

ORGANIC SEMINAR

Discovery and Application of Neurotoxin and Antibiotic Natural Product Biosynthesis

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Nature is a remarkable chemist capable of constructing a vast array of structurally diverse compounds, many of which possess therapeutically useful bioactivities. The McKinnie lab uses an interdisciplinary approach to better understand the role of enzymology in establishing the chemical complexity within natural product biosynthesis. Moreover, we leverage these enzymes to perform challenging regio-, chemo- and enantioselective reactions under ambient conditions, in aqueous solvents, and without requiring protecting groups. This talk will focus on our efforts towards three structurally divergent natural products from different biological hosts. We will first highlight the biosynthesis of potent freshwater cyanobacterial anticholinesterase guanitoxin, with an emphasis on the unusual pyridoxal-5'-phosphate enzymology involved in its construction. The second story will involve the kainoid synthase family of non-heme iron (II) α -ketoglutarate-dependent dioxygenases from marine micro- and macroalgae. These unusual enzymes catalyze the oxidative cyclization of *N*-prenylated L-glutamic acids to form bioactive pyrrolidine rings – our work to mechanistically understand and biocatalytically apply these enzymes will be emphasized. And lastly, we will share our recent understanding of site-selective vanadium-dependent haloperoxidases that regioselectively halogenate marine actinobacterial metabolites to modulate their physical properties and biological activities. These cumulative stories showcase our interdisciplinary efforts to better understand and apply natural product biosynthetic enzymology.



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