IN VITRO ANALYSIS OF MONOCYTE-ENDOTHELIAL CELL INTERACTIONS MEDIATED BY INFLAMMATORY CYTOKINES

Chong Chen and Damir Khismatullin

Department of Biomedical Engineering, School of Science and Engineering, Tulane University, New Orleans, LA 70118

Abstract
Monocyte rolling and adhesion on vascular endothelium play a vital role in many inflammatory diseases including atherosclerosis. Cell-derived inflammatory cytokines, such as tumor necrosis factor (TNF-α) and histamine, upregulate the expression of cell adhesion molecules on the endothelial surface but they may activate different types of adhesion molecules and thus differentially influence monocyte-endothelial cell interactions. In this work, we study the differential role of TNF-α and histamine in rolling and adhesion of THP-1 (human acute monocytic leukemia cell line) on a confluent monolayer of HUVEC (human umbilical vein endothelial cells) under shear flow and static conditions in vitro. All flow experiments were conducted in the Bioflux 200 microfluidic shear flow system (Fluxion Biosciences) that provides a convenient and efficient way to study cell-cell interactions for a wide range of wall shear stresses (up to 20 dyne/cm²). According to our data, both TNF-α and histamine enhance the adhesion and rolling of THP-1 on HUVEC. However, histamine plays the most important role in monocyte rolling, while TNF-α is primarily involved in firm adhesion. Flow cytometric analysis shows that histamine-activated HUVEC express more P-selectin than TNF-α-activated HUVEC. This indicates that P-selectin is the primary cell adhesion molecule involved in monocyte rolling. Our current work focuses on understanding the combined role of shear flow and endothelial dysfunction by oxidized low density lipoprotein (oxLDL) in monocyte rolling and adhesion. OxLDL is known to be a key factor in development of atherosclerosis. The preliminary data show that monocytes roll slower on oxLDL-activated on HUVEC than on nonstimulated endothelium, but the effect of oxLDL is less pronounced than that of histamine.