Susan G. Komen

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Novel devices to capture circulating tumor cells

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Lead Organization: University of Michigan

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Public Abstract:

Breast cancer spreads from the breast to distant organs, where it develops metastases, which are the primary cause of mortality. The metastatic process requires that the breast cancer cells escape from their site of origin and travel in the blood system to the distant organs. When these cells are in transit, they are called "circulating tumor cells," or CTC. We and others have shown that the presence of CTC in the blood of patients with early breast cancer, or in patients with already established metastatic breast cancer, is associated with worse prognosis – in other words, the time to development of distant metastases, the time to progression if the patient already has metastases, and the time to mortality, is shorter for those patients with elevated vs. not elevated CTC levels. We have also shown that patients who do not reduce their CTC after one cycle of first-line chemotherapy appear to not be responding to that treatment, and appear not to respond to other types of chemotherapy either, and that their survival time is quite poor (median is approximately 13 months).

These data suggest that just counting CTC is not sufficient to direct patient care. Rather, CTC might serve as a "liquid biopsy," permitting detailed characterization for markers that might predict benefit from "targeted" therapies, the goal of "Precision Medicine." CTC might have several advantages over true biopsies. True biopsies are invasive, expensive, and difficult to perform repeatedly. Further, a biopsy only provides information about the specific site from which the tissue was drawn, while CTC in blood presumably come from all the sites, and therefore provide a more comprehensive portrait of the patient's entire tumor burden.

Recently, our laboratory and several other investigators, have shown that CTC can, indeed, be characterized for expression of important breast cancer markers, such as estrogen receptor, BCL2, HER2, Ki67, apoptosis, and markers of epithelial-mesenchymal transformation (EMT), which appears to be an important step in

metastases. CTC can also be characterized for genetic abnormalities that might predict specific therapeutic responses.

However, currently available methods to capture CTC are limited to a relatively small volume of blood (3-30 milliliters) which is drawn at a specific time. We have developed a prototype CTC capture system that is placed into a subject's venous system (like an intravenous catheter) and stays there for several hours. Blood will be diverted from the vein into a capture device that the patient wears on her arm and then back into the patient's venous system.

We hypothesize that this system will provide us with many more CTC for characterization, and that these CTC will be more representative of the patient's cancer than is a single blood draw. We will test this hypothesis in three specific aims: 1) we will refine the prototype system and test it in a canine (dog) cancer-bearing model; 2) we will determine if CTC captured in this system can be characterized (we will determine the genetic and protein expression status) and if they can be cultured in vitro; and 3) we will conduct pilot trials in patients with metastatic breast cancer.