**Exploring an endogenous role for dopamine transporter-mediated dopamine efflux in modulating neurotransmission in *Drosophila melanogaster***

Sandra Jones Ph.D., Jonathan Javitch M.D., Ph.D.

Skj2124@columbia.edu

**My research aims to understand how dopamine (DA) homeostasis is maintained and how DA dysfunction contributes to mental health disorders.** Nearly 1 in 5 U.S. adults live with a mental health disorder and the high rate of comorbidity among mental illness and substance abuse calls for research into common molecular risk factors. DA plays critical roles in reward, learning, memory, and arousal, with abnormal DA signaling linked to neuropsychiatric disorders such as Schizophrenia, attention-deficit/hyperactivity disorder (ADHD), autism, and drug abuse. The dopamine transporter (DAT) functions presynaptically in DA neurons to reuptake DA at release sites and terminate postsynaptic DA signaling. DAT variants are implicated in neuropsychiatric disorders and DAT is the primary molecular target responsible for the rewarding properties of the psychostimulant amphetamine (AMPH). AMPH promotes non-exocytotic release of DA by inducing the reverse transport of non-vesicular cytoplasmic DA through DAT, a process known as DA efflux. Whether this DAT-mediated DA efflux has a physiological or pathophysiological role independent of AMPHs is unclear. Using genetic, imaging, pharmacological, and behavioral assays in *Drosophila melanogaster*, we will test whether DAT-mediated efflux is triggered as a stress response to aberrant cytosolic DA or whether it plays a role in synaptic plasticity required for learning and memory.