Susan G. Komen
Research Grants – Fiscal Year 2014

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Breast cancer cell sensitivity to radiotherapy in the presence of PARP inhibitors

Investigator(s): Lori Pierce, M.D.
Lead Organization: University of Michigan
Grant Mechanism: KS **Grant ID:** SAC110029

Public Abstract:
Currently, breast conservation therapy for patients with localized invasive breast cancer includes surgical resection followed by radiation therapy, with chemotherapy given to selected patients. While molecular prognostic tools, such as OncotypeDx, can be used to help guide decisions regarding chemotherapy in subsets of breast cancer patients, no similar tools exist to inform decisions regarding radiation therapy. Therefore, there is a clear need to identify the inherent radiation sensitivity of each patient's breast cancer, and to develop approaches of combining targeted drugs with radiation therapy for patients with aggressive tumors that have a high chance of local recurrence following radiation alone. To this end, we have previously generated a radiation sensitivity signature, named RadiotypeDx, in a series of laboratory studies assessing the expression of genes which can distinguish between radiation sensitive and radiation-resistant breast cancer cell lines. In the current proposal, we now seek to assess the perform a nee of this signature in clinica I specimens from patients with breast cancer, by using previously published gene expression data collected from tumor samples from cohorts of breast cancer patients. In addition, we hope to evaluate for associations between radiation resistance, as predicted by RadiotypeDx, and breast cancer cell line sensitivity to hundreds of drugs, as an approach for discovering potential therapeutic strategies which may overcome radiation resistance. Lastly, we plan to test the top therapeutic strategies, as nominated from our analyses, in laboratory models of breast cancer. We believe that successful completion of this project will allow us to identify and confirm biological markers of breast cancer resistance to radiation, and to develop new strategies for increasing the sensitivity of aggressive breast cancers to radiation therapy. In doing so, we hope that this project provides a scientific foundation for our next generation of clinical trials in this area.