

“Shear Dependent Shedding of the Endothelial Glycocalyx and the Mechanics of Leukocyte-Endothelium Adhesion”

It is well recognized that as blood flow exits the capillary circulation into the small veins (post-capillary venules) leukocytes (White Blood Cells, WBC's) may adhere to the venular wall in response to stimulation of receptor mediated adhesion molecules on the WBC and endothelial cells (EC). WBC-EC adhesion may obstruct the lumen of venules and reduce flow and oxygen transport to tissue. The mechanics of WBC-EC adhesion is known to revolve around the binding of specific ligands on the WBC and their counterparts on the EC. These adhesion molecules are buried within a layer of polysaccharides and proteins (glycocalyx) on the EC surface that appears to shield them to preclude indiscriminate adhesion. Analysis of alterations in the polysaccharide content on the surface of the EC during flow reductions (ischemia) and inflammation suggest that glycans may be enzymatically shed from the EC surface to facilitate WBC-EC adhesion. This process may be inhibited by various agents which affect endothelial cell signal transduction or inhibit the activity of matrixmetalloproteases. The results of these studies suggest that the composition of the endothelial glycocalyx reflects a balance of shear dependent removal of glycans and the continued biosynthesis of new glycans. Understanding the mechanical and chemical factors that affect the composition of the glycocalyx may lead to new therapeutic treatments of inflammation and the low flow state.