528c Micropatterns of P-Selectin Enhance Cell Capture and Rolling

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Leukocyte capture and transient adhesion, or rolling, along the endothelium is mediated by the selectin family of proteins and their ligands. This is a vital process of the innate immune response system, since blocking ligation of selectins with their ligands diminishes leukocyte adhesion. Parallel-plate flow chambers using uniform surface distributions of selectins have been used to study the biophysics of receptor-ligand bonds and the stochastic nature of leukocyte rolling. It has been recently shown that P-selectin exists as a punctate distribution *in vivo* or on cultured monolayers of endothelial cells. Thus, we developed a patterned surface distribution of selectins to serve as a better model of *in vivo* surface distributions to test the effect that non-uniform distributions of molecules have on the dynamics of cell adhesion. We performed *in vitro* experiments and detailed numerical simulations to examine the effects of a punctate protein distribution on leukocyte capture and rolling. By utilizing microcontact printing, we created a parallel-plate flow chamber with a patterned protein surface. These surfaces consisted of a repeating grid of 3μm x 3μm P-selectin coated squares. We also created an adhesive dynamics simulation that includes a micropatterned surface distribution, and a more accurate model of neutrophil mechanical properties and P-selectin:PSGL-1 bond dissociation kinetics. Our simulation includes the effects of cellular deformation, elasticity of the microvillus:receptor-ligand complex, receptor:cytoskeletal dissociation, viscous microvillus extrusion, and two structure-dependent receptor-ligand bond dissociation pathways[1]. We find, *in vitro* and *in silico*, that the micropatterned surface causes a decrease in average rolling velocity, and an increase in the rolling flux of human neutrophils, as compared to equivalent experiments with uniform surfaces.

1. King, M.R., V. Heinrich, E. Evans, and D. A. Hammer. 2005. Nano-to-Micro Scale Dynamics of P-selectin Detachment from Leukocyte Interfaces: III. Numerical Simulation of Tethering Under Flow. Biophys. J. 88:1676–1683