"Rare Opportunities for Progress in ADHD Neurobiology: A Tale of Leaky Dopamine Synapses"

The biological mechanisms underlying risk for Attention-Deficit Hyperactivity Disorder (ADHD) are poorly understood, though genetic, pharmacological and imaging studies point to perturbations of brain dopamine signaling pathways. In a search for heritable, functional changes in dopamine modulatory genes in subjects with ADHD, we identified multiple, rare coding variants in the presynaptic dopamine transporter (DAT, SLC6A3). DAT is responsible for the efficient elimination of synaptic dopamine, and is the target of the most commonly prescribed ADHD medications. In my lecture, I will describe our efforts to establish the in vitro and in vivo impact of one of these variants (DAT Val559), a novel interaction observed with ADHD medications, and the opportunities for insights into ADHD neurobiological mechanisms afforded by the DAT Val559 mouse model.