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### The use of small molecule proteasome modulation in human diseases

Natural products isolated from plant, animal or fermentation has long been the main source for compounds used in the chemotherapeutic intervention of cancer. However, in the later part of the 20th century, the advances of combinatorial chemistry have taken center stage in the drug discovery process and natural product synthesis took a temporary backseat for these new chemical processes. Combinatorial techniques and compound repurposing have resulted into large libraries in a very cost-efficient manner that can be screened for their biological activities against a desired target. Although cost-effective, these libraries suffer from a lack of diversity with respect to the structural complexity, stereochemistry and chemical space. In addition, the enforcement of restrictions of structural complexity and “drugability rules”, further narrows the chemical space and thus limits the discovery of novel drug-target interactions. Research in the Tepe lab is primarily focused on the synthesis and use of natural products and natural product mimics to discover new drug-targets interactions. As part of this effort, the Tepe lab has developed a range of new heterocyclic reactions structurally inspired by complex marine sponge metabolites. Target identification of these natural product mimics revealed several unprecedented drug-target interactions, including mechanistically unique proteasome inhibitors and activators. Here we will present our journey towards the discovery of small molecules capable of inducing novel drug-target interactions with a specific focus on the small molecule regulation of proteasome activity.

### Biography

Jetze J Tepe received his PhD from the University of Virginia in 1998 with Prof. T L Macdonald and completed his Post-doctoral studies with Prof. R M Williams at Colorado State University in 2000. Research in his lab is primarily focused on the synthesis and use of natural products and their analogues to interrogate proteasome-mediated signaling pathways. Using the new synthetic methods, drug-like derivatives of natural products are prepared and interrogated for their clinical significance *in vitro*, cell culture and animal models. For his academic drug discovery efforts aimed at multiple myeloma, he received the American Cancer Research Scholar award, Senior Award from the Multiple Myeloma Research Foundation in 2008 and Multiple Myeloma Senior Award in 2010 and the International Myeloma Senior Award in 2013.

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