The measurement of molecules within cells and organelles is analytically challenging and in the early stages of development. Certain mass spectrometric techniques possess excellent sensitivity and specificity and have the advantage of not requiring antibody or fluorescent tags. These include secondary ion mass spectrometry (SIMS); matrix-assisted laser desorption/ionization; capillary electrophoresis-electrospray ionization (ESI) MS; laser capture microdissection coupled with ESI; and live single-cell mass spectrometry (Masujima method).

As part of our research we intend to use single cell metabolomics to study the effect of drug compounds on cellular metabolism. Using the Masujima method for single cell analysis, one can detect hundreds to thousands of endogenous metabolites within cells and organelles at the attomole level. Using this approach, we propose studying the effect of drugs on real-time changes in biochemical pathways in specific regions of live cells. Individual metabolites can be identified using high-resolution mass spectrometry, MS/MS, and Principal Component Analysis. Stable isotopically-labeled analogs of endogenous metabolites may be used for quantitative measurements within the cytosol or organelles. Using this methodology, a new paradigm for drug screening based on single cell analysis of signaling networks has been proposed. Screening of new chemical entities using human cells, like biopsies, could be...
envisioned. One may study and potentially quantify cell signaling networks and correlate changes to cell and disease states with the ultimate goal of identification of efficacy and toxicity earlier in the drug screening process. One may also gain a better understanding of cell function with this approach.

**Selected Publications**

Structure-based drug design of novel, potent, and selective azabenzimidazoles (ABI) as ATR inhibitors. [2]

Structure-based drug design of novel potent and selective tetrahydropyrazolo[1,5-a]pyrazines as ATR inhibitors. [3]

Evaluation of an accurate mass approach for the simultaneous detection of drug and metabolite distributions via whole-body mass spectrometric imaging. [4]
Shahidi-Latham SK, Dutta SM, Prieto Conaway MC, Rudewicz PJ.

Click here [5] for additional publications.

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