Biomimetic Microcontrolled Materials for Guiding Cell Migration

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Cell migration is an essential component of tissue development and homeostasis, embryological morphogenesis, inflammation, tissue repair, angiogenesis and immune surveillance(1). Cell migration also plays a key role in determining the structure and growth rate of bioartificial tissues(2). Thus, significant attention has recently focused on developing biomimetic materials capable of guiding migration. As such, the ability of the patterning modality to create internally complex materials capable of controlling cell migration within scaffolds would represent a substantial advance.

In the present study, we establish the feasibility of patterning bioactive features into optically transparent, photoactive materials using an adaptation of conventional, i.e., single photon absorption (SPA), photolithography. Although SPA photolithography has been used to create topographical microstructures on surfaces(3), it has not, to the our knowledge, been developed for the internal modification of pre-formed materials. As we show, SPA photolithography allows for rapid and inexpensive biochemical and biomechanical patterning of existing photoactive materials in 3D.

To demonstrate the feasibility of using these internally micropatterned PEG hydrogels to guide cell migration, we patterned rectangular channels of fluorescently-labeled ACRL-PEG-RGDS into 1.5 mm thick collagenase-degradable hydrogels. The collagenase-sensitive peptide sequence used for the base hydrogel was GGPGQGILQGGK(4), which was derivatized with monoacrylated PEG at each terminus. Previous studies of cell migration into collagenase-degradable PEG hydrogels have shown that, in addition to sufficient levels of MMP, appropriate levels of a peptide capable of promoting integrin-mediated cell adhesion, such as peptide RGDS, must be present for cell migration to occur(5). Hence, by patterning ACRL-PEG-RGDS only in specific regions of the degradable hydrogel, we should be able to spatially confine cell migration to these regions.

Patterned hydrogels (n = 3) were placed into transwell inserts and HT-1080 fibrosarcoma cells, a commonly used cell type in migration studies(6), were seeded on top of the gels. After four weeks in culture, cells were labeled with Orange Cell Tracker and DAPI, and migration was assessed using confocal microscopy. Cell migration was isolated to the fluorescently-labeled RGDS channels, with the average extent of cell migration into the patterned regions being roughly 150 μm.

As demonstrated herein, internally complex materials generated using SPA photolithography can be used to guide cell migration, and thus this approach represents a powerful avenue for the exploration of a range of fundamental questions in biotechnology. Possible extensions of this technique are numerous, and include the creation of microvascular networks in 3D tissue engineered scaffolds via controlled endothelial cell migration.

References

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