Susan G. Komen
Research Grants – Fiscal Year 2014

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How does circulating cholesterol promote breast cancer growth and metastasis?

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Lead Organization: Icahn School of Medicine at Mount Sinai
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Public Abstract:
Women with obesity and Type 2 diabetes are at a higher risk of developing aggressive forms of breast cancer and are at greater risk of dying from breast cancer than women without these conditions. Therefore, it appears that woman's metabolic health may impact her risk of breast cancer recurrence and survival. While there are many metabolic abnormalities that occur with obesity and Type 2 diabetes, which may contribute to this increased risk, one potential contributing factor is elevated circulating cholesterol. Cancer cells require cholesterol to make essential cell components, and need more cholesterol to make new cells and spread. Cells also use cholesterol to make hormones, including estrogen and estrogen-like hormones. Therefore, a greater supply of cholesterol from the blood may provide cancer cells with fuel and hormones to grow and spread more rapidly. However, it is unknown whether it is only specific types (such as hormone receptor negative breast cancer) or all types of breast cancer that will grow more rapidly in the setting of high circulating cholesterol. Additionally, it is unknown whether using cholesterol-lowering medication to reduce circulating cholesterol levels will reduce the growth and spread of breast cancers. To address these unknowns, I will use mice with high cholesterol levels, as genetically engineered mice allow me to examine the effects of cholesterol on breast cancer in isolation from other metabolic abnormalities that occur with obesity and diabetes. My animal studies so far have found that human estrogen receptor (ER)-negative breast cancers become larger and spread to the lungs of mice with high cholesterol, more than in mice with normal cholesterol levels. In this project I will examine if cholesterol also increases the growth of ER-positive breast cancer. I will prevent the cancer cells from taking up cholesterol by manipulating the genes of the cancer cells and see if this reduces their growth. I will treat the mice with cholesterol lowering medication to determine if lowering their cholesterol levels will reduce the growth of specific types of breast cancer. Through these studies I aim to determine if different subtypes of breast cancer respond differently to high circulating cholesterol levels, if different cholesterol profiles have differing effects on breast cancer growth, if inhibiting the cholesterol uptake by tumor cells reduces their growth and spread, and if cholesterol lowering medication will reduce the growth of specific types of breast cancer. Furthermore, I will study the fate of cholesterol in tumor cells to understand how breast cancers use cholesterol to grow and spread. I hope to use the results of these studies to optimally treat the metabolic conditions of obese and diabetic patients with breast cancer.