

## Bankhead-Coley Cancer Research Program

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*Biochemistry and Molecular Biology  
University of Florida*

*2009 Program  
Bridge (1-year project)*

**Project Title:** Defining Molecular Alterations in Chromatin Structure During Gene Silencing in Breast Cancer

**Project Summary:** Cancer is a disease of the genome. Genomic alterations that cause cancer are changes in DNA sequence (genetic changes) and DNA structure (epigenetic changes). Among the epigenetic changes occurring in cancer cells is epigenetic silencing, which results in decreased expression of anti-cancer tumor-suppressor genes (TSGs). We are using cutting-edge molecular genetics approaches to study multiple molecular events that occur during epigenetic silencing in both cultured breast cancer cells and mammary tumors. In Aim 1, we are studying silencing of the TG2 gene, a TSG silenced in breast cancer, using a cultured cell line in which we can induce TG2 to undergo epigenetic silencing. In addition to this study, we plan to treat human breast cancer cells with 5-azadC, a drug that reverses gene silencing, and monitor molecular events that occur during TSG re-silencing following the removal of 5-azadC. In Aim 2, we are studying epigenetic events during tumor development. Since this work is not feasibly conducted in humans, we will use an engineered mouse line that is highly prone to developing mammary tumors. We will dissect mammary glands from these mice at various time points and examine epigenetic changes within several TSGs prior to and during the development of mammary tumors. Beyond improving our knowledge of the molecular basis of cancer, defining early epigenetic events has promise in providing patients with better prognostic and diagnostic cancer markers.