Dynamic RNA Imaging and Synaptic Epitranscriptomics

Summary

Brain development and function are dependent on dynamic gene expression. Although the advent of functional genomics and system biology has enabled unbiased detection of RNAs and proteins, our understanding of the complex gene regulatory mechanisms lacks temporal and spatial precision, hindering the translational breakthroughs that will be driven by better understanding of human brain function and neurological diseases. To solve this problem, we have focused on understanding post-transcriptional regulation pathways by “seeing, analyzing, and mimicking” RNA molecules. We demonstrate that RNA molecules are highly mobile in living cells and their dynamic behavior can be drastically altered by chemical modifications. Studies concerning RNA chemical modifications are collectively called “epitranscriptomics”, a recently emerged field but quickly evolving and transforming the landscape of gene expression regulation. We show that one of the most abundant internal modifications of messenger RNA, N6-methyl-adenosine (m6A), marks thousands of mRNAs in neuronal processes whose decoding impacts expression of a core genetic program underlying synapse organization, plasticity, and neurodevelopment. Finally, we identify a cellular pathway for epitranscriptomic regulation through m6A in the context of brain development, Autism, and Schizophrenia.