Susan G. Komen
Research Grants – Fiscal Year 2013

This research grant was approved by Komen's national board of directors for funding, and will be funded upon the execution of a grant agreement between Komen and the grantee institution(s).

Molecular Markers for Progression from In Situ to Invasive Breast Cancer

Investigator(s): James Hicks, Ph.D.; Jorge Reis-Filho, M.D., Ph.D.

Lead Organization: Cold Spring Harbor Laboratory
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Public Abstract:
As imaging methods for detecting early stage breast cancer have become increasingly more sensitive, a growing number of women are being diagnosed with very early stage cancers. Ductal Carcinoma In Situ (DCIS) is a non-invasive breast cancer where the cancer cells are still contained within the duct. A large percentage of women diagnosed with DCIS do not require any treatment as many DCIS lesions will not recur or progress to invasive cancer. While some women opt for no treatment, aggressive surgery, including mastectomy and radiotherapy is not uncommon. Absent reliable indicators of which lesions will recur or escape the duct and invade the surrounding breast tissue, women diagnosed with DCIS are faced with difficult decisions. They are forced to make treatment choices without evidence-based science to guide those choices. Having a way to determine a DCIS lesion is harmless would spare countless women from unnecessary medical intervention. Conversely, understanding what drives some DCIS to progress may provide an opportunity for potential earlier intervention with systemic or endocrine therapy. The basis of this research proposal is to use new molecular methods to determine the genetic basis of DCIS. We seek to identify which genes, when mutated, develop into DCIS. Then, we will identify which of those mutated genes are found in DCIS cells that have the ability to escape from the duct, invade the surrounding breast tissue and form a full blown invasive cancer. We have the opportunity to study rare, frozen specimens where both the non-invasive DCIS and invasive breast cancer (IBC) are side by side in the same lesion. Frozen specimens are necessary for extraction of undamaged DNA. We plan to study 80 pairs of DCIS and IBC using complementary deep DNA sequencing methods and ultimately identify the individual single cells that are leading to the development of DCIS and the progression of DCIS to invasive disease. To succeed, this proposal requires a combination of novel molecular technology and sophisticated statistical methods that are uniquely available through our proposed collaboration between Cold Spring Harbor Laboratory and Memorial-Sloan Kettering Cancer Center. Results from this project are likely to provide reliable methods of identifying potential diagnostic markers and predictors of the behavior of individual DCIS cases. Development of prognostic markers holds tremendous promise for DCIS patients. Collaborative interactions with their clinicians to make medically sound treatment decisions can be based upon scientifically accurate, personalized information.