FABIAN SPILL, University of Birmingham

Cellular and Subcellular Geometry and Mechanics as Determinants of Cell Migration

The migration of epithelial cells plays a critical role in physiological processes such as wound healing. In this context, cells utilize distinct migration modes based on the geometric properties of gaps: lamellipodial crawling at convex edges and purse-string-like movements at concave edges. Despite advances in identifying biochemical pathways, the underlying mechanisms determining these mode switches in response to curvature remain unclear. Our study addresses this by focusing on the endoplasmic reticulum (ER), a dynamic organelle whose morphology depends on cellular geometry. Through a combination of experimental data and theoretical modeling, we show that the ER undergoes curvature-specific morphological reorganizations that act as a determinant of migration modes. At convex edges, the ER forms tubular networks that align perpendicularly, facilitating lamellipodial crawling. At concave edges, the ER reorganizes into dense sheet-like structures favoring actomyosin-driven purse-string contractions. Our mathematical model describes the ER as a flexible fiber whose morphology-dependent strain energy guides these transitions, revealing a lower energy state when ER tubules or sheets form in accordance with local edge curvature. This study positions the ER as a critical player in cellular mechanotransduction, providing a mechanistic link between subcellular organization and cellular migration strategies. Our findings offer insights into how cellular and subcellular geometries dynamically influence the physical properties and behaviors of cells, forming a basis for understanding migration regulation in complex tissues.