



Susan G. Komen

Research Grants – Fiscal Year 2015

This research grant was approved for FY2015 Research Programs funding. This grant will be funded upon the execution of grant agreements between Komen and the grantee institutions.

Receptor activator of nuclear factor-kB (RANK)-axis and mammographic density

Investigator(s): Adetunji Toriola, M.D., Ph.D.

Lead Organization: Washington University School of Medicine

Grant Mechanism: CCR Basic and Translational

Grant ID: CCR15332379

Public Abstract:

Background: Although a dense breast as seen on a mammogram is one of the strongest risk factors for breast cancer, there is very limited knowledge on how it can be modified to reduce a woman's risk of breast cancer. Increased breast density (heterogeneously or extremely dense breast) is common and is seen in >27 million women aged 40-79 years in the US. It is estimated that 28% of breast cancer cases are attributable to increased breast density. Importantly, a decrease in breast density over time is associated with reduced breast cancer risk; hence, strategies to reduce breast density could have great utility in the primary prevention of breast cancer. Further, as legislation that requires disclosure of breast density information directly to women becomes mandatory in many states in the US, women with increased breast density will be more sensitive to identifying ways to reduce their elevated risk of breast cancer. In this proposal, I will investigate for the first time the associations of the receptor activator of nuclear factor-kB (RANK) pathway with mammographic density. The RANK-axis was recently demonstrated to play an important role in the proliferation of breast parenchyma in pre-clinical studies. Hence, inhibiting the RANK-axis could be a novel strategy to reducing breast density and subsequently, breast cancer risk.

I hypothesize that RANK-axis will be associated with mammographic density.

Approach: I will evaluate my hypotheses in 365 women, recruited from among >25,000 women who undergo annual screening mammogram at the Joanne Knight Breast Health Center, Washington



University School of Medicine, St. Louis, Missouri. Mammographic density will be evaluated by two radiologists with expertise in breast imaging using a Food and Drug Administration approved computer program that permits quantitative analysis of breast parenchymal density on a mammogram. In addition to mammogram, the women will provide a sample from a blood draw to assess the biomarkers of interest.

Innovation and Impact: This proposal is very innovative and has substantial public health importance. Findings from the study have the potential to greatly enhance scientific knowledge of breast density and could provide initial data that will allow for targeting RANK-axis in breast cancer prevention in millions of women. A RANKL inhibitor (denosumab) is already in clinical use, which will allow for a speedy translation of study findings and could provide a path to primary prevention of breast cancer in the very near future. As noted recently RANKL inhibition represents a “unique chance to potentially prevent breast cancer in millions of women - not in 20 years, but right now”. My proposal has the unique opportunity to set that in motion.

