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A FORCE TO BE RECKONED WITH: WHEN MECHANICS GUIDE EPITHELIAL MORPHOGENESIS

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During development, simple epithelial sheets give rise to a diverse array of tissues with complex forms and specialized functions through regulated and robust tissue choreography. Mechanical forces, originating both from the microenvironment and generated within morphing tissues, play a pivotal role in shaping organs and ensuring proper form. Simultaneously, epithelial decision-making processes contribute to tissue patterning by accurately specifying correct cell types within cellular structures, thereby creating functional tissues. To robustly and successfully achieve form and function, tissue mechanics and epithelial decision-making must be tightly interlinked. In this presentation, I will discuss how we use bioengineering approaches to disentangle the roles of mechanical forces in morphogenesis and cell patterning in in-vitro human pluripotent stem cell (hPSC)-derived model systems. Specifically, I will highlight how mechanical forces direct cell patterning and symmetry breaking in human neural tube organoids using a combination of global and local actuation (mechanical stimulation) devices integrated with a single-cell transcriptomics atlas. Furthermore, I will explore the significance of the extracellular matrix (ECM) as a dynamic mechanical landscape during early development. In particular, I will discuss my recent findings on the reciprocal relationship between cell-driven ECM flow and epithelial morphogenesis. We will examine how symmetry-breaking events at morphogenesis sites are essential for driving and guiding ECM flow, while ECM flow, in turn, is critical for sustaining morphogenesis. I will also present insights from in-silico modeling of this reciprocal relationship, along with findings from single-cell transcriptomic analyses that reveal how ECM flow contributes to a primitive streak-like phenotype in this pre-/early streak in-vitro gastrulation model.

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