

Bankhead-Coley Cancer Research Program

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*Cancer Biology
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*2007 Program
New Investigator (3-year project)*

Project Title: The Role of the FOXO3a Transcription Factor in Breast Cancer

Project Summary: Breast cancer is the second leading cause of cancer-related death in women. Although some risk factors and genetic pre-dispositions involved in the development and progression of breast cancer have already been described, many factors regulating tumor growth and metastasis remain unknown. In order to develop effective therapies that stop breast cancer growth and spreading via the blood and lymphatic system, the respective underlying biological and molecular events have to be investigated further. We found in our preliminary data that a cellular protein named FOXO3a is upregulated in invasive ductal tumors and that tumor cells depleted from this protein formed smaller tumors in a mouse model for breast cancer. FOXO3a is a so-called "transcription factor," a protein that can regulate genes that control cellular processes such as survival, proliferation, and migration. So far, no knowledge is provided regarding the role of FOXO3a in breast cancer development and progression in vivo. This grant aims to define the role of the FOXO3a transcription factor in breast cancer. The overall hypothesis guiding our application is that the transcription factor FOXO3a promotes normal breast cell transformation, breast tumor growth, metastasis, and thus the malign phenotype. We will use a mouse breast cancer model (Aim 1) and two different 3-dimensional (3-D) cell culture models (Aim 2) to test this hypothesis. The 3-D cell culture models resemble either normal breast acinar structures or breast cancer-like spheroid structures. Importantly, we have found that data obtained with cell lines in these 3-D models allows predicting tumor formation and metastasis in in vivo animal models. As a potential mechanism of how FOXO3a regulates tumor progression, we will also analyze the role of FOXO3a in the regulation of genes that allow the degradation of extracellular matrix, an important step in tumor progression and metastasis (Aim 3). The long-term objectives of this project are to define the role of FOXO3a in breast cancer progression and metastasis in vivo and to determine if FOXO3a expression or activity could serve as a biomarker for the malign potential of breast tumors. The identification of a transcription factor such as FOXO3a as a regulator of genes that are involved in tumor formation would be of great benefit for the development of assays that allow pharmacological screening for drugs that inhibit its activity and thus prevent tumor growth or metastasis.