DEPARTMENT OF BIOLOGY | UNIVERSITY of WASHINGTON

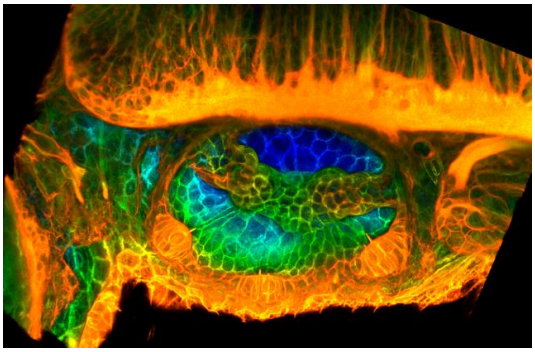
# Faculty Search Biology Seminar

By: Akankshi Munjal

Harvard Medical School | Postdoctoral Fellow, Department of Systems Biology

https://connects.catalyst.harvard.edu/Profiles/display/Person/141890

## Building an integrated framework for tissue morphogenesis with the zebrafish inner ear



**Wednesday, February 03, 2021**
**12:00 PM PST**

How simple tissues give rise to geometrically complex organs with robust shapes and functions is a fundamental question in biology with important implications in disease and translational medicine. The current mechanistic framework explains how upstream genetic and biochemical information pattern cellular mechanics and thereby tissue dynamics. In this framework, the main driving force is cell-intrinsic and generated by actomyosin contractility. The extracellular matrix (ECM) that surrounds most cells is considered to be a passive mechanical scaffold that may shape these forces through differential stiffness. I will present a case which inverts this expectation. Zebrafish semicircular canals form from invaginations in the otic epithelium (buds) that extend and fuse to form the hubs of each canal. We find that conventional actomyosin-driven behaviors are not required. Instead, local secretion of hyaluronan, made by the enzymes *ugdh* and *has3*, drives canal morphogenesis. Charged hyaluronate polymers osmotically swell with water and generate isotropic extracellular pressure to deform the overlying epithelium into buds. The mechanical anisotropy needed to shape buds into tubes is conferred by a polarized distribution of cellular protrusions, linked between cells, that we term cytocinches. Hyaluronate-pressure shaped by anisotropic tissue stiffness may be a widespread mechanism for powering morphological change in organogenesis and tissue engineering. We are now investigating the molecular underpinnings and the transcriptional identity of the canal forming cells using single-cell RNA sequencing. In my independent research program, I will use the zebrafish inner development to investigate emerging behaviors in tissue morphogenesis as a result of under-explored players such as the mechano-chemical roles of the ECM, feedback interactions between patterning and morphogenesis, and the contribution of tissue geometry in determining robust organ shape. My long-term vision is to build an integrated framework for tissue morphogenesis encapsulating generalizable design principles through a description of how multi-scale interactions and feedback give rise to information and mechanics, and to use insights from fundamental research to advance translational medicine.

Seminar Speaker Host: Jay Parrish