Drug addiction is a chronic relapsing disorder driven by molecular changes that occur in the brain in response to habitual drug use, and currently available pharmacotherapies have shown only limited efficacy reducing drug use and relapse in addicts. Drug exposure produces profound changes in lipid and protein signaling processes during dependence and withdrawal that ultimately underlie many aspects of the resulting behavioral dysfunction, and collectively these molecules comprise a largely untapped resource of potentially druggable targets that can be directly translated into clinical therapeutics. Accordingly, the fundamental objective of my research is (1) to identify the novel molecular changes caused by drug exposure using advanced mass spectrometry-based platforms and (2) validate a functional role in neurological disorders. To address this issue, I employed a multidisciplinary approach to identify and validate novel lipid and protein pathways dysregulated by nicotine exposure and identified the 2-arachidonoylglycerol (lipid signal) and phosphodiesterase 10A (protein target) as two potential druggable targets of nicotine dependence. Ultimately, this research program aims to discover novel therapeutics to facilitate novel treatments for neurological dysfunction.