



**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.

Genomic predictors of chemotherapy-induced toxicity

Investigator(s): Brian Schneider, M.D.

Lead Organization: Indiana University

Grant Mechanism: KS

Grant ID: SAC110056

Public Abstract:

The side effects from chemotherapy is an important problem that can adversely impact patients' quality of life and can also result in truncated therapy that may have adverse implications with regard to efficacy. Specifically, taxane-induced peripheral neuropathy can be irreversible and dramatically interfere with daily functions. Also, therapy induced heart failure can impact both quality of life and may be life-threatening. The frequency and severity of these toxicities are highly variable from patient to patient and this heterogeneity may be due to simple differences in our inherited genetics. We have previously evaluated common genetic variations throughout the entire genome of over 3300 patients in a large breast cancer trial (E5103) where patients received commonly used breast cancer drugs. In this proposal we plan to further explore some of the provocative genetic difference identified in this trial to better predict the likelihood of experiencing peripheral neuropathy and congestive heart failure. Specifically we will plan to validate our initial findings for taxane-induced neuropathy in a large independent breast cancer trial (E1199). We will also evaluate for rare genetic variants in the same trial, E5103, using a cutting edge genomic technology called next generation sequencing. The discovery of validated inherited genetic markers to better predict these toxicities a priori has the potential to allow for better counseling, preferentially select drugs and regimens, and may ultimately shed insight on the underlying cause of these toxicities which can lead to novel preventative therapies.