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Cellular Force, and Geometry Sensing (Over Time) Can Detect Matrix Rigidity: Local Modules Produce Global Signals

MICHAEL SHEETZ, Columbia University

The shape and behavior of mammalian cells is defined by an interplay between extracellular signals and the cellular responses. Although the chemical nature of the external signals is important, there is a growing realization that the physical aspects of the external environment are equally important. In particular, the stresses, rigidity and form of the external environment have major effects on cell behavior. Of particular importance is rigidity since cancerous cells can often grow on soft agar or in a fluid phase without force production. For most mammalian cells there are relatively few types of motility that are evident from quantitative analyses of rapidly spreading fibroblasts (Dubin-Thaler et al., Biophys. J. 86:1794-1806, 2004). One motile phase that we have studied extensively involves periodic contractions (24 s period) in local regions of the leading edge of the cell (Giannone et al., Cell, 116:431-443, 2004). The periodic signal is carried radially from the cell edge toward the center and is part of a general mechanism for rigidity-directed movement and pathfinding. Another motile phase involves the movement of individual collagen fibers in a hand-over-hand fashion (Meshel et al., Nature Cell Biol. 7:157-164, 2005) where the form of the fiber is being sensed. Rigidity and form sensing in these systems is dependent upon the cytoskeleton and force-dependent tyrosine phosphorylation through oncogenes (Sawada and Sheetz, J Cell Biol. 156:609-15, 2002; Tamada et al., Developmental Cell, 7:706-718, 2004). Recent studies indicate that the cell rigidity sensing occurs preferentially at the leading edges of moving cells and involves forces of 10-20 pN generated by displacements of 50-100 nm (Jiang et al., Biophys J. In Press). We will discuss how cells organize motility tools in motile phases (Döbereiner et al., Phys. Rev. Letters. 93:108105-1-4, 2004) in a dialogue with the environment to define cell morphology and behavior over time..