Pharmaceutical Sciences Seminar
Wednesday, January 31, 2018
Room 2548 C.C. Little Building
4:00 – 5:00 p.m.

"A Comprehensive Raman-based Microanalytical Methodology for the Chemical Characterization of Alveolar Macrophages"

Presented by:

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Abstract: Over the past 500 years, significant advances in medical sciences have been made but adverse drug reactions still represent a major healthcare concern for individual patients and clinicians as well as an economic burden on hospitals and pharmaceutical companies developing new drug candidates. Bioaccumulation of xenobiotics (e.g. drug molecules, environmental toxins, food additives, etc.) has been reported for a multitude of compounds and in many cases, has been linked with the concurrent accumulation of phospholipids within various organs and cell types, termed phospholipidosis (PLD); the presence of foamy, lipid-laden, macrophages has historically served as the histopathological hallmark. Despite an abundance of research endeavors surrounding PLD over the past 30 years, the relationship between drug exposure, lipid accumulation, and observed organ toxicity has yet to be firmly established. Amiodarone, the most widely used antiarrhythmic drug in the clinical setting, is notorious for inducing PLD and causing pulmonary toxicity, an often-fatal side effect for which there is currently no diagnostic criteria. Since pulmonary alveolar macrophages are readily accessible in humans and animals via bronchoalveolar lavage (BAL), we believe these cells could feasibly serve as a clinical correlate between drug-induced PLD and observed pulmonary toxicity. **The long-term goal of this project is the development and validation of a robust Raman microscopy-based cytoanalytical methodology to enable chemical characterization of BAL cell populations and elucidate the molecular composition of these cells in absolute quantitative terms, to better assess the health status of the respiratory system.**

Accordingly, I will present how our research addresses the need for a robust, quantitative chemical imaging methodology that can be reliably utilized in the clinical setting to acquire physiologically-relevant information relating the alveolar macrophage phenotype to the health status of individual patients, thereby providing a more personalized, risk-benefit assessment for administration of medication with potential lung toxicity, such as amiodarone. As such, the project will pursue three distinct, clinically-relevant specific aims: 1) Utilizing algorithmic data-processing and statistical modelling to characterize drug exposure and bioaccumulation properties in a clinically-accessible macrophage population; 2) Development of an ultra-quantitative Raman-based cytoanalytical methodology for measurement of the absolute protein, lipid, nucleic acid, and drug content on a single-cell basis; 3) Demonstrating how quantitative spectral analysis of Raman cytochemical datasets can be used to discover new information about the structure, function, and role these cells play in the pathogenesis of different pulmonary diseases. I will discuss how *expanding this analysis beyond just amiodarone to the bioaccumulation of other xenobiotics (e.g. chemotherapeutics, antidepressants, food additives, environmental toxins, dust particles, etc.) will provide a more detailed understanding of our molecular composition and the natural balance of biomolecular components that enable us to remain alive and healthy.*

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