Photodegradable Hydrogels for Selective Capture and Release of Rare Mammalian Cell

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Statement of Purpose: This paper describes the fabrication of capture surfaces for the specific capture and selective release of rare mammalian cells using photodegradable poly(ethylene glyocol) (PEG) hydrogels. Microfludic devices have been shown to capture rare cells from complex fluids, such as blood, at higher purity and yield than alternative methods. For the capture of circulating tumor cells (CTCs), high surface area microfluidic post arrays were first introduced [1], followed by the description of a microvortex-generating herringbone channel [2]. A current limitation to microfluidic CTC capture is the inability to selectively release cells in a viable state. Several approaches have been proposed to overcome this problem including reversible alginate coatings upon flat capture surfaces [3] and thermally reversible polymer surfaces [4]. These methods utilize bulk release of the entire capture surface and, with it, pure viable cells. They cannot, however be conveniently applied to complex geometries. The use of photodegradable PEG hydrogels allows for the molding of complex structures directly within microfluidic channels and the selective release of CTCs via local UV exposure. Using photodegradable PEG improves yield, purity, and viability of mammalian cells which are anticipated to provide earlier cancer detection, improved diagnostics, and prognostics.

Methods: The hydrogel-forming monomer solution consisted of photodegradable poly(ethylene glycol) (PEGdiPDA, [5]), poly(ethylene glycol) monoacrylate, photoinitiator, and acrylated NeutrAvidin. A polydimethylsiloxane (PDMS) channel was placed in conformal contact with an acrylated glass slide and filled with the PEG solution, which was photopolymerized using collimated visible light (400-500nm). After polymerization the channel mold was removed and a PDMS straight channel was bonded over the capture surface onto the glass slide. The polymerized hydrogel surface was functionalized with biotinylated EpCAM antibody. A suspension of A549 human lung carcinoma cells were passed over the functionalized PEGdiPDA hydrogel surface to verify capture. Captured cells are released from the hydrogel surface with light (up to 405nm, [5]) and expanded in culture.

Results: Two capture surface geometries were fabricated: flat control surfaces and herringbone patterned surfaces. Flat capture surfaces have limited interaction with cells, resulting in a low cell capture yield. To increase cell-hydrogel interaction, a herringbone patterned device was created. This surface introduces recirculating flows (Figure 1) which cause more cell-hydrogel interactions, and therefor a higher yield of captured cells [1]. Studies with herringbone patterned PDMS devices have previously reported high recovery of spiked cell (91.8%) from whole blood, but poor purity (14%). While captured cells were largely viable (95%), they could not be released from the device and could only be cultured in vitro [2]. Currently, we have been able to show successful capture of A549 cells spiked into phosphate buffered saline solution (PBS) on both surface geometries. Successful release of cells from the capture surface by using UV light has been observed (Figure 1). Initial capture numbers showed 6% of the cells ran over the flat surfaces were captured and 15% were captured on the herringbone surfaces. Our PEG-based herringbone capture surfaces display improved recovery over flat surfaces while enabling specific release of target cells, and therefore higher purity.

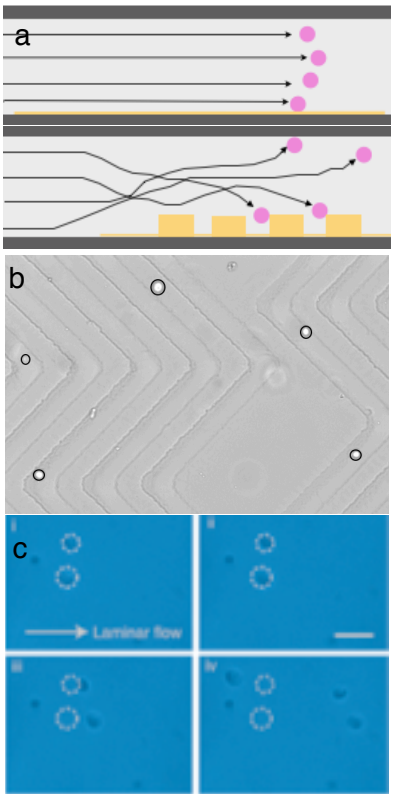

Figure 1. (a) The top image depicts the flow profile in a flat channel, and the bottom image depicts the recirculating flow that occurs within a herringbone channel. (b) Cells captured on a herringbone gel. (c) Cells being released from a gel after capture. Scale bar, 60μm

Conclusions: The use of photodegradable PEG and microfluidic devices to create capture surfaces has successfully been shown to capture and selectively release cells, and mold into complex geometries. Improvements in yield, purity, and viability of mammalian cells are anticipated to provide earlier cancer detection, improved diagnostics and prognostics.

References:

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