Surface Engineering in Microfluidic Devices for the Isolation of Smooth Muscle Cells and Endothelial Cells

Shashi K. Murthy,[1] Brian Plouffe,[1] and Milica Radisic.[2]
[1]Northeastern University, Boston, USA and the [2]University of Toronto, Toronto, Canada.

Statement of Purpose: Microfluidic cell separation systems have emerged as attractive alternatives to traditional techniques in recent years. These systems offer the advantages of being able to handle small sample volumes and at the same time achieve highly selective separation. Conventional separation techniques, including both fluorescence-activated cell sorting (FACS) and magnetic-activated cell sorting (MACS), typically require a pre-processing incubation step to attach ligated tags (such as fluorescent dyes or magnetic beads) to cell surfaces prior to separation. These techniques are also constrained by infrastructure and high cost. Microfluidic devices with surface-immobilized adhesion molecules eliminate the need for pre-processing incubation and are a low cost alternative.

Methods: The adhesion peptides coated on to the microfluidic device surfaces val-ala-pro-gly (VAPG) and arg-glu-asp-val (REDV). These peptides are known to bind selectively to smooth muscle cells and endothelial cells, respectively, in static systems. Surface attachment of the peptides was performed using silane chemistry and NHS-ester coupling. The geometry of the microfluidic devices used in this work is such that the shear stress changes linearly as a function of flow channel length, allowing simultaneous evaluation of the effects of surface chemistry and fluid shear on cell adhesion. Cell adhesion was examined in a shear stress range of 1.3-4.0 dyn/cm^2. Experiments were performed with three cell lines: mooth muscle (A7r5), endothelial (H5V), and fibroblast (3T3-J2) in single cell-type as well as mixed suspensions.

Results/Discussion: Under the flow and surface conditions described above, endothelial cells show significantly higher adhesion to REDV-coated devices compared to smooth muscle cells and fibroblasts (Figure 1). Correspondingly, smooth muscle cell adhesion in VAPG-coated devices is much greater than that of endothelial cells and fibroblasts. This selective binding behavior is also observed when mixed suspensions of the three cell types are flowed into both types of peptide-coated microfluidic devices.

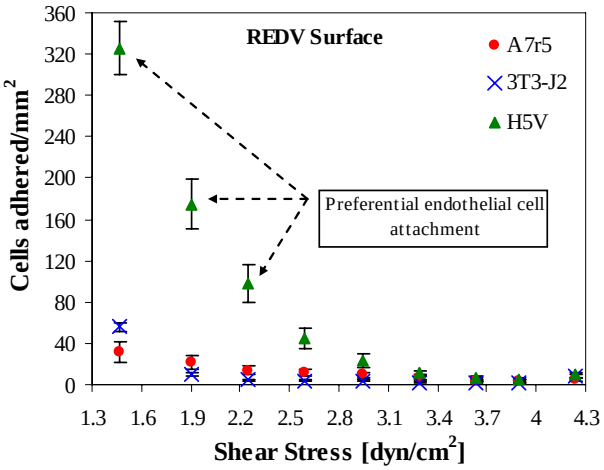

Figure 1. Adhesion of smooth muscle (A7r5), endothelial (H5V), and fibroblast (3T3-J2) cells as a function of shear stress in a microfluidic device coated with REDV. Endothelial cells show significantly higher adhesion compared to the other cell types.

Conclusions: These results suggest that microfluidic devices coated with REDV and VAPG can be used as effective separation tools. This method can find applications in areas such as tissue engineering and diagnostics, where there is a need to either enrich a particular cell type or indentify and isolate rare cell types.