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Modeling of Local Inflammatory Factors Regulating Targeting Nanocarriers to Inflamed Endothelium

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Extended Abstract

Endothelial cells form the inner lining of blood vessels and are exposed to various factors like hemodynamic conditions (shear stress, laminar, turbulent flow), biochemical signals (cytokines) and interaction with other cell types (smooth muscle cells, monocytes, platelets etc). Blood vessel functions are regulated by interactions among these factors. The occurrence of a pathological condition would lead to localized upregulation of cell adhesion molecules on the endothelial lining of the blood vessel. This process is promoted by circulating cytokines such as tumor necrosis factor-alpha (TNF-α), which leads to expression of intercellular adhesion molecule-1 (ICAM-1) on the endothelial cell surface among other molecules. ICAM-1 is critical in regulating endothelial cell layer dynamic integrity and cytoskeletal remodeling and also mediates direct cell-cell interactions as part of inflammatory responses and wound healing. In this study we developed a novel biomimetic blood vessel model by culturing confluent, flow aligned, endothelial cells in a microfluidic platform, and performed real time *in situ* characterization of flow mediated localized pro-inflammatory endothelial activation. The model mimics the physiological phenomenon of cytokine activation of endothelium from the tissue side and studies the heterogeneity in localized surface ICAM-1 expression and F-actin arrangement. Fluorescent antibody coated particles were used as imaging probes for identifying endothelial cell surface ICAM-1 expression. The binding properties of particles were evaluated under flow for different particle sizes and antibody coating densities[1]. This allowed the investigation of spatial resolution and accessibility of ICAM-1 molecules expressed on the endothelial cells, along with their sensitivity in receptor-ligand recognition and binding. This work has developed an *in vitro* blood vessel model[2] that can integrate various heterogeneous factors to effectively mimic a complex and physiologically relevant endothelial microenvironment.

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