Our research program provides an interdisciplinary blend of synthetic and medicinal chemistry that includes the total synthesis of natural products, the discovery of new reactions, as well as the evaluation for their cellular mechanism and medicinal properties. Natural products are still the primary source for medicines, and marine sponge metabolites represent a highly diverse and complex class of natural products with remarkable biological activities. Our laboratory is focused on the total synthesis of marine sponge alkaloids, to examine their potent anti-cancer and anti-neurodegenerative properties.

**The Oroidins:** The oroidin family of alkaloids is a highly diverse and complex class of biologically active secondary marine sponge metabolites containing characteristic pyrrole-2-carboxamide and 2-aminoimidazoline (or derivatives thereof) moieties. Members of this group include the highly publicized palau’amine as well as the structurally related phakellins and phakellstatins. Our group recently developed a novel NBS mediated addition of guanidines to olefins, which was used in the total synthesis of dibromophakellin and many of its analogues. Cellular studies in our lab subsequently identified the human proteasome as a target responsible for the exiting biological properties these compounds elicit.

**Natural Product Inspired Scaffold Design:** Our scaffold design program aims at the development of small molecular weight scaffolds containing a high degree of diversity. The skeletal diversity of our scaffolds is inspired by natural products, but unlike their natural counterparts these scaffolds are readily optimized for their pharmacokinetic and pharmacodynamic properties. For example, our imidazolone-based Chk2 inhibitors (left below), can protect normal cells from ionizing radiation (IR) without interfering with IR-induced killing of tumor cells. Another example includes the imidazolone-based proteasome modulators, which elicit remarkable in vivo anti-cancer efficacy (right below). More recently, we are modifying our natural product scaffolds to prevent the aggregation of proteins such as alpha-synuclein and tau, which are involved in the pathogenesis of Parkinson’s and Alzheimer’s disease, respectively.

**SELECTED PUBLICATIONS**

Substituted quinolines as noncovalent proteasome inhibitors, McDaniel, Tanner J.; Lansdell, Thereasa A.; Dissanayake, Amila A.; Azevedo, Lauren M.; Claes, Jacob; Odom, Aaron L. and Tepe, Jetze J., Medicinal Chemistry, synthetic and medicinal chemistry, 2016, http://dx.doi.org/10.1016/j.bmc.2016.04.005


