

Bankhead-Coley Cancer Research Program

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Molecular Oncology
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Bridge (1-year project)

Project Title: MicroRNAs Regulated by TGFbeta-dependent and -independent Pathways in Breast Cancer-initiating Cell and Metastasis

Project Summary: Metastasis, the process by which cancer cells move away from the primary tumor and establish new tumors in distant locations, accounts for 90 percent of all cancer death in breast cancer patients. In order to address this life-threatening problem, it is crucial to understand the molecular and cellular mechanisms that cause primary tumor to metastasize. It has been well documented that breast cancer stem cells underlie the relapsing nature of advanced disease and that transforming growth factor (TGF) beta plays a key role in regulating breast cancer stem cell self-renewal and promoting breast cancer metastasis. In addition, inhibition of the TGFbeta pathway resulted in a reversal of the breast cancer stem cells. We have recently established three breast cancer stem cell lines and shown differential expression of microRNAs (which regulate gene expression) between breast cancer stem cells and their parental cells. Because a single microRNA could regulate hundreds and even thousands of protein-coding genes, we hypothesize that the microRNAs have a critical role in regulation of cancer stem cell and metastasis. To test this, we will 1) Perform microRNA microarray analysis in all three breast cancer stem cell lines treated with/without TGFbeta inhibitor and 2) Determine whether modulation of key microRNAs reverses breast cancer stem cell phenotype, including growth in mammosphere, chemoresistance, tumorigenesis, and metastasis. These investigations will significantly enhance our understanding of the role of microRNAs in breast cancer stem cell and metastasis and provide potential therapeutic targets for treatment of this disease.