

ORGANIC SEMINAR

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"Structure-based Drug Discovery of Kynurenine Pathway Modulators as Tool Compounds for Neurodegenerative Disease and Aging-related Disorders"

The Kynurenine Pathway (KP) is the primary pathway for tryptophan catabolism in humans and produces nicotinamide adenine dinucleotide (NAD/NAD⁺) from dietary tryptophan. Dysfunction along the KP in the central nervous system (CNS) can lead to the accumulation of the neurotoxic metabolite quinolinic acid (QUIN), which has been linked to several neurodegenerative diseases including, but not limited to Alzheimer's, Parkinson's, and Huntington's. In the periphery, however, free QUIN is rapidly converted to NAD/NAD⁺, a ubiquitous enzyme cofactor with several protective functions including DNA repair and mitochondrial biogenesis, among other anti-aging processes. In this seminar, I will discuss the structure-based drug design of inhibitors of the α -amino- β -carboxymuconate- ϵ -semialdehyde decarboxylase enzyme (ACMSD) to stimulate NAD/NAD⁺ biosynthesis in the periphery, and degraders of the tryptophan 2,3-dioxygenase enzyme (TDO) to inhibit QUIN biosynthesis in the CNS.