Susan G. Komen

Research Grants – Fiscal Year 2015

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Genomic and functional circulating tumor cell analysis for personalized therapy

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Lead Organization: Massachusetts General Hospital

Grant Mechanism: CCR Clinical **Grant ID:** CCR15224703

Public Abstract:

Despite major advances in genomics, real-time monitoring of breast cancer has been challenging because it is difficult to obtain tumor biopsies, particularly for hormone receptor positive breast cancer which is the predominant subtype involved in bone metastasis.Obtaining multiple serial biopsies would be required to evaluate dynamic change in tumor biology and discern the best therapy at a given time for an individual patient and is a challenge. In principle, molecular analyses of tumor cells in blood can serve as a “liquid biopsy” and rationally guide therapy selection based on tumor characteristics. While conceptually promising, detection of circulating tumor cells (CTCs) has been technically challenging beyond counting of cells, which has had limited value in guiding therapy decisions.

Recent advances have made it possible to isolate CTCs for sophisticated molecular analysis, and even culture them in the laboratory for drug testing, as recently demonstrated by a collaborative effort between myself and Cancer Center investigators. This is ground-breaking because it allows real-time monitoring of circulating breast cancer cells and individualized drug testing to potentially identify which therapy would work best for that individual at any given point of time. This clinical proposal builds on these exciting hypotheses and has been carefully developed with the input and advice of the mentorship committee and patient advocates including Ruth Fax, an experienced advocate who will serve on my mentoring committee. The study will evaluate the clinical application of CTCs for detecting tumor

evolution and rational therapy selection, and will provide a foundation to build models for utilizing CTCs in clinic to personalize therapy selection for an individual with breast cancer.

Successful clinical application of CTC genotyping and functional analyses could have tremendous positive impact for patients with breast cancer. It will provide a more accurate snapshot of the current biological state of the cancer for identification of actionable targets and help select the right drug for the right patient. Furthermore, real-time close monitoring of the tumor could facilitate early identification of emerging resistant subclones and guide therapy switch that could overcome treatment resistance in breast cancer. This could allow us be one step ahead of tumors and potentially lead to a significant reduction in breast cancer morbidity and mortality. While the research is currently being proposed for hormone receptor positive breast cancer, if proved to be successful, the same principles could be applied for research in other subtypes including triple negative breast cancer. Thus, this study has the potential to lay clinical foundation of personalized therapy selection based on real-time monitoring of breast cancer biology, and sustain the quest to successfully treat and ultimately cure breast cancer.