RESEARCH*
  Axelrod, J. D., Majors, J.
  1989; 17 (1): 171-183

• VITAMIN-D AFFECTS PROLIFERATION OF A MURINE T-HELPER CELL CLONE  *JOURNAL OF IMMUNOLOGY*
  1987; 138 (6): 1680-1686

• UNIQUE CYTOCHALASIN-B BINDING CHARACTERISTICS OF THE HEPATIC GLUCOSE CARRIER  *BIOCHEMISTRY*
  Axelrod, J. D., Pilch, P. F.
  1983; 22 (9): 2222-2227

• UNIMPAIRED SIGNAL TRANSDUCTION BY THE ADIPOCYTE INSULIN-RECEPTOR FOLLOWING ITS PARTIAL PROTEOLYTIC FRAGMENTATION  *JOURNAL OF BIOLOGICAL CHEMISTRY*
  Pilch, P. F., Axelrod, J. D., COLELLO, J., Czech, M. P.
  1981; 256 (4): 1570-1575