Department of Chemistry Seminar

“Imaging Mass Spectrometry of 3D Cell Cultures”

Three dimensional cell cultures are attractive models for biological research. They combine the flexibility of cell culture with some of the spatial and molecular complexity of tissue. For example, colon cancer cell lines form spheroids, in vitro mimics of poorly vascularized tumors. The spheroids are composed of a central necrotic core, a middle quiescent layer and an outer proliferative layer of cells, similar to a rapidly growing colon tumor. Our laboratory has characterized the distribution of endogenous proteins via MALDI imaging mass spectrometry in colon spheroids and determined that the molecular gradients correlate with the pathophysiological changes in the structure. Currently, we are interrogating the spatial distribution of proteins following the loss of function of the protein E-cadherin, a critical regulator of the metastatic process. Given the flexibility of cell culture, we can manipulate E-Cadherin expression and monitor the spatial changes in protein expression and phenotypic alterations that accompany E-Cadherin knockdown. We have also developed an approach to employ 3D cell cultures to evaluate the penetration of compounds into cellular masses. Most novel drugs are initially evaluated with 2D cultures before moving directly to costly animal studies. 3D cultures provide an ideal testbed to minimize these studies. Working with the chemotherapeutics oxaliplatin and irinotecan, our data supports differential penetration of these clinically relevant drugs. Our future studies include evaluation of drug and imaging probe libraries to evaluate the functional moieties that contribute to penetration of compounds, including the development of novel statistical workflows to evaluate imaging data generated from 3D cell cultures. We are also employing microfluidic devices to enable dynamic dosing, thus investigating the pharmacokinetics and pharmacodynamics of chemotherapy regimes in these attractive model systems.

BIO

Amanda was born and raised in Pittsburgh, PA. She earned her A.B. in chemistry at Cornell University in 1999, where she did undergraduate research in the laboratory of Prof. James M. Burlitch, synthesizing copper phthalocyanine nanoparticles.

In the fall of 1999, she began her graduate studies in analytical chemistry at the University of Illinois, Urbana-Champaign, joining the laboratory of Prof. Jonathan V. Sweedler. Her thesis work focused on the development of mass spectrometric and bioinformatic strategies to predict and identify neuropeptides. Following the completion of her Ph.D. in 2004, Amanda was invited to participate in the annotation of the newly sequenced honey bee genome as a post-doctoral fellow in the laboratories of Prof. Gene E. Robinson and Prof. Sandra L. Rodriguez-Zas at the University of Illinois. The focus of her research was constructing a methodology to utilize detected gene products, both mRNA and proteins, to decipher an unannotated genome.

In August of 2005, Amanda began her position as the Sallie Rosen Kaplen Post Doctoral Fellow at the National Cancer Institute, National Institutes of Health in the laboratory of Dr. Thomas Ried. During her time in the Ried lab, she utilized RNA interference screening techniques followed by microarray analysis to elucidate genes that regulate the viability of colorectal cancer cells. In the fall of 2009 she began her independent career as the Walther Cancer Assistant Professor in the Department of Chemistry and Biochemistry at the University of Notre Dame and was tenured in 2015. Currently, she is an Associate Professor of Chemistry and Biochemistry.

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Friday, November 11, 2016
SEH B1220
2:00 - 3:00 p.m.
Refreshments will be served at 1:45 p.m.