



Susan G. Komen

Research Grants – Fiscal Year 2015

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Optimizing therapy for early-stage triple-negative breast cancer

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Lead Organization: Stanford University

Grant Mechanism: Komen Scholars

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Public Abstract:

The current approach to the treatment of early stage triple-negative breast cancer (TNBC) has changed little in 15+ years. However, a growing body of evidence suggests that platinum chemotherapy drugs may be more active against tumors in BRCA1 and BRCA2 gene carriers and potentially other TNBC tumors with altered DNA repair function. Recent clinical trial data in all patients with TNBC suggest that platinum chemotherapy agents can increase the rate of favorable response when added to standard chemotherapy drugs given prior to surgery, yet toxicity is increased and the benefits do not appear to be equally experienced by all patients.

Optimizing therapy for this high-risk group of patients, by giving platinum treatment to those most likely to benefit and sparing toxicity for those unlikely to benefit, is a high priority.

Given the clinical potential of drugs such as platinum, new methods to assess the DNA repair capacity of tumors (functional versus dysfunctional) have been developed. We have shown that these tumor-based tests can identify TNBC patients, with and without an inherited risk of breast cancer due to BRCA1 or BRCA2 gene mutations, most likely to benefit from chemotherapy drugs like platinum. As such, the clinical trial proposed will directly address the customized chemotherapy treatment of women with newly diagnosed early-stage TNBC on the basis of the tumor's DNA repair function (functional versus dysfunctional). If successful, this trial will provide important evidence with great potential to lead to a shift in the treatment approach for newly diagnosed breast cancer with tumor DNA repair dysfunction.



Interestingly, recent studies have also documented that the body's immune system plays an important role in prognosis and chemotherapy response in TNBC. The presence or absence of the body's immune cells around a tumor in the breast has been shown to influence how likely that tumor is to respond to chemotherapy. Interestingly, we have shown that tumors lacking a normal capacity to repair DNA damage appear to be the same tumors that are more likely to have infiltrating immune cells around the tumor cells and are more likely to respond favorably to chemotherapy treatment. As part of this proposal, we will further evaluate this interplay between immune cell infiltration and DNA repair dysfunction in TNBC. A better understanding of the relationships between tumor immunity and DNA repair dysfunction may provide important insights regarding the response to both standard chemotherapy drugs and novel immunotherapy drugs currently in early clinical testing in TNBC.

