Imaging Mass Spectrometry of 3D Cell Cultures

Amanda Hummon, Department of Chemistry, University of Notre Dame

Abstract: 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.