ANALYTICAL SEMINAR

Capillary Electrophoresis Mass Spectrometry for Single-Cell Discoveries

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Analytical tools capable of characterizing cells are essential to understanding normal development and designing efficient therapeutics. Even today, after sequencing entire genomes, there is limited information on how molecules downstream, such as proteins and metabolites, contribute to cell processes. A major limitation has been a lack of sufficiently sensitive mass spectrometry (MS) technologies that can measure these biomolecules with scalability in space and time and compatibility for live development, a prerequisite for functional biology. In this presentation, we will discuss technological developments from our laboratory to transform MS proteomics and metabolomics to single cells using custom-built capillary electrophoresis instruments. We used these technologies to determine the proteomic and metabolomic profile of identified cells in live *Xenopus laevis* frog embryos and neurons in mouse brain tissues. Molecular measurements with separation using capillary electrophoresis and detection by (trapped ion mobility) time-of-flight or orbitrap mass spectrometry revealed quantitative molecular differences between cells of different phenotypes. Through follow-up functional experiments, we discovered molecules capable of altering normal cell fate decisions in the chordate embryo and the behavior of the resulting tadpole. The technology was scalable to smaller cells, including electrophysiologically identified neurons in the mouse brain. Proteome profiling revealed reproducible differences between dopaminergic, serotonergic, and parvalbumin interneurons. Microprobe capillary electrophoresis mass spectrometry expands the analytical toolbox of cell biology and neuroscience.

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