



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

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Cancer mutations and prognosis in premenopausal, early-stage breast cancer

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Lead Organization: The University of Melbourne

Grant Mechanism: CCR Basic and Translational

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Public Abstract:

Diagnosis of breast cancer at a young age, particularly younger than 40 years old, is relatively uncommon and it is unclear why it is often associated with poorer outcomes. There has been very little biological research focused on the reasons why this may be so. Mutations are changes or abnormalities in the DNA of genes that can signal uncontrolled growth, a characteristic of cancer. Using state of the art technology called “next generation sequencing”, the purpose of this project is to define the “mutation landscape” or how cells grow abnormally in premenopausal estrogen receptor (ER)-positive breast cancer. We plan to do this by using samples from patients who participated in a large phase III clinical trial called SOFT (Suppression of Ovarian Function Trial). The focus of this trial was to determine if complete blockade of estrogen function can improve outcomes in premenopausal women diagnosed with breast cancer. Over 3000 premenopausal women world-wide participated in the study with nearly one-third younger than 40 years of age at the time of diagnosis. At the end of 2014, results of the SOFT study will be reported and it is expected the results will change the way women with this type of breast cancer are treated. During the study, tumor and normal tissue samples were collected in over 70% of women, providing an incredible resource for further studies to help understand the biology of the disease and its links to clinical outcomes. For example, normal cells go through a natural process of dying but when oncogenes are activated they can cause the cells not only to survive but also to multiply. One of the processes this study will focus on is the implications of PIK3CA mutations, an oncogene present in around 40% of ER-positive breast cancers. PIK3CA mutations are clearly a significant factor in breast cancer growth but we would like to know whether it is associated with a good prognosis when combined with endocrine or hormone therapies and we would also like to know what additional mutations result in a poor prognosis. NGS also allows us to potential identify many hundred’s of mutations with minimal quantity of DNA. Because a large number of women participated in the SOFT study we are confident the results we will obtain will give us a huge amount of new information about important previously unknown mutations and how they are associated with relapse and survival in breast cancer diagnosed in young women. The information that will be obtained from this project are extremely likely to provide results that will directly affect patient care and help physicians make important decisions about adjuvant therapy in this group of patients. This research project will also help us identify novel drug targets and hence give us new ideas for treatment and prevention strategies in young women.