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Title: Understanding Drug Disposition & Safety in Lung by Mass Spectrometry Imaging

Abstract: Mass spectrometry imaging (MSI) of lung tissues offers particular challenges due to their complexity and fragility. However, many drug projects require new insights into compound distribution in the lung at both a global and high resolution level. Development of inhaled drug treatments of respiratory disease requires the optimization of delivery and retention in certain lung substructures to maximize the localized effect. Furthermore, new methods for assessing drug induced lung toxicity are also needed. In this lecture, salmeterol is used to investigate the local delivery of a drug after inhalation or intravenous administration and its pulmonary tissue deposition. Then, drug safety in lung will be evaluated using benchmark compounds and MSI to enable a fast detection and early prediction of drug induced toxicity. Two examples dealing with Phospholipidosis (PLD, a lipid storage disorder characterized by the accumulation of phospholipids in lysosomes) and lung lesions (inflammation & epithelial damages) will be discussed. These truly multimodal studies exemplify the power of combining established imaging and pathology methods with the full range of MSI platforms to tackle real world molecular toxicity in modern drug discovery. Finally, Imaging Mass Cytometry (IMC) as the next major evolution of MSI technique will be introduced. IMC can be briefly described as the combination of MSI, flow cytometry and immunohistochemistry (IHC) enabling multi-parametric and spatially resolved single-cell proteomic analysis.