Susan G. Komen
Research Grants – Fiscal Year 2014

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Molecular and clinical characterization of breast cancer heterogeneity in Israel

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Public Abstract:
Breast cancer is composed of different diseases which vary according to the origin of the cancer cell types as well as their location. Breast cancer originates and progresses as a result of molecular processes. Our aim in this study is to understand the molecular processes that are the basis of breast cancer development, progression, metastasis and resistance to therapy.
As cancer progresses, new mutations (genetic alterations) occur and accumulate in the cancer cells. Our working hypothesis is that early identification of such genetic signatures will shed light on tumor evolution and will lead to the development of rationally targeted and individualized therapy.
We address several clinically relevant questions and plan to detect and analyze the genetic differences underlying the following processes:
1.To understand the molecular mechanism(s) of the development of invasive cancer (IDC – invasive ductal carcinoma) from locally confounded cancer (DCIS – ductal carcinoma in-situ). We propose to investigate tumor evolution by analyzing the mutational spectrum of a certain patient's tumors at different stages of the disease progression.
2.Characterization the breast cancer evolution throughout the timeline of pre-operative (neo-adjuvant) chemotherapy. We plan to identify expression signatures that predict recurrence at the biopsy stage.
Overall, in addition to the contribution of this study to the improvement of breast cancer prevention and management, it has also the potential to contribute to cancer study in general. The produced data from these studies have the following potential: A. providing the research community with a basic understanding of the tumorigenic process. B. detecting a set of potential biomarkers involved in these processes. Identifying the cases prone either to resist therapy, or cause tumor progression, or recur; would justify more aggressive therapy, while avoiding unnecessary morbidity. On the other hand, identification of low-risk patients can help reconsider the most appropriate treatment management thus avoiding short- and long-term morbidities, as well as side effects undermining patients' quality of life.
3.The mechanism(s) lead to the significant difference in the response rate to treatment (pathological complete response) between young and older patients receiving pre-operative chemotherapy (neo-adjuvant).