



Susan G. Komen

Research Grants – Fiscal Year 2015

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Examining the role of cholesterol metabolites on the estrogen receptor signaling pathway

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Lead Organization: Duke University

Grant Mechanism: Komen Scholars

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Public Abstract:

There are increasing associations between obesity and cancer, particularly estrogen receptor positive breast cancer, but the reasons for this are unclear. A leading hypothesis is that obesity is linked to estrogen receptor positive breast cancer through high cholesterol and high levels of cholesterol byproducts. A recent breakthrough paper in *Science*, showed that higher levels of cholesterol byproducts were associated with more aggressive breast cancers. They also found that in the presence of increased amounts of cholesterol, breast cancers were more likely to be resistant to standard treatments. These interesting findings have never been evaluated in human breast cancer patients.

We propose a study of 12 breast cancer patients on anti-hormone treatments for their estrogen receptor positive breast cancer to evaluate the total cholesterol and cholesterol byproducts in their blood prior to anti-cholesterol treatment and then at three time points on anti-cholesterol treatment. Additional studies on pre-treatment breast cancer biopsies in the laboratory will provide information about the characteristics of the tumor including levels of cholesterol byproducts, tumor aggressiveness, and gene expression. We would then have each patient



undergo two additional biopsies of the tumor to repeat these same tests while on anti-cholesterol treatment. We will evaluate the optimal dose of rosuvastatin, the anti-cholesterol medication, the safety of rosuvastatin in these patients, and, with the blood work and tumor studies, determine if there are ways of predicting which patients would benefit from this treatment the most. We believe that estrogen receptor positive breast cancer patients will respond better to standard anti-hormone treatment while on anti-cholesterol treatment. We believe that rosuvastatin is a safe, inexpensive treatment with few side effects and it is taken by mouth as a daily tablet, unlike most cancer treatments.

This project is particularly interesting because anti-cholesterol medications, such as rosuvastatin, are inexpensive and widely available. Therefore, this study could have immediate clinical impact and rapidly provide better treatment options for breast cancer.

