School of

Biological Sciences

Spring 2022 Seminar Series

2022 Rilett lecture:

Presynaptic Choline Transporters: From Gene to Mouse to Disease

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Acetylcholine, the first identified neurotransmitter, and perhaps the best defined in terms of synthesis, inactivation and signaling, still poses questions whose resolution mean the difference between a healthy, happy life and a life of emotional, cognitive, autonomic, and even fatal disorders. These questions encouraged us some two decades ago to clone and characterize human and mouse choline transporters. Unlike other neurotransmitters that are removed from the synapse after release by high-affinity transport mechanisms, acetylcholine is rapidly inactivated after release by the enzyme acetylcholinesterase, which produces acetate and choline, the latter the biosynthetic precursor to acetylcholine. Indeed, it is the uptake of choline that is rate limiting in the synthesis of acetylcholine, particularly under states where acetylcholine release is high and/or sustained. We have characterized the regulatory mechanisms that position sufficient choline transporters at the presynaptic membrane to achieve optimum recapture of choline, efforts that reveal a remarkable coupling between the acetylcholine release process and choline transport. Moreover, through studies of choline transporter deficient mice, we have demonstrated the essential role the transporter plays in cholinergic signaling and extended these efforts to identify humans with transporter dysfunction. My lecture will trace the arc of these studies, ending with most recent work that demonstrates cognitive deficits from a choline transporter coding variant in the transporter found in 10% of the US population.

Thursday, April 21, 2022 at 4:00 p.m. in FSA 133