Department of Bioengineering
THE UNIVERSITY OF UTAH

SEMINAR SERIES

"Engineered models of microvascular systems for basic and translational research"

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11:45 am – SMBB Auditorium

Sorenson Molecular Biotechnology Building (USTAR Bldg) – Second Floor

Anjelica Gonzalez' appointment as Assistant Professor in the Department of Biomedical Engineering at Yale University has provided a supportive and convenient platform for her research, focused on the development of biomaterials for use as investigational tools and therapeutic devices. Anjelica's group focuses on the investigation of extracellular matrix regulation of vascular immunological processes. Anjelica attended Utah State University, earning a B.S. in Irrigational and Biological Engineering and continued on at Baylor College of Medicine to pursue a PhD in Computational Biology.

Gonzalez has a dedicated interest in training the next generation of scientists to think in an interdisciplinary manner and approach problems from a scientifically global perspective. In this spirit, the Gonzalez lab combines organic chemistry, molecular biology, computational modeling and image analysis to develop materials that direct immunological processes. This work has special significance to an array of inflammatory diseases and disorders, including wound healing, tissue fibrosis and cancer.

To date, Anjelica's research has been acknowledged by national organizations, including the National Institutes of Health, NBC, American Society for Investigative Pathology, American Physiological Society and The Hartwell Foundation.

Presentation Abstract:

The three components of the microvascular wall, endothelial cells (EC), pericytes (PC) and extracellular proteins, uniquely influence microvessel susceptibility to leukocyte migration. EC-PC paracrine and contact-mediated dependence is well established in angiogenesis and vascular maintenance, but presents an uninvestigated aspect of neutrophil extravasation in the lungs, eyes and brain—tissues with a high PC to EC ratio.

Our work presents an innovative, human cell model of the postcapillary venule in which neutrophils extravasate through a cytokine-activated EC layer, PC-deposited protein layer, and PC layer, closely mimicking the microenvironment encountered by activated neutrophils. This comprehensive model can be decomposed to investigate the role of cell contact, paracrine signaling, and PC-deposited proteins in mediating inflammation. Each interaction dictating the process and mechanisms of neutrophil extravasation into extravascular tissue space. Proof-of-concept studies using cytokines (IL-1β, TNFα, and MCP-1(CCL2)) confirm the replication of crucial neutrophil and vascular responses while also elucidating their underlying mechanisms. We demonstrate that in early stages of human inflammation, PC attenuate neutrophil attraction whereas EC promote neutrophil recruitment. We also demonstrate that PC-deposited matrix proteins can modulate neutrophil transmigration through EC monolayers, potentially resulting from matrix-EC and matrix-neutrophil signaling.

Inflammation is a highly dynamic process reliant on system-wide signaling to determine human vasculature susceptibility to neutrophil extravasation. The use of human cells and biomaterials in this highly physiologically relevant model enables the isolation and manipulation of cell-cell and cell-matrix interactions that would not be possible in in vivo studies. Our work on this model continues to further incorporate protein-specific biomaterials and mechanical cues to extend its application to identify critical regulators of inflammation and to address immunological pathologies.