

528d The Effects of Cytoskeleton Disruption in Membrane Tether Formation and Leukocyte Rolling

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Leukocyte rolling and initial interactions with vascular endothelium at inflammatory sites are mediated by adhesion molecules expressed on the cell-surface and the shear stress associated with blood flow. Cytoskeletal rearrangement in circulating neutrophils is a critical element of cellular activation, rolling and adhesion. Intracellular actin dynamics may be triggered by numerous signaling mechanisms, including binding of endothelial P-selectin to a specific receptor, P-selectin glycoprotein ligand-1 (PSGL-1), on the neutrophil surface. However, the exact mechanism of this process is still unknown. In the present study we examined the effects of direct inhibition of actin turnover on velocity of human neutrophils and CHO-cells rolling over P-selectin substrates in a model system. Three different actin inhibitors, Latrunculin A, Cytochalasin B, and Jasplakinolide, targeting different steps of actin polymerization were applied. Velocity of cells rolling over surfaces coated with P-selectin at different site densities was measured at shear rates of 50, 100, 200, 400 and 800 s⁻¹. Disturbances in actin polymerization produced by these inhibitors resulted in significant increase of the rolling velocity of neutrophils at high shear rates and dramatic changes in membrane tether formation.