BIOMATERIALS

Forces in Biomolecular Systems SFB 863

Cells as smart materials: Quantitatively dissecting and rebuilding mechaniobiological units

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Abstract:

Living cells are capable of processing a variety of mechanical signals encoded within their microenvironment, which can in turn act through the cellular structural machinery to regulate many fundamental behaviors. In this sense, cells may be regarded as "smart materials" that dynamically and locally modulate their physical properties in response to environmental stimuli. Here we discuss our recent efforts to dissect, control, and mimic these phenomena. First, we have used laser nanosurgery to spatially map the nanomechanical properties of actomyosin stress fibers. We have combined this approach with advanced molecular imaging tools (FRAP, FRET) to relate intracellular tensile forces to the conformational activation of mechanosensory proteins at the cell-microenvironment interface and the activities of specific myosin activators and isoforms. Second, we have used the tools of synthetic biology to precisely control the expression and activation of mechanoregulatory proteins in single cells using multiple mutually orthogonal inducer/repressor systems. This capability has enabled us to quantitatively elucidate relationships between signal activation and phenotype and to deconstruct complex signaling networks. By combining these genetic approaches with advanced culture paradigms and in vivo models, we have been able to explore how mechanobiological signals may help drive stem cell differentiation and tumor invasion in the central nervous system. We are now beginning to close the loop by engineering proteins that mimic the stimulus-responsive features of cellular structural networks and may serve as smart, genetically-encoded mechanochemical building blocks.

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