



**Susan G. Komen**

**Research Grants – Fiscal Year 2015**

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**The role of breast cancer exosomes in organotropic metastasis**

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**Public Abstract:**

Cancer spread, or metastasis to distant vital organs such as bone, lung and brain is the most devastating feature of breast cancer, accounting for over 40,000 deaths in the United States each year. Over the past decade, we have gained a better understanding of how cells in the body other than breast cancer aid in the growth and spread of cancer. It is crucial now to investigate the cancer cell-host cell interactions that drive malignant behaviors of susceptible epithelial cells in the breast as well as their secondary homes. In 1889, Stephen Paget first proposed that cancer spread is a non-random event, yet why cancer in general and breast cancer in particular spreads to specific organs remains one of the greatest mysteries in cancer biology. There are growing number of studies demonstrating tumor-derived microvesicles, referred to as exosomes, may alter the environment in target organs in which cancer will develop. However, what mechanisms drive this process occurs, and the specific role of exosomes in tumor progression remains unknown. In this study, I will be using a well-characterized human breast cancer cell line model to investigate the role of exosomes in breast cancer progression. My preliminary data shows that the breast cancer organ-specific cell line derived exosomes home to the future metastatic sites where the cancer cells of origin are known to spread. Furthermore, pre-treatment with lung-homing breast cancer exosomes can instruct cancer cells that lack the capacity to colonize the lung to now spread to the lung. In this study I am investigating which molecules packaged in organ-specific exosomes are responsible for exosome homing to organ specific sites of cancer spread. I will identify



which cells in each future metastatic organ are responsible for uptaking breast cancer exosomes and also what changes are induced in these cells by cancer exosomes. The ultimate goal of this novel and unique proposal is to establish the clinical, biological and functional relevance of breast cancer-derived exosomes in organ specific cancer spread, and to establish whether exosomes that home to future metastatic niches contain unique cargos that are therapeutically targetable or can be used as biomarkers for early diagnosis of cancer spread.

