DIRECTING CELLULAR TRAFFIC USING GEOMETRIC AND BIOMOLECULAR CUES

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Keiichiro Kushiro

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ABSTRACT

Directing Cellular Traffic Using Geometric and Biomolecular Cues

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Directed cell migration plays a principal role in various aspects of important cellular phenomena such as wound healing, development and cancer metastasis. Although the mechanism of gradient stimulus leading to directed cell migration is well understood and exploited, the geometrical and topographical cues that cause directed migration has been largely unexplored. With the advent of accessible microfabrication techniques to precisely control the topography of the extracellular matrix (ECM) on substrates, researchers are just starting to study the complex mechanical signals that can alter directed cell motility. A key challenge now is to parse out the precise factors that affect directional movement of cells on certain micropatterns, use that understanding to design strategies to enhance the motility and bias of directed cell migration, and further apply these concepts to multiple cell types and higher-order cell systems.

Here, we investigate the tunability of directional bias through various geometrical manipulations using quantitative analysis of cell movement on micropatterns. We observe that MCF-10A epithelial cells in general jump with an unnaturally high bias between teardrop-based islands with specific gap distance, asymmetry and positional placement. Throughout the studies, we observe that lamellipodial protrusions and unilamellar

morphology play a crucial role in dictating not only the directional bias of epithelial cells, but also their speed and persistence, and find that moderate alteration of Rac1 signal leads to an unexpected flip of bias. We further extend the concept of directional bias to design patterns to successfully control cell flux and effectively partition cell population, as well as induce unilamellar morphology in different cell types to promote directed cell motility. We also investigate the combinatorial effect of hybrid micropatterns in enhancing motility and unravel the unique properties and possible mechanisms behind directed cell motility on teardrop-based micropatterns.

Our results demonstrate a new type of directed cell motility using a micropattern that involves the use of physical constraints to stabilize the unilamellar morphology and guidance of the unilamella in the correct direction through purely geometrical cues. These studies offer multiple design strategies to modulate the cell motility and directional bias on micropatterns for various applications, such as tissue engineering.

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