PROJECT TITLE: Nanodevices to delay or prevent thrombosis

Starting date: June 1, 2017
Minimum duration: We can offer several degree projects, long or short, involving nanodevice/particle synthesis, microfluidics visualization of UL-vWF, and impact on thrombus formation.

Hosting PI and location:
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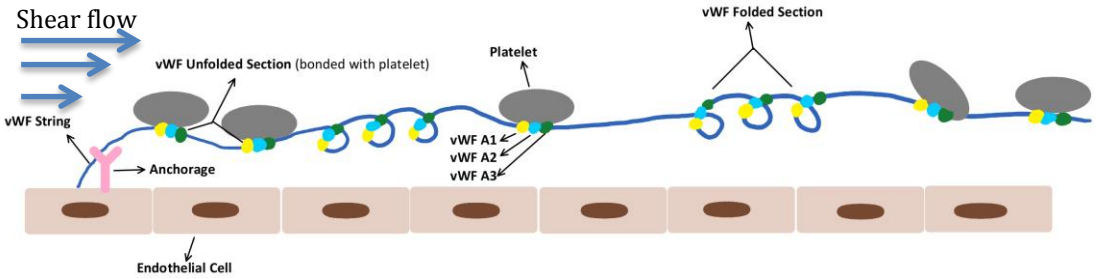
Project description:
Intra-arterial thrombosis causes heart attacks and strokes. Prevention of these fatal events is a worthy goal. The mechanism behind arterial occlusions by thrombosis has been elucidated through a series of recent observations. In particular, platelet accumulation is stimulated by pathologically high shear conditions, where circulating platelets stick to the wall without activation. Adhesion and rapid accumulation to occlusion requires platelet–vWF interaction under high shear rates. The high shear rates cause elongation of the vWF protein to expose A1 receptors in sufficient quantity to capture fast-moving circulating platelets almost instantaneously.
As the vWF capture of circulating platelets is a key step in the formation of an occlusive thrombus, it is possible that inhibition of this capture may retard development of the thrombus. Instead of biochemically altering the kinetics of the bonding via a small molecule or genetic variant, one may be able to retard the interaction by separating the vWF protein from the platelet under high shear rates.
The long-term goal of this project involves development of novel mechanisms to control interaction of vWF with platelets.



The aim of this project is to visualize nanoparticle and platelet interaction with ultralong vWF (UL-VWF) at low shear rate, as shown in the figure. The visualization of particles must be at low flow and shear rate, otherwise the particles will be moving too fast to visualize. This can be achieved by formation of UL-VWF anchored to the endothelial cells at one end. Activated EC secrets UL-VWF, anchored at one end to the EC membrane and unfolding completely due to the shear stress of the flowing plasma. A portion of the UL-VWF multimers remain attached to the surface of activated endothelial cells and can bind platelets. Particles and platelets added to the plasma are tracked by florescent microscopy to visualize their competing interaction with the UL-VWF. The results will provide insight for potential development of 'nanodevices' for control of cell interaction with the vWF.

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