



**Susan G. Komen
Research Grants – Fiscal Year 2014**

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Biomechanical profiling as a biomarker for breast cancer progression

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Lead Organization: Duke University

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Public Abstract:

The normal cellular functions of breast epithelial cells is controlled by a family of related proteins that make up the transforming growth factor-beta (TGF- β) superfamily. The TGF- β superfamily normally inhibits breast cancer formation. However, most human breast cancer cells become resistant to these tumor suppressor effects. We have demonstrated that most human breast cancers lose expression of one of the proteins on the cell surface that binds TGF- β superfamily proteins, the TGF- β receptor, T β RIII. When breast cancer cells spread, they often stop appearing like, acting like and expressing proteins like normal epithelial cells, instead appearing like, acting like and expressing proteins like cells that make up connective tissue in the body in a process called epithelial to mesenchymal transition (EMT). The TGF- β superfamily and T β RIII both have a role in EMT, and EMT appears to have an important role in the progression of breast cancer from localized cancer to metastatic cancer. While we know that the ability of breast cancer cells to move and invade in the laboratory is a good measure of how aggressive an individual's breast cancer might be, these studies take hours to days to perform. More rapid measures that could predict how an individual's breast cancer will behave are needed to make better and more individualized treatment decisions. One potential measure is to examine the stiffness of the cell and the cell's outer membrane. We and our collaborators have set up a system to measure these biophysical properties and have used this system to assess the role of T β RIII in cancer, defining a role for T β RIII in regulating the stiffness of cancer cells relative to normal epithelial cells. We now propose to investigate whether loss of T β RIII expression during breast cancer progression is responsible for the decrease in cancer cell stiffness that allows the breast cancer cells to become more motile and invasive. We will address this question first by measuring the properties of breast cancer cells before and after EMT, including their ability to move and invade and then correlating that with the stiffness of the cancer cells. We will then optimize our ability make these same measurements on specimens from mouse models of breast cancer. We will then examine the stiffness of cancer cells from these mouse models and correlate these biophysical properties with more standard biomarkers for breast cancer behavior and clinical outcomes. Our ultimate goal is to use these measurements on breast cancer tissues to assess how breast cancers form, how each individual's breast cancer is different and how they might be treated differently. These biophysical measurements could also create new, rapidly obtained biomarker to diagnose or decide how to treat breast cancer patients on an individual basis.