Extracellular and Intracellular Phenomena in Microfluidic Flow

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Adhesion-based microfluidic cell separation techniques have been utilized for a wide range of applications, from cancer diagnostics to tissue engineering. The efficacy of adhesion-based microfluidic cell separation is governed by two factors: the affinity of cells to the ligands utilized for capture (typically antibodies or peptides) and the magnitude of fluid shear forces. The design of adhesion-based microfluidic cell separation systems is generally carried out with the implicit assumption that cells are quiescent during the separation process. While this assumption probably applies to the majority of applications where adhesion-based microfluidic separation has been utilized, not enough is known about how such changes might occur, particularly with respect to sensitive cells such as stem/progenitor cells and cells known to respond to shear forces. Therefore, this work focuses on understanding the role shear stress, ligand density, receptor density and binding strength play in cell adhesion within microchannels.

To thoroughly investigate these parameters the following tasks were performed: (1) Cells were pre-incubated in a ligand prior to flowing them into microchannels functionalized with the same ligand as a means of evaluating the effect shear stress had on receptor expression. (2) Microchannel surfaces were functionalized with varied ligand density, and cell attachment on these surfaces enumerated to determine the effect ligand density had on cells of varied receptor density. (3) Cells were incubated in ligand functionalized microchannels over a range on times and the cells detached by flow to evaluate the strength of the receptor-ligand bond. (4) Mouse embryo derived cells were subjected to shear stress using two shear platforms as a means to determine the effect shear stress has on hematopoiesis.

Overall this work shows that ligand density, receptor density and binding strength are key factors that should be considered when developing an efficient capture platform. More specifically cells pre-incubated with a ligand that was also functionalized in the microchannel responded to shear stress and the ligand by upregulating receptors. This upregulation was shown to be mediated by p38 mitogen-activated protein kinase receptor recycling. We further show that high cell capture is mitigated by both receptor presentation and a strong ligand-receptor bond. Cell capture can also be affected by the ligand density on the channel surface which this work shows by isolating two phenotypically similar cells using devices having varied ligand density. Finally it is shown that with minimal shear stress cells (mouse-embryo derived) can differentiate into blood cells.