Susan G. Komen
Research Grants – Fiscal Year 2014

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Novel anti-metastamiR therapy for metastatic breast cancer

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Public Abstract:
One hundred percent of breast cancer patients diagnosed when cancer is still localized to the breast has a 5-year survival rate. However, in patients diagnosed after cancer has spread to other organs of the body (cancer has metastasized), the 5-year survival rate dramatically drops to only 24%. Because metastatic breast cancer is not currently considered curable, women with metastatic disease are unable to envision a long life without breast cancer. We now have the tools to revolutionize therapeutic strategies to treat and, ultimately, cure patients with metastatic breast cancer. Small RNAs, called microRNAs (miRNAs), are powerful regulatory molecules that can inhibit expression and protein production of over 60% of human genes by binding to target genes. This proposal is designed to develop a novel cancer therapy using miRNAs to inhibit metastatic tumor growth. Many of the proteins made from miRNA-regulated genes control the ability of cancer cells to move to other tissues in the body. In metastatic cancers, metastasis-promoting miRNAs, or pro-metastamiRs, can become overexpressed which results in inhibition of genes that suppress metastasis. Alternatively, metastasis inhibiting miRNAs, or anti-metastamiRs, can be down-regulated, which allows metastasis-inducing genes to become overexpressed providing the drive to send tumor cells to other sites in the body. Research studies have shown that reintroducing the missing anti-metastamiRs back into the cancer cells will reduce the growth and development of metastatic disease in tumor-bearing mice. This study will optimize reintroduction of anti-metastamiRs lost in metastatic breast cancer cells and demonstrate efficient and effective delivery of these anti-metastamiRs to the metastatic tumors. Our lab has co-developed a nanovector that can deliver these anti-metastamiRs specifically to tumor cells without affecting normal cells, thereby reducing toxicity to normal cells. Clinical trials using our nanovector have already shown the capability of delivering genes to metastatic lesions with minimal side effects. This project will have a significant impact on cancer therapies by demonstrating the effectiveness of miRNA-based therapies using nanotechnology for treatment of metastatic breast cancer. Successful completion of this proposal can lead to new therapeutic options for women with metastatic breast cancer. Drug resistance is one of the major challenges in treating metastatic breast cancer. miRNA-based therapies can alter cellular pathways to reactivate cell death programs. Using miRNA-based therapies in combination with existing therapies, such as chemotherapy or radiation therapy would provide a new way of treating breast cancer patients with drug resistant metastatic disease.