The Department of Chemistry and Biochemistry

Seminar Series

Presents a Seminar Titled:

"Measurement of Mechanical Tension Across Endothelial Cell - Cell Junction Proteins"

Presented By

Dr. Daniel Conway

Assistant Professor
Department of Biomedical Engineering,
Virginia Commonwealth University

Cells are exposed to a wide variety of tissue-specific mechanical forces. These mechanical forces play important roles in development, homeostasis, and disease. A major obstacle in the study of how cells respond to forces is the inability to resolve forces across specific proteins. Recently, a calibrated FRET biosensor was developed that can be inserted into any protein and used to visualize the amount of tension across the protein. Using this technique, I developed VE-cadherin and PECAM-1 tension sensors to measure the tension changes across these two proteins in endothelial cells exposed to fluid shear stress. Fluid shear stress from blood flow acting on the endothelium critically regulates vascular morphogenesis, blood pressure, and atherosclerosis; therefore, elucidating how ECs sense flow is important for understanding both normal vascular function and disease. Onset of shear stress triggered a rapid decrease in tension across VE-cadherin, which paralleled a decrease in total cell-cell junctional tension. Flow triggered a simultaneous increase in tension across junctional PECAM-1, and this increase in tension was dependent on PECAM-1 association with vimentin. The data argue against the current model of passive transfer of force through the cytoskeleton to the junctions, but instead argue that force triggers an active rearrangement of the cytoskeleton and the formation of new connections alter forces on the junctional proteins. I am currently working with specific VE-cadherin and PECAM-1 mutants that do not experience changes in tension at onset of shear stress to identify which signaling events are tension-dependent. I will also discuss my current efforts to measure tension across other proteins.

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