

**Melody Swartz**

William B. Ogden Professor

Institute for
Molecular EngineeringThe University of Chicago
Chicago, IL*Vlasta Klima
Balloun Lecture***Thursday,****March 1, 2018****11:00 a.m.****171 Durham Center****Iowa State University**

Lymphatic Vessels in Inflammation and Cancer: New Roles in Immune Regulation and Implications for Immunotherapy

In tissues, interstitial fluid flow is mechanically coupled to lymphatic drainage, and both are often increased in acute inflammation as well as in the tumor microenvironment where steeper-than-normal pressure gradients exist at the tumor margin due to higher fluid pressure in tumors. It has long been assumed that local lymph formation is driven primarily by pressure gradients generated by interstitial fluid stress and downstream lymphatic pump function, but we have found that vesicular transendothelial transport also contributes significantly to lymph formation and is actively regulated by the lymphatic endothelium according to inflammatory stimuli, allowing fine control of the delivery of antigens, cells, and chemokines to the local lymph node. While exploring how lymphatic endothelial cells actively control such delivery, we have discovered new roles that the lymphatic endothelium plays in the regulating immunity, including direct antigen presentation to T cells. In some types of inflammation, local lymphatic expansion and activation occurs, in turn changing the biomechanical and cytokine environments that alter the immune microenvironment. For example, in some cancers, we found that tumor-associated lymphangiogenesis leads to the activation of TGF- β and increased interstitial flow, both of which promote fibroblast differentiation and matrix remodeling. Lymphatic activation also triggers the release of cytokines that attract immune cells that, together with TGF- β , can promote an immune suppressive microenvironment and help the tumor escape from host immunity. Finally, our lab is exploring ways to translate this new knowledge towards strategies for immunotherapy.

Melody A. Swartz is a Professor in the Institute for Molecular Engineering at the University of Chicago, where she holds the William B. Ogden Chair and a joint appointment in the Ben May Department for Cancer Research. She holds obtained her BS from Johns Hopkins and PhD from MIT, both in Chemical Engineering. Her PhD focused on lymphatic physiology and biomechanics in the lab of Rakesh Jain, after which she undertook postdoctoral studies in mechanobiology at Brigham & Women's Hospital in the lab of Jeffrey Drazen. She was an Assistant Professor at Northwestern University in the Department of Biomedical Engineering before moving to the Ecole Polytechnique Fédérale de Lausanne (EPFL), where she was promoted to Full Professor and spent 13 years in the Institute of Bioengineering and the Swiss Institute for Experimental Cancer Research. Trained as a bioengineer, she uses quantitative approaches in immunobiology and physiology, including biotransport and biomechanics, to develop a deeper understanding of how the lymphatic system regulates immunity in homeostasis and disease, particularly in cancer and chronic inflammation. Her lab applies this knowledge to develop novel immunotherapeutic approaches in cancer, including lymph node-targeting vaccine approaches, as well as in vitro model systems that recapitulate relevant features of the 3D, perfused tumor microenvironment.

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