ABSTRACT EXAMPLE

Geometric Determinants of Directional Cell Motility Revealed Using Microcontact Printing

Eric C. Chang
Harvard Medical School, HST, 2005

Donald E. Ingber, MD, PhD
Department of Pathology & Surgery
Children's Hospital
Boston, MA

ABSTRACT

Cell shape plays a central role in cell proliferation, apoptosis, differentiation and migration. Analysis of this structural form of cell regulation has been limited by the availability of culture systems that allow control of cell shape independent of other variables, such as the concentration of soluble growth factors and insoluble extracellular matrix (ECM) adhesive ligands. Our approach to cell shape control involves use of microfabrication to pattern adhesive islands of defined size, shape, and position on the micron scale that are coated with a saturating density of ECM and surrounded by non-adhesive boundary regions. With this novel technique, we will investigate how the direction in which cells extend their leading edge can be controlled by constraining cell shape within various adhesive islands that differ in corner angles.

Mammalian cells redirect their movement in response to changes in the physical properties of their extracellular matrix (ECM) adhesive scaffolds, including changes in available substrate area, shape or flexibility. Yet, little is known about the cell's ability to discriminate between different types of spatial signals. Here we utilize a soft lithography-based, microcontact printing technology in combination with automated computerized image analysis to explore the relationship between ECM geometry and directional motility. Fibroblast cells were cultured on fibronectin-coated adhesive islands with the same area (900 um^2) but different geometric forms (square, triangle, pentagon, hexagon, trapezoid, various parallelograms) and aspect ratios. These quiescent cells remained constrained by the adhesive region and did not extend lamellipodia. In contrast, when cells adherent to square islands were stimulated with platelet-derived growth factor (PDGF) to promote motility, the cells extended F-actin-rich lamellipodia and vertical membrane ruffles preferentially from their corner regions. In addition, by imposing these simple geometric constraints through ECM, cells were directed to deposit new fibronectin fibrils in these same corner regions. Prelimary data indicated that mammalian cells can sense edges within ECM patterns that exhibit a wide range of angularity and that they use these spatial cues to guide where they will deposit ECM and extend new motile processes during the process of directional migration.