

Bankhead-Coley Cancer Research Program

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*Anatomy and Cell Biology
University of Florida*

*2009 Program
Florida Research Challenge
(2-year project)*

Project Title: Identification of Chemical Modulators of Histone Modifications through High-Throughput Screening

Project Summary: Histone acetyltransferases (HATs) and histone deacetylases (HDACs) play important roles in shaping epigenetic landscapes in the cell. They are enzymes whose activities are fundamentally altered in cancer cells, resulting in abnormal epigenetic modifications. Such epigenetic alterations are implicated in causing human cancer. Fortunately, unlike genetic mutations, epigenetic modifications are reversible by chemical agents that modulate the activities of HATs, HDACs, and other enzymes. Consequently, such agents have important therapeutic potentials for treating cancer. Indeed, one agent that inhibits HDACs was approved for clinical therapies against cancer by the FDA, and multiple clinical trials are ongoing for treating diverse human cancers. However, currently available inhibitors of HATs and HDACs suffer noted limitations such as toxicity and low efficacy. We have engineered cell lines that show promise for identifying novel and more effective agents for inhibiting HATs and HDACs. As a joint effort between University of Florida and Scripps Florida as well as access to one of the best screening facilities in the world, we propose to use engineered cell lines to screen one of the largest drug-discovery chemical libraries. The outcomes of this grant include the discovery of important lead compounds as potential anticancer agents that may benefit cancer patients. The immediate impact of this grant is that the anticipated results will form the foundation for securing long-term federal funding in Florida.