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The role of the cytoskeleton in the formation and properties of membrane tethers

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Membrane tethers play a critical role in cell adhesion and cell motility. This can be observed in the arrest of neutrophils on the endothelial wall of blood vessels during inflammatory response. Tethers are employed to slow down neutrophils when they are attracted to the periphery of the vessels due to chemotactic gradients set up by cytokines. As a result of slowing down, the neutrophil has time to form specific bonds with endothelial cells and start extravasating from the circulatory system into the surrounding tissue. Metastasizing cancer cells use a similar mechanism. A wide array of factors affects the mechanical characteristics of tethers. A major contribution is provided by the interaction between the cytoskeleton and the membrane. Interbilayer slip and the interaction between the membrane and the glycocalix are additional determinants of tether properties. Previous studies have shown a strong dependence of force needed to extract and pull a tether on the interaction between the membrane and the cytoskeleton. It has also been shown that disrupting the integrity of the cytoskeleton significantly reduces the tether force. The focus of this study was to further elucidate the contribution of the cytoskeleton-lipid bilayer interaction to the tether force, in particular how it affects cell membrane surface viscosity. Atomic Force Microscopy based force spectroscopy was used to determine the tether force and surface viscosity of the membrane prior and after the actin microfilament system had been depolyermerized by latrunculin-A. Two cells lines, Chinese Hamster Ovary (CHO) and Human Brain tumor (HB) cells were investigated. The tether force was determined when the membrane was stretched by a cantilever moving at a constant velocity over a range 3 to 21 micron/s. Surface viscosity was obtained from the slope of the linear force-speed curve. Quantitative information on tether forces and membrane surface viscosities allow for a better understanding of the mechanism responsible for the arrest of neutrophils during their attachment to the endothelial wall.