Susan G. Komen
Research Grants – Fiscal Year 2014

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Alterated ubiquitin signaling networks regulating breast cancer proliferation

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Lead Organization: The University of North Carolina at Chapel Hill
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Public Abstract:
When compared to normal cells, breast cancer cells exhibit numerous differences. These changes can be thought of as traffic signals that are inappropriately turned to green, allowing the cancer to grow in an uncontrolled fashion. In this analogy, breast cancer cells are cars, speeding through a network of city streets without restraint. Since there is a giant network of streets with green lit intersections, turning a single traffic light back to red, in an effort to halt the flow of cars, is a tremendous challenge. To halt traffic requires a detailed map indicating which signals are green and pinpointing high traffic intersections through which all traffic must pass (the bridges and tunnels of breast cancer). My goal is to decode this complex map that permits the unrestrained growth of breast cancer cells. I have recently developed and applied large-scale technologies that simultaneously examine thousands of possible changes in human cells. First the first time, we will apply this technique to identify changes that occur in breast cancer. This analysis will reveal changes in breast cancer that researchers have been unable to identify using current technologies. In doing so, we expect to identify potential therapeutic targets that promote cancer growth. We will focus on the basal-like, triple negative breast cancer (TNBC) subtype. Basal-like TNBC is the most aggressive breast cancer subtype, with the fewest treatment options and the worst prognosis. Systematically identifying changes will determine where best to direct efforts to halt breast cancer growth. Our previous studies identified a molecule named FoxM1 that we will evaluate as a possible therapeutic target. FoxM1 is turned on in basal-like TNBC where it drives growth, making it an attractive target for stopping cancer. Unfortunately, practical reasons prevent us from directly turning off FoxM1. We have developed an alternative strategy, turning off FoxM1 by attacking the cellular machines that protect it from being destroyed. We predict that this strategy of attacking the guards that protect FoxM1 will produce a similar outcome to targeting FoxM1 itself. Importantly, these guards are amenable to drug discovery, suggesting this will be a viable approach for treating TNBC in the future. Taken as a whole, this application will better define the map of alterations that occur in the most aggressive form of breast cancer and evaluate a potential drug target. Our goal is to better understand the changes that occur in breast cancer by revealing and evaluating potential therapeutic targets to improve the lives of patients with this disease.