Scaling down with Bruker: metabolite and neuropeptide measurements in individual cells and organelles

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In the postgenomic era, one expects the suite of chemical players in a tissue to be known and their functions uncovered. Perhaps surprisingly, many chemicals remain poorly characterized. One reason for this lack is the large chemical heterogeneity observed within the cells of almost every tissue, and that much of this heterogeneity is not exclusively encoded by the genome but depends on cellular context. Here we highlight recent efforts using both the Bruker SolariX FTICR and the timsTOF Pro to characterize broad range of compounds within individual pancreatic islets and brain regions, moving down to individual neurons and cells, and finally, to individual cellular organelles. With these instruments, we can measure multiple classes of analytes, sometimes on the same samples, including lipids, fatty acids, and peptides. Here we highlight the ability to perform in depth peptidome measurements from individual human islets using the timsTOF Pro to reveal neuropeptide and hormone variability in the islets. Moving on to single cells, we demonstrate both lipid and peptide characterization efforts from individual islet and brain cells with the SolariX. As another example, one of the more difficult post-translational modifications to characterize is the isomerization of an amino acid from the L-form to the D-form; using the ion mobility capabilities of the timsTOF Pro, we are able to confirm novel d-amino acid containing neuropeptides from small volume tissues and even from individual cells. Lastly, our new methodology to characterize the lipids and peptides in individual organelles such as the dense core vesicles enables subpopulations of the vesicles to be distinguished based on their chemical contents. These two instruments combine to form a powerful platform to probe cellular and subcellular chemical heterogeneity at unprecedented scale and detail.

Biography:

Jonathan Sweedler is the James R. Eiszner Family Endowed Chair in Chemistry, Director of the School of Chemical Science, and affiliated with the Institute of Genomic Biology and the Beckman Institute for Advanced Science and Technology. His research interests focus on developing new mass spectrometry

approaches for assaying small volume samples, including metabolomics and peptidomics. Recent efforts have created a range of high throughput single cell mass spectrometry approaches to probe cell heterogeneity. He has used these new tools to characterize small molecules and peptides in a range of animal models across the metazoan and in samples as small as individual cells and cellular domains. Sweedler, with large international teams of biologists and technologists, has performed comprehensive interrogation of the genome, transcriptome and peptidome in a range of animal models to uncover new neuromodulators, neurotransmitters and signaling peptides involved in wide range of functions and behaviors.

Sweedler has published more than 500 manuscripts and presented 600 invited lectures. He has received numerous awards including the ACS Award in Analytical Chemistry and the ANACHEM Award. He is currently the Editor-in-Chief for Analytical Chemistry.