Susan G. Komen
Research Grants – Fiscal Year 2014

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Targeting epithelial-stromal crosstalk networks in breast cancer

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Public Abstract:
Breast cancer takes years to develop and results from a complex set of interactions between breast epithelial cells, which undergo the genetic changes leading to breast cancer, and the supporting stromal cells in the cancer micro-environment, which provide essential supporting factors to enable the initiation, growth, progression, and metastasis of breast cancer. The epithelial and stromal cells interact through a complex process known as "epithelial-stromal crosstalk". While previous work -- both in our laboratory and by many other breast cancer researchers -- has shown the importance of epithelial-stromal interactions in breast carcinogenesis, our knowledge of the specific proteins involved in epithelial-stromal crosstalk in breast cancer remains limited. The long-term goal of our Susan G Komen Career Catalyst Research grant project is to identify novel epithelial-stromal crosstalk partners in breast cancer, and to use this knowledge to lead to improved breast cancer diagnostics and therapeutics, enabling improved breast cancer prevention, treatment, and cure rates. To work towards this goal, we will first perform a genome-wide computational analysis to identify the most important epithelial-stromal crosstalk partners contributing to breast cancer. This analysis will leverage a large set of publicly available paired expression profiling data obtained separately from both the epithelial and stromal tissue regions from normal breast samples as well as from invasive breast cancer samples. After completing these computational analyses, we will evaluate the expression of a subset of top-ranking epithelial-stromal crosstalk partners (total of 9 - 15) on a large set of benign and malignant breast tissue samples obtained from women enrolled in the Nurses' Health Study, which is one of the nation's largest and longest running studies of factors impacting breast cancer risk and survival. Using these data, we will: 1) identify epithelial-stromal cross-talk partners whose expression in benign breast tissue is associated with risk of future breast cancer; and 2) identify epithelial-stromal cross-talk partners whose expression in breast cancer is associated with breast cancer molecular phenotypes and patient survival. If successful, these analyses will result in the identification of markers that will allow physicians to more accurately predict a woman's future risk of breast cancer and to more accurately predict a breast cancer patient's prognosis. Further, if successful, the epithelial-stromal cross-talk partners identified in our analyses will represent novel drug targets for breast cancer prevention, treatment, and ultimately, cure.