Neuronal Subtype-Specific Translational Changes Following Extended-Access Cocaine Self-Administration in Mice

Erika C. Andrade[a], Johana Alvarez[a], Eric F. Schmidt[a], Paul Greengard[b], Nathaniel Heintz[a]

[a] Laboratory of Molecular Biology, Howard Hughes Medical Institute, The Rockefeller University, 1230 York Avenue, New York, NY 10065, USA
[b] Laboratory of Molecular and Cellular Neuroscience, The Rockefeller University, 1230 York Avenue, New York, NY 10065, USA

Studies aimed at understanding the molecular basis of drug addiction have focused largely on the mesolimbic dopamine system and related structures. From these studies, long-lasting alterations in transcription are a clear consequence of repeated exposure to drugs of abuse. What remain elusive are the specific contributions of neuronal subtypes within these regions to addiction. To better understand the contributions of different cell-types, bacterial artificial chromosome (BAC) transgenic mice which drive the expression of EGFP-tagged ribosomal protein L10a in defined cell populations (known as bacTRAP transgenic lines) were trained to self-administer cocaine. Cell-types of interest include those found in the mesolimbic dopamine system, specifically D1 and D2 medium spiny neurons in dorsal striatum and nucleus accumbens. Following 2.5 weeks of extended cocaine self-administration, polysomal mRNAs were isolated by affinity purification and analyzed by RNA-seq to identify translational profiles of each cell type. Results from these studies provide insight into the neurocircuitry most affected by cocaine use as well as genes and pathways most affected.