Susan G. Komen
Research Grants – Fiscal Year 2014

This research grant was approved by Komen's national board of directors for FY2014 Research Programs funding. This grant will be funded upon the execution of grant agreements between Komen and the grantee institutions.

Mutational Landscape of Invasive Lobular Breast Cancer

Investigator(s): Christos Sotiriou, M.D., Ph.D.
Lead Organization: Jules Bordet Institute
Grant Mechanism: KS **Grant ID:** SAC110043

Public Abstract:
Significant gains have been achieved in the field of breast cancer research over the last two decades. The complexity of breast cancer is now better understood. However, most of the research programs conducted so far focused on the most common subtype of breast cancer (invasive ductal carcinoma - IDC), leaving behind specific subtypes of breast cancer such as invasive lobular carcinoma (ILC). Invasive lobular carcinoma represents the second most common type of breast cancer, but knowledge about the optimal treatment of this disease subset remains suboptimal. Tumor grade assessed at the microscope is an important feature for choosing appropriate treatments after breast cancer surgery. However, in the subset of invasive lobular carcinoma, the importance of tumor grade remains controversial. With the support of Susan G. Komen for the Cure, the Breast Cancer Translational Research Unit of the Institute Jules Bordet (IJB) in Brussels already conducted a comprehensive research program aiming to elucidate the biological underpinnings of ILC. Genetic material extracted from ILC tumor samples have been studied using modern techniques. Using microarray gene expression technology, which measures the expression of thousands of genes, we were able to evaluate the importance of grade in ILC using a gene signature named genomic grade index. We demonstrated for the first time that genomic grade index represents an important prognostic tool in invasive lobular carcinoma. We further expanded our molecular understanding of ILC by interrogating other aspects of their biology, such as DNA methylation in order to uncover epigenetic modifications that may be involved in the biology of lobular carcinomas, and copy number changes in ILC compared to IDC. During the last couple of years, significant advances have been done in the sequencing technology, which now allows interrogating for the presence of mutations in a relatively large number of samples in a reasonable period of time. In this project, which is the direct and logical continuation of the above described research, we will aim to provide the mutational landscape of cancer genes in ILC in the largest cohort of ILC samples ever sequenced (1093 samples from 653 unique ILC patients) using targeted sequencing. This will allow us to identify recurrently mutated genes in ILC, which could then potentially be targeted by some specific treatment. Altogether, we believe that this effort will be fundamental for a better classification of ILCs, and a subsequent tailored treatment of ILC with improvement in patients' outcome.