

## Bankhead-Coley Cancer Research Program

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Bridge  
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**Project Title:** Interplay of Epigenetic Mechanisms in Gene Silencing

**Project Summary:** Tumor suppressor proteins are essential components of normal cells that protect against cancer formation by regulating cell growth, DNA repair, blood vessel formation, invasion and metastasis. Mutations in DNA were the first means recognized to inactivate tumor suppressor gene function and lead to increased incidence of cancer. More recently, however, tumor suppressor function was also found to be lost by changing the way the genes that encode them are packaged in the cell so that they are turned off or silenced. This process, termed epigenetic, is caused by adding small methyl chemical groups to either DNA or histone proteins, which DNA wraps around to conserve space. Thus, epigenetically-silenced genes are compacted and inaccessible to other proteins needed to induce gene expression. However, because the DNA is not mutated, it may be possible to reverse epigenetic silencing of tumor suppressor genes and thus inhibit cancer initiation. Oncogenes also play a vital role in promoting cell growth and preventing cell death; however, they can lead to cancer when unregulated. This proposal's objective is to determine mechanisms by which specific changes in DNA methylation and gene packaging occur in cells during oncogene-induced silencing of tumor suppressor genes in breast cancer. By understanding these processes, we expect that specific and reversible targets will be identified for therapeutic use in possible prevention and treatment of breast cancer initiation and progression.