Small Molecule Probes for Interrogating Biological Pathways

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Small-molecule probes with potency and selectivity towards a specific biological target and/or pathway have been instrumental for studying biological processes. These compounds have been used as chemical biology tools to dissect the intricacies of biological pathways, elucidate various disease states, validate potential therapeutic targets and serve as starting points for novel therapeutics. In the University of Kansas Specialized Chemistry Center (SCC) we provide hit-to-lead optimization for small-molecule probe production to modulate a variety of biological targets. As part of the SCC I have had the opportunity to participate in multidisciplinary collaborative research for discovery and development of numerous probes. Select projects include the discovery of activators of the unfolded protein response apoptotic pathway, a cellular mechanism implicated in several disease states including cancer, and development of inhibitors for Trypanosoma brucei Hexokinase 1, a potential antiparasitic therapeutic target. In addition to SCC research, I have performed independent research in an effort to repurpose the antihistamine terfenadine for antimicrobial use. These projects, and the impact the small-molecule probes have had on their respective fields, will be described.