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.

Prioritizing adjuvant targeted therapy for TNBC patients via molecular profiling

Investigator(s): Justin Balko,Pharm.D., Ph.D.
Lead Organization: Vanderbilt University
Grant Mechanism: CCR Basic and Translational **Grant ID:** CCR14299052

Public Abstract:

Patients with triple-negative breast cancer (TNBC) tend to have a much worse prognosis that patients with HER2-positive or hormone (estrogen receptor)-positive breast cancer. This is mainly because the only therapy that is effective in TNBC is chemotherapy. Sometimes patients diagnosed with surgically-resectable TNBC are given chemotherapy right after diagnosis, before they undergo surgery, called neoadjuvant chemotherapy (NAC). The goals of NAC are to shrink the tumor and give the patient a better chance of having surgery that does not remove as much of the breast. Another goal of NAC is to kill any tumor cells that are in the rest of the body, but may not yet have developed into metastasis. When surgery is performed after NAC, sometimes the tissue with is removed has no evidence of any living tumor cells, and this is called a pathologic complete response (pCR). These patients do very well after surgery, and many are cancer free for decades or longer. However, if there are living tumor cells in the specimen (called residual disease), almost all of these patients recur in the next decade; some even within only a few years. However, patients with residual disease do not typically undergo any drug therapy after surgery, because there is no way to know if it is working, and there are no therapies that are known to work to reduce recurrences after surgery in TNBC. The goals of our proposal are to: 1) Determine if certain drugs, called MEK inhibitors, are likely work in combination with NAC to increase rates of pCR (giving TNBC patients a better prognosis). Our published data suggest that they may work in a certain group of patients with TNBC. Further validation of this in more advanced models will be needed so that we can start a clinical trial in patients in the near future. 2) Determine if MEK inhibitors may be given after NAC and surgery to reduce the possibility of metastatic recurrence. 3) To try and identify which genes are mutated in the cells remaining after NAC in TNBC patients which could be markers of response to these inhibitors in the time period after surgery. We will perform the proposed studies in mouse models in which we will grow patient's tumor cells, or whole tumor transplants (called patient-derived xenografts). We will then treat the mice with MEK inhibitors (or other drugs) to try and cure the mice. If this works, it will provide the data we need to start a clinical trial to help patients with TNBC.