Title: Understanding the Wiring of the Brain: Genome-Wide Analysis of Local Protein Synthesis

Presented by: Joshua Ainsley

Authors: Joshua Ainsley; Laurel Drane; Jonathan Jacobs; Leon Reijmers, Department of Neuroscience, School of Medicine, Tufts University

Abstract:

Translation of mRNA into proteins can occur in a highly regulated spatial pattern within cells. Indeed, subcellular localization and translation of mRNA supports functional differentiation between cellular compartments. In neuronal dendrites, local translation of mRNA provides a rapid and specific mechanism for changing the strength of the synaptic connection between cells and memory formation, and might be involved in the pathophysiology of certain brain disorders. Despite the widely accepted importance of dendritic mRNA translation, little is known about which mRNAs can be translated in dendrites in vivo and when their translation occurs. By collecting ribosome-bound mRNA from the dendrites of CA1 pyramidal neurons in the adult mouse hippocampus, we found that dendritic mRNA rapidly associates with ribosomes following a novel experience. High throughput RNA sequencing (RNA-Seq) allowed for accurate quantification of gene expression in dendrites before and after the animals were exposed to a novel experience. The large amount of data generated with RNA-Seq techniques required advanced statistical methods for proper analysis. By using machine learning classification techniques, we revealed an unexpected breadth of ribosome-bound dendritic mRNAs, including mRNAs expected to be exclusive to the soma. Our findings are in agreement with a mechanism of synaptic plasticity that engages acute local translation of functionally diverse dendritic mRNAs and highlight the utility of machine learning methods in quantitative biology.