In the postgenomic era, one expects the suite of chemical players in a brain region to be known and their functions uncovered. However, many cell-to-cell signaling molecules remain poorly characterized and for those that are known, their localization and dynamics are oftentimes unknown. A suite of small-scale measurement approaches are described that allow the investigation of individual neurons and small brain regions; these approaches include capillary scale separations, direct mass spectrometric-based profiling and mass spectrometry imaging. Several applications of single cell microanalysis are highlighted including the discovery of unusual metabolites to characterizing the neuropeptides in single cells. Single cell assays allow differences in the metabolome and peptidome from supposedly homogeneous populations of cells to be explored. As a further example, a unique matrix assisted laser desorption / ionization time of flight mass spectrometry approach is used to probe thousands of endocrine cells for their peptide content. Current technology efforts involve extending the depth of metabolome coverage and adapting our approaches to high throughput single cell assays. By obtaining information from tens of thousands of individual cells, rare cells are found and subtle differences in cell populations are measured. Imaging mass spectrometry and dynamic sampling of the extracellular environment also provide a functional context for the discovery of novel cell to cell signaling molecules. Our overarching goal is to uncover the complex chemical mosaic of the brain and pinpoint key cellular players in physiological and pathological processes.

Host: Leslie Sombers