Name: Jennifer M. Loftis
Email: loftisj@ohsu.edu
PI Name: Ursula Sandau
PI email: sandauu@ohsu.edu

Plasma extracellular vesicles and their miRNA cargo as biosignatures for neuropsychiatric impairments in methamphetamine use disorders

Jennifer M. Loftis[1,2,3,4,7]; Erika Duggan[5]; Sierra J. Smith[6]; John P. Nolan[5]; Julie A. Saugstad[6]; Ursula S. Sandau[6]

[1]VA Portland Health Care System, Portland, OR; [2]Department of Psychiatry, Oregon Health & Science University, Portland, OR; [3]Methamphetamine Research Center, Oregon Health & Science University, Portland, OR; [4]Department of Behavioral Neuroscience, Oregon Health & Science University, Portland, OR; [5]Scintillon Institute, San Diego, CA; [6]Department of Anesthesiology & Perioperative Medicine, Oregon Health & Science University, Portland, OR; [7]Clinical Psychology PhD Program, OHSU, Portland, OR

Methamphetamine addiction is a major socioeconomic and healthcare burden, and ~70% of people with a methamphetamine use disorder also meet criteria for a co-occurring mental health diagnosis that may persist into remission and impede recovery. A major hurdle to treatment is a lack of objective blood-based biomarkers for methamphetamine addiction and its associated neuropsychiatric impairments, making it difficult to evaluate and improve treatment strategies.

Biosignatures based on objectively quantifiable blood biomarkers that relate to neuropsychiatric data could be used clinically to monitor recovery from methamphetamine use. Extracellular vesicles (EVs) are mediators of cell-to-cell communication, and studies support an emerging role for EV miRNAs in processes that underlie addictive behaviors. Here, we isolated EVs using size exclusion chromatography from the plasma of adults with active methamphetamine use (MA-ACT) and age and sex-matched controls (CTL). Multiplexed bead-based assays were performed to measure the relative abundance of 37 EV subtypes. EV MiRNA expression levels were determined by RT-qPCR arrays.

Normalized EV subtypes and EV miRNA data were correlated to measures of *i*) methamphetamine use characteristics and *ii*) neuropsychiatric function. Plasma EVs positive for inflammatory markers (CD44 and CD45) significantly correlated to measures of craving in MA-ACT as well as anxiety and memory impairments in MA-ACT and CTL participants. Five EV miRNAs also significantly correlated with clinical features of methamphetamine addiction (e.g., frequency of use, lifetime exposure), anxiety, memory, and pain. These studies demonstrate the use of plasma EVs and their miRNA cargo as biomarkers for neuropsychiatric impairments in methamphetamine use disorder.