



**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.

Application of lipidomics to a sulindac intervention of pain

Investigator(s): Jessica Miller, Ph.D.

Lead Organization: University of Arizona

Grant Mechanism: CCR Clinical

Grant ID: CCR14299136

Public Abstract:

PI Career Goals and Training Plan: The Komen Career Catalyst Award would provide Dr. Jessica Miller with the opportunity to participate in training activities such as classes, workshops, journal clubs and clinical activities focused on breast cancer research. The proposed individualized training program will provide the skills necessary to conduct clinical trials, apply metabolomics to those trials, and to translate research findings to patient care. Ultimately, Dr. Miller's goal is to become a tenured professor conducting research identifying clinically relevant markers of breast cancer risk, and determining appropriate breast cancer prevention agents (of lifestyle modification) that will modulate that risk profile. Funding for this work will also provide Dr. Jessica Miller with the opportunity to participate in training activities such as classes, workshops, journal clubs and clinical activities focused on breast cancer research. The proposed individualized training program will provide the skills necessary to conduct clinical trials, apply metabolomics to those trials, and to translate research findings to patient care. Her overarching career goal is to apply methodology from several different disciplines, including analytical chemistry, nutrition, cancer prevention, medicine, and statistics, to design and test hypotheses that make important contributions to the field of breast cancer prevention. Research Plan: A major challenge in the management of ER+ disease is the high rate of early discontinuation of and poor adherence to adjuvant hormone therapy (HT) such as AI which ultimately results in recurrence and mortality from breast cancer. Side effects of AIs include menopausal symptoms, sexual dysfunction, bone loss, and function-limiting chronic joint stiffness and pain. The molecular mechanisms of AI-associated pain, however, are still unknown. An R01-funded clinical study of women with a diagnosis of invasive breast cancer on aromatase inhibitors (AI) + sulindac (a nonsteroidal anti-inflammatory drug: NSAID) is currently underway. Understanding the determinants of AI-associated pain as well as demonstrating a benefit with sulindac would provide clinical opportunities to improve adherence to AI and ultimately reduce breast cancer mortality. The target of NSAIDs is cyclooxygenase 2 (COX2), COX2 metabolizes the fatty acid, arachidonic acid to produce inflammatory metabolites. Arachidonic acid is also metabolized by cytochrome P450 and lipoxygenase enzymes to produce other biologically active metabolites. We propose to extend the aims of the R01 trial to conduct an analysis of targeted arachidonic acid metabolite signatures in blood and urine pre and post-AI+sulindac intervention in these women. We will relate these metabolites in blood and urine to pain scores. The study should help guide future research that will identify molecular targets of pain for the ultimate goal of improving AI adherence and reducing death from breast cancer.