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FIRST PERSON

First person – Vaibhav Pai

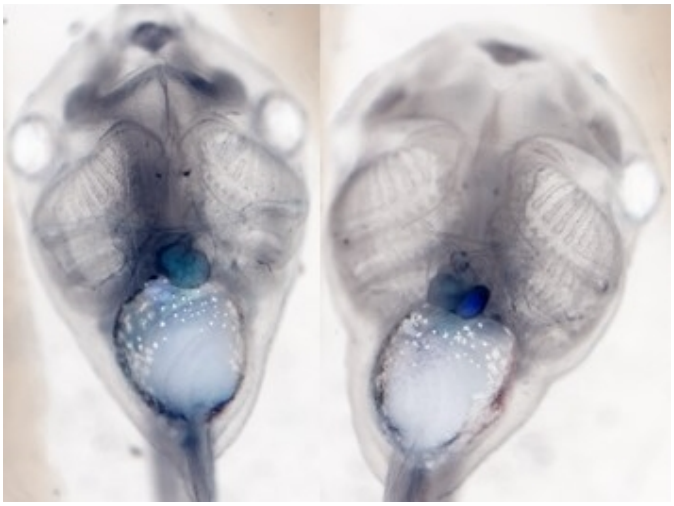
First Person is a series of interviews with the first authors of a selection of papers published in Biology Open, helping early-career researchers promote themselves alongside their papers. Vaibhav Pai is first author on 'HCN4 ion channel function is required for early events that regulate anatomical left-right patterning in a nodal and lefty asymmetric gene expression-independent manner', published in BiO. Vaibhav is a Research Associate working in Michael Levin's group at the Allen Discovery Center at Tufts University, investigating bioelectric control of embryonic organ formation and how bioelectric networks interact with the classic genetic and biochemical networks in this process.

Vaibhav Pai

What is your scientific background and the general focus of your lab?

I have a BSc in genetics and microbiology, and an MSc in biophysics. My PhD was in systems biology and physiology, where under the mentorship of Dr Nelson Horseman, I studied the role of endogenous electrical potential across mammary epithelial cells in milk synthesis and secretion and how these potentials are regulated by the serotonin biochemical pathway. I also studied how this bioelectrical–biochemical coupling gets co-opted during cancer. Currently, I am a Research Associate working in Michael Levin's group which is a part of Allen Discovery Center at Tufts University.

My current work focuses on endogenous bioelectrical signals as patterning information conduits during embryogenesis, which help guide the formation of various organ systems, particularly neural systems (eye and brain). I try to understand how these bioelectrical systems interface with the known genetic and biochemical signals classically studied in the embryonic development context.



Ventral view of a Xenopus tadpole with a reversal of asymmetric organ placement and their coiling following injection with a dominant-negative HCN4 channel at the early cleavage stage.

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How would you explain the main findings of your paper to non-scientific family and friends?

It is very easy to determine our left side from our right side, right? Imagine explaining to an alien over the phone which hand is its left hand. In reality, it is an incredibly difficult problem to solve for a spherical mass of cells – an embryo. Underlying the symmetric exteriors of the body, the internal organs are placed in a left–right asymmetrical manner inside the body cavity. During embryonic development, cells need to talk to each other to coordinate building complex organs like heart and gut, and place them correctly inside the body cavity. Using frog embryos, we showed that part of their conversations is electrical in nature, with the first demonstration of a role of the HCN4 ion channel in this developmental process. We also showed that this electrical conversation occurs without engaging the classic gene expression, suggesting a new, possibly parallel and compensatory method for left–right asymmetric organ placement inside the body cavity.

"The extent of patterning information carried by the bioelectric signals and their ability to reorganize and change major body plan anatomical outcomes has been beyond my wildest imagination."

What are the potential implications of these results for your field of research?

These data identify a novel, developmental role for HCN4 channels and reveal a new Nodal–Lefty–Pitx2 asymmetric gene expression-

independent mechanism upstream of organ positioning during embryonic left–right patterning. This discovery underlies the endogenous bioelectric signaling that is an important component of developmental and regenerative patterning, and adds to the toolbox of available targets for understanding and control of growth and form. This interplay between bioelectrics, transcriptional regulation and resultant anatomical patterning presents exciting opportunities for understanding developmental and evolutionary dynamics. It is possible that the study of compensatory redundant pathways will reveal new approaches for harnessing the robustness of developmental mechanisms for regenerative medicine.

What has surprised you the most while conducting your research?

The biggest surprise has been the sensitivity of the developmental programs to specific bioelectrical signals and yet their robustness to physiological noise. The extent of patterning information carried by the bioelectric signals and their ability to reorganize and change major body plan anatomical outcomes has been beyond my wildest imagination.

What, in your opinion, are some of the greatest achievements in your field and how has this influenced your research?

The ability of electrical signals to influence biological processes has been long known. Lionel Jaffe made a major advance by discovering the role of endogenous bioelectric signals in regulating embryonic developmental processes using the vibrating probe which he co-invented with Richard Nuccitelli. In the past 15 years, Michael Levin has leveraged the magnificent advances made in molecular genetics, biophysics of ion channels/pumps and ion fluxes, and physiology to develop strategies to understand the morphological information carried by bioelectric signals in the context of development, regeneration, and cancer. This has initiated several new areas of research and laid the framework for my research to explore how bioelectric signals control embryonic organ formation and how they integrate with the classical genetic and biochemical networks. This understanding can be exploited to develop tractable strategies addressing issues of birth-defects, regenerative medicine, and synthetic biology.

What's next for you?

Currently, I am applying for faculty positions at universities where I can pursue my research and teaching interests.

Reference

Pai, V. P., Willocq, V., Pitcairn, E. J., Lemire, J. M., Paré, J. -P., Shi, N. -Q., McLaughlin, K. A. and Levin, M. (2017). HCN4 ion channel function is required for early events that regulate anatomical left-right patterning in a nodal and lefty asymmetric gene expression-independent manner. *Biol. Open* **6**, doi:10.1242/bio.025957.