Susan G. Komen
Research Grants – Fiscal Year 2014

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Predictors of bone metastasis in breast cancer

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Lead Organization: University of Washington School of Medicine Alliance
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Public Abstract:
Metastases involving the bone are the first site of recurrence in 25-40% of recurrent breast cancer patients. Eventually, bone metastases are seen in up to 60-80% of metastatic breast cancer patients. Development of bone metastases involves complex interactions between breast cancer cells and the bone environment. Tumor cells that circulate through the blood and end up in the bone produce a variety of factors which directly and indirectly stimulate bone breakdown (resorption). In turn, this bone breakdown releases growth factors stored in the bone that may increase tumor cell growth and survival. This interaction generates a "vicious cycle" of tumor growth and bone destruction. Understanding the biology of this process may offer useful insights to determine which patients and which tumors are at particular risk for developing bone metastasis, and in developing therapy to prevent or reduce the development of bone metastases. We are exploring whether we can identify features found on breast cancer cells at the time of diagnosis that may make the cancer cells more likely to spread to and survive in the bone, and whether we can predict for which cancers might spread to the bone versus other sites, such as the liver or lungs. We are also studying whether elevated bone breakdown at the time of breast cancer diagnosis, as detected by elevated markers of bone turnover found in the blood, can predict for which newly diagnosed breast cancer patients have an increased risk of developing bone metastases. Bisphosphonates, a class of drugs that are potent inhibitors of bone breakdown and commonly used to treat osteoporosis, can also reduce complications due to established bone metastase in breast cancer. The Southwest Oncology Group 80307 clinical trial is comparing 3 different bisphosphonates with different potencies and administration routes in 6,000 early stage breast cancer patients to see if these drugs can decrease breast cancer recurrence, by disrupting the interactions between breast cancer cells and the bone at an early time point in treatment. As part of this study, tumor and serum samples have been collected to help us identify predictors of bone recurrence. We have hypothesized that tumor and patient characteristics, specifically blood markers of bone turnover and tumor expression of bone-related proteins, can predict for which patients and tumors are at highest risk for bone recurrence. If adjuvant bisphosphonates are found effective in reducing bone recurrence in breast cancer in the large studies, it would be desirable to be able to predict which patients are most likely to develop distant metastases, and which are most likely to relapse in bone as the first recurrence site. Identifying predictors of metastasis in general, and bone metastases specifically, would allow selective use of bisphosphonates while avoiding side effects and cost in patients unlikely to benefit. The ability to predict likely sites of future metastasis at the time of breast cancer diagnosis will allow us to better tailor adjuvant breast cancer treatments to the patients and tumors most likely to benefit.