Susan G. Komen
Research Grants – Fiscal Year 2014

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Translating lobular breast cancer 'omics' to improved patients outcome

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Lead Organization: Dana-Farber Cancer Institute
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Public Abstract:
Invasive lobular carcinoma (ILC) represents the second most common subtype of breast cancer, and is mostly represented by hormone receptor (HR) positive tumors. At the clinical level ILCis considered as a different breast cancer subtype with distinct responsiveness to available systemic therapies and distinct patterns of disease relapse. Despite recognized differences, most of the translational and clinical research conducted in breast cancer has not considered ILC as a separate disease entity. In our previous work we demonstrated significant differences between ILC and invasive ductal cancer (IDC). Using a technique called gene expression, we demonstrated that ILC tumors are most likely classified as luminal-A (LA) or luminal-B (LB) molecular subtypes (HR positive subtypes with low- or high-proliferative activity, respectively). Following our initial translational findings, we performed a clinical project using data from the international phase III study – BIG 1-98. We evaluated the magnitude of benefit of letrozole versus tamoxifen in the subsets of ILC and IDC tumors, considering previous findings (i.e., LA and LB) classification. The results of this effort showed greater magnitude of benefit for letrozole when compared to tamoxifen in the subset of invasive lobular carcinoma. For this application, we plan to build upon our previous results to further unravel the molecular underpinnings ILC. In the first aim we will investigate the differential effectiveness of endocrine therapies using a technology called chromatin immunoprecipiation (Chip-seq). This technology (Chip-seq) will provide us a detailed map of estrogen receptor (ER) binding sites in tumor DNA. The initial set of experiments will be performed using cell lines and a subsequent validation will be performed using tumor biopsies from a prospective clinical study. The second aim of the project is to characterize mistakes in the tumor cell DNA for which targeted therapies are being developed (i.e., somatic mutations). A technology called OncoPanel will be used in this project. The third aim of this project will interrogate a subset of invasive lobular carcinoma, for which minimal research has been conducted. This refers to ILC tumors with mixed IDC features (mixed tumors). We will investigate the outcome of this group of patients in comparison to ILC using clinical and pathologic data of 811 patients followed over a 10-year period since the diagnosis. The scientific information obtained during this effort will be crucial to inform the design of a clinical trial dedicated to the treatment of invasive lobular carcinoma. We believe the proposed research is timely and relevant with potential to improve treatment and increase survival within a 10-year period.