A cytocompatible photoresponsive hydrogel to study cell response to dynamic topographies

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Introduction: In tissues, cells need to continually interact with topographically changing extracellular environments. However, most studies on cellular responses to topographical cues have focused on static conditions, neglecting the dynamic, spatiotemporal variations found in native tissues. To address this gap, we introduce a simple and effective approach: a dynamic cell culture platform utilizing a light-responsive spiropyran-containing poly(N-isopropylacrylamide) (Sp-pNIPAM) hydrogel.

Methods: We produced surface-constrained Sp-pNIPAM hydrogels coated with a thin elastomeric layer to minimize buffer interference. Upon blue light illumination (455 nm) through a mask, the stable, hydrophilic protonated merocyanine form in the exposed areas isomerizes to the hydrophobic spiropyran form, resulting in local hydrogel shrinkage and a controlled microscale change in hydrogel surface topography.

Results: Optical interferometry showed that a variety of topographies, defined by the mask features, can be successively and reversibly generated in the same hydrogel samples within ~15 min, without any measurable change in surface strain, stiffness, and roughness. When cells were cultured on the hydrogels, no significant difference in cell viability and DNA damage was observed before and after (masked) illumination. Recurring light-induced topographical changes was observed to result in reorganization of cell nuclei and focal adhesions, where fibroblasts form their focal adhesions (FAs) largely on the dynamic regions but shift their nuclei away from the dynamic regions. This dynamic conditioning was further found to be associated with epigenetic modifications and modulation of fibroblast phenotype.

Conclusions: Overall, our hydrogel-based platform offers a new approach to dissect the dynamic interplay between cells and their microenvironment and shines a new light on the cell’s ability to adapt to topographical changes through FA-based mechanotransduction.