

Cell type-specific biotin labeling *in vivo* resolves regional neuronal proteomic differences in mouse brain

Sruti Rayaprolu¹, Sara Bitarafan⁴, Juliet Santiago^{2,3}, Ranjita Betarbet², Sydney Sunna^{2,3}, Lihong Cheng^{2,3}, Hailian Xiao^{2,3}, Ruth Nelson⁶, Prateek Kumar⁶, Pritha Bagchi^{2,3}, Duc M. Duong^{2,3}, Annie M. Goettemoeller⁵, Viktor János Oláh⁵, Matt Rowan⁵, Allan I. Levey², Levi B. Wood⁴, Nicholas T. Seyfried³, Srikant Rangaraju⁶

¹Department of Neurology, University of Florida, Gainesville, FL 32607, USA. ²Department of Neurology, Emory University, Atlanta, GA 30322, USA. ³Department of Biochemistry, Emory University, Atlanta, GA 30322, USA. ⁴Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, GA, 30332 USA. ⁵Department of Cell Biology, Emory University, Atlanta, GA 30322, USA, ⁶Department of Neurology, Yale School of Medicine, New Haven, CT 06511, USA

Proteomic profiling of brain cell types using isolation-based strategies pose limitations in resolving cellular phenotypes representative of their native state. We generated a novel mouse line for cell type-specific expression of biotin ligase TurboID, leading to *in vivo* biotinylation of proteins. Using adenoviral and transgenic approaches to label neurons, we show striking protein biotinylation in neuronal soma and axons throughout the brain and quantified over 2,000 neuron-derived proteins spanning synaptic proteins, transporters, ion channels and disease-relevant druggable targets. Next, we compared Camk2a-neuron and Aldh1l1-astrocyte proteomes, and resolved brain region-specific proteomic differences within neurons, some of which may underlie selective vulnerability to neurological diseases. Leveraging the cellular specificity of proteomic labeling, we used an antibody-based approach to uncover differences in neuron and astrocyte-derived signaling phospho-proteins and cytokines. This approach will facilitate the characterization of cell-type specific proteomes in a diverse number of tissues under both physiological and pathological states.

Presenter Name and contact information:

Sruti Rayaprolu, Ph.D., Associate Scientist
Department of Neurology
Center for Translational Research in Neurodegenerative Diseases
1Florida Alzheimer's Disease Research Center
University of Florida, College of Medicine
Gainesville, FL, USA
Email: sruti.rayaprolu@ufl.edu