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DEPARTMENT OF CHEMISTRY

# Exploiting Natural Product Scaffolds to Design Protein-Protein Interaction (PPI) Stabilizers


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14-3-3 proteins are eukaryotic adapter molecules that regulate hundreds of client proteins by forming transient protein complexes. Certain of these PPIs play a direct role in the pathobiology of cancer and neurological disorders. Thus, there is strong interest in designing chemical tools to interrogate the role(s) of individual 14-3-3•client protein interactions in disease-relevant biochemical pathways. In this regard, the fungal phytotoxin fusicoccin A (**FC**) harbors special potential because it targets 14-3-3 functions in vivo. FC engages a select group of 14-3-3•client protein contacts and enhances these PPIs via simultaneous interactions with both proteins. This unique biological activity has stimulated efforts to develop non-natural variants of FC with tailored pharmacological profiles; however, synthetic entry to highly oxidized and architecturally complex diterpene framework of FC has emerged as a key limitation. Herein, we describe a modular approach to this motif that leverages a UV-light promoted oxidative cycloisomerization reaction. This chemistry provides stereocontrolled access to the fused 5-8-5 carbocylic ring system of FC in a single step and, importantly, enables the first fully synthetic entry point to this terpene natural product.


Date: Wed, Oct. 3, 2018
Time: 4:30-5:30 pm
Location: 208 Clark Hall

Students, meet the speaker over coffee and cookies in the Bennett Conference room at 3:30 pm