

Bankhead-Coley Cancer Research Program

Briegel, Karoline

*Biochemistry and Molecular Biology
University of Miami*

*2008 Program
Bridge (1-year project)*

Project Title: The Role of T Box Transcription Factor 2 (TBX2): A Novel Therapeutic Target in Breast Cancer

Project Summary: These studies aim to elucidate the molecular mechanisms underlying tumor development in familial breast cancer. T-box transcription factor 2 (TBX2), a protein that normally regulates fetal development, is present in abnormally high amounts in breast tumors of patients with a family history of breast cancer. Hereditary breast cancer is characterized by deleterious mutations in the breast cancer susceptibility genes BRCA1/2 and early onset as well as poor clinical outcome. At present, very little is known about the molecular mechanisms that lead to breast cancer development in these patients.

Published research as well as our own work strongly suggests that reactivation of TBX2 in BRCA1/2-mutant breast cells may facilitate breast tumorigenesis. For example:

- 1) TBX2 possesses characteristic features of an oncoprotein (cancer-causing protein).
- 2) TBX2 has the potential to induce cellular changes in primary breast tumor cells that are prerequisite to cancer metastasis.
- 3) Reactivation of TBX2 may endow cancer cells with an increased resistance against chemotherapy.

In this grant we are testing the hypothesis that TBX2 overexpression and familial BRCA1/2 gene mutations have a cooperative effect on promoting breast cancer development. The goal of Aim1 is to analyze the consequences of abnormal TBX2 expression on tumorigenesis of BRCA1-associated breast cancers in a mouse model that harbors both genetic events. This model is being used to determine tumor incidences as well as the molecular events downstream of TBX2 function in regulating neoplastic transformation. The purpose of Aim 2 is to assess the role of TBX2 in tumor progression of BRCA1-associated breast cancers in a cell culture model. Specifically, we are examining if abnormal activation of TBX2 makes these cancer cells more resistant to chemotherapy.

A better understanding of these mechanisms will be pivotal for the future development of preventive and more specific therapies of currently difficult-to-treat forms of breast cancer.