

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.

Targeting the stem cell niche in aggressive breast cancers

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Lead Organization: University of Wisconsin - Madison

Grant Mechanism: CCR Basic and Translational

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Public Abstract:

Obesity is one of the most important risk factors for postmenopausal women for the development of

breast cancer. Women with a higher body mass index develop tumors that are larger at the time of diagnosis that are more clinically aggressive. Obese women also have an increased risk for the development of metastases and a shorter time before tumors can recur. Obesity also has been shown to enhance other risk factors for breast cancer. Understanding the differences in the breasts between obese and lean women could have a significant impact on our ability to treat obese women with breast cancer. One possibility for the difference in breast cancer development between lean and obese women is changes that occur in the fatty tissue surrounding the cells of the breast that are able to make milk during lactation. In this fat, a type of white blood cells, which are named macrophages, are increased. These macrophages are activated within the obese fat tissue to produce factors, which can increase the type of breast cells that may later form tumors in obese women. These activated macrophages also act in the early forming tumors to increase aggressive cells and change the environment of these growing tumors cells, to an environment that strongly promotes tumor growth. In this project, we will study how macrophages, activated by obese fat, change the populations of breast cells and identify the factors that are responsible for this change. We will examine how these same factors increase cells that are aggressive and resistant to treatment within the tumor and promote an environment that enhances tumor development. Many of the types of factors that macrophages produce are also involved in autoimmune diseases, such as rheumatoid arthritis. Because the factors that macrophages secrete

have already been investigated for these other conditions, drugs which are used to treat these other illnesses may have substantial usefulness to either safely treat obese women at high risk for developing cancers early, such as women with a family history of breast cancer, or in conjunction with other clinically used treatments to increase the success for treating obese women with breast cancer.