

## Bankhead-Coley Cancer Research Program

***Wu, Lizi***

*Molecular Genetics & Microbiology  
University of Florida*

*2010 Program  
Technology Transfer Feasibility  
(1-year project)*

**Project Title:** Evaluation of Novel Notch Inhibitors for In Vivo Efficacy

**Project Summary:** Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy, and T-cell ALL is an aggressive subset of ALL with poor clinical outcome. The genetic abnormality involving a gene called NOTCH1 cell surface receptor has been identified in more than 50 percent of T-ALL patients. Such abnormality results in the Notch signaling cascade that is constantly activated (“turned-on”), and this overactive signaling is sufficient to induce generation and progression of leukemia in animal models by promoting cell growth and survival. Moreover, hyperactive Notch signaling is critically involved in the pathogenesis of a variety of solid cancers such as breast cancer, lung cancer, pancreatic cancer, prostate cancer, brain cancer, and melanoma. Therefore, the Notch signaling pathway is a promising therapeutic target in the treatment of a broad range of cancers with Notch activation. We have identified small-molecule compounds that prevent aberrant Notch signaling by targeting a unique protein complex and inhibiting leukemic cell growth in vitro. In this research, we will evaluate anti-tumor effects of our lead small-molecules using mouse models of leukemia. Therefore, this project will help to establish the feasibility of developing our novel inhibitors as potential, effective targeted therapeutic agents for a broad range of cancers with aberrant active Notch signaling.