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## **Exploring the CNS Epitranscriptome by MS-Based Approaches**

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Natural RNA is decorated with over 140 known post-transcriptional modifications (PTMs), which define structure and modulate function. We have developed an approach for PTM characterization and quantification based on direct mass spectrometric analysis with no front-end chromatography. The approach can be applied to either total RNA extracts from whole cells/tissues to obtain global PTM profiles, or individual RNA strands isolated by antisense affinity capture to monitor specific modifications. Capitalizing on this approach, we have shown that PTMs are involved in the response to heat-shock and osmotic stress in yeast. The concerted application of gene silencing techniques revealed that their presence on long non-coding RNAs is regulated by established signaling pathways. In analogous fashion, we have also found that the genomes of several RNA viruses –including HIV-1– contain a plethora of modifications that are regulated by host signaling pathways. Based on these premises, we are now investigating whether dopaminergic and GABAergic pathways may be capable of regulating the modification of viral RNAs in different types of CNS cells infected with HIV-1. This report will introduce the technology, discuss the challenges of the approach, and illustrate the results of our initial studies on human neurons, astrocytes, and microglia.