A Cell-Laden Microfluidic Hydrogel for Tissue Engineering and Diagnostics

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Statement of Purpose: The encapsulation of mammalian cells within the bulk material of microfluidic channels may be beneficial for a variety of applications ranging from tissue engineering to cell-based diagnostics. In this work, we present a technique for fabricating microfluidic channels from cell-laden agarose hydrogels.

Methods: Using standard micromolding techniques, 3% liquid low-melt agarose containing cells was molded against a SU-8 patterned silicon wafer (Figure 1). To generate sealed and water-tight microfluidic channels, the surface of the molded agarose was heated at 71°C for 3 s and sealed to another surface-heated slab of agarose. Proper channel sealing was verified by flow of fluorescent dye using a syringe pump. Additionally, cell media was delivered through the channel via a syringe pump in cell experiments and initial cell viability as well as viability over time were analyzed by live/dead assay of channel cross-sections.

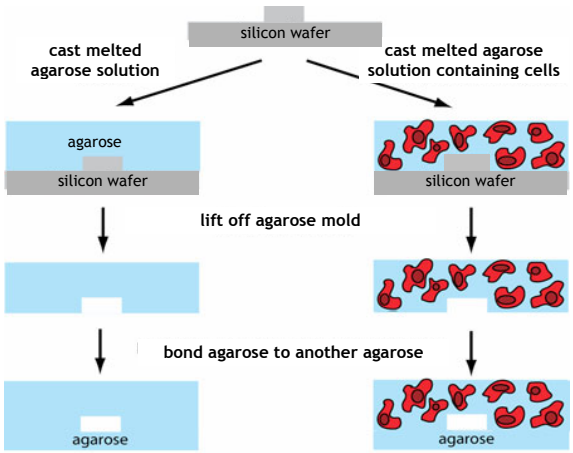

Figure 1.

Results/Discussion: Channels of different dimensions and aspect ratios ranging from (width x height) 50 x 70µm to 1000 x 150µm were generated to show that agarose is a capable of reproducing high-fidelity patterns with sharp corners (data not shown). Furthermore, channel sealing was verified by flow of fluorescent dye to determine that agarose, though highly porous, is suitable material for performing microfluidics. The specific processing conditions were found to be extremely important for proper sealing; while too little heating resulted in inadequate sealing, too much heating resulted in melting of the agarose channel features. Fluorescence imaging of cells showed them to be embedded and homogeneously distributed within the bulk material. Due to diffusion transport limitations through the bulk agarose material from the microchannel, cell viability over time with media flow through the channels produced an expected and characteristic pattern (Figure 2).

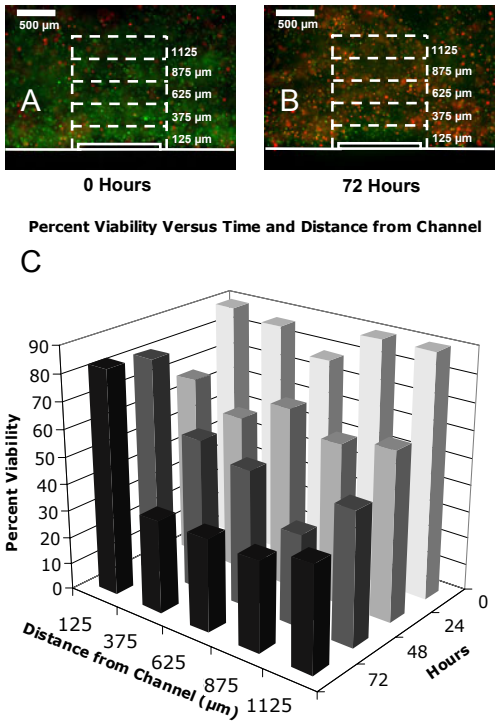

Figure 2.

While most cells remained viable upon initial device fabrication, only those cells near the microfluidic channels remained viable after 3 days, forming a 'ring' of viability. This result suggests the efficacy of perfused networks of microchannels for nutrient delivery and waste removal to maintain high cell viability of cells embedded within large hydrogels.

Conclusions: Agarose was shown to be a useful material for microfluidics and perfused cell-laden scaffolding. It is capable of forming sealed microfluidic channels while simultaneously allowing nutrient diffusion into the bulk material. Further development of this technique may lead to the generation of more biomimetic synthetic vasculature for tissue engineering, diagnostics, and drug screening applications.