

Bankhead-Coley Cancer Research Program

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2009 Program
New Investigator (3-year project)

Project Title: Novel Insights in Tamoxifen Regulation of MGMT Expression in Human Breast Cancers and Its Therapeutic Relevance

Project Summary: With more than 200,000 new cases per year, breast cancer is the most commonly diagnosed cancer and second leading cause of cancer-related deaths among women in the United States. The most commonly used hormonal therapies for breast cancer have brought about positive outcomes for many patients; however, after years of treatment, most patients develop drug resistance to these treatment options. Therefore, there is an urgent need for innovative/improved therapeutic strategies that avoid/overcome drug-related resistance and increase the overall survival of breast cancer patients. Recent reports show that cancer cells recognize and efficiently repair the therapy-induced DNA damage. This repair mechanism plays a major role in drug resistance to cancer cells, thereby having the potential to negatively impact the therapeutic efficacy. Human breast cancers are known to possess higher levels of a unique DNA repair protein called MGMT than normal breast. We identified that prolonged treatment with tamoxifen (commonly used anti-estrogen therapeutic agent for breast cancer) also induces MGMT expression. Therefore, we propose that the observed MGMT activity in breast tumors may cause resistance to therapies and usage of anti-estrogens along with MGMT blockers will not only overcome drug resistance but will also increase the efficacy of anti-estrogen drugs, ultimately decrease tumor burden, and increase the overall survival of breast cancer patients.