Curvature: a dynamic regulator of cell migration mode and motility

Cas van der Putten, Maike Werner, Daniëlle van den Broek, Carlijn Bouten, and Nicholas Kurniawan[1]

[1]*Department of Biomedical Engineering, and* [2]*Institute for Complex Molecular Systems, Eindhoven University of Technology, Eindhoven, The Netherlands*

The intrinsic architecture of tissues subject cells to geometrical cues in the form of mesoscale curvatures [1]. While the effect of nano- and micro-scale topographical cues have been extensively studied, surprisingly little is known about the cell response to geometries larger than cell size. To study the effect of curvature in a systematic and high-throughput manner, we developed a microfabricated chip containing arrays of concave and convex structures with a wide range of size (μm to mm) [2]. We observed distinct cell migration modes on these structures: on concave surfaces cells showed undirected but fast migration, whereas migration on convex surfaces was persistently directed towards the direction that imposes the least cell bending. Moreover, we found an unexpected negative correlation between migration speed and persistence that emerged universally across all structures and for all tested cell types. The scale-dependent effect of mesoscale curvature was found to be sensitive to cell phenotype and activation state and was accompanied by changes in the F-actin organization and the levels of phosphorylated myosin and nuclear lamin-A. Thus, our findings demonstrate a complex interplay between cell contractility, nuclear mechanics, and adhesion morphology in dynamically guiding cell migration on physiologically-relevant 3D structures.

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