Susan G. Komen for the Cure
Research Grants – Fiscal Year 2012

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Activatable Molecular Probes for Personalized Breast Cancer Therapy

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Awarded: $180,000.00

Grant Mechanism: Postdoctoral Fellowship

Public Abstract:
From person to person, variations in breast tumor physiology and the accumulation of random mutations by these tumors, which is a hallmark of cancer, makes breast cancer a highly variable disease. These variations between afflicted women contributes to variations in treatment response, which often leads to treatment failure. Periods of unsuccessful treatment need to be avoided to prevent the breast tumor from progressing to more aggressive disease states. The successful treatment of a disease as heterogeneous as breast cancer necessitates a personalized therapeutic strategy tailored to the specific tumor physiology of each individual. In this proposal, we hypothesize that such a personalized therapeutic strategy can be achieved by monitoring the activity of cellular machinery responsible for sensing DNA damage in real time in the tumor of the patient. Measuring the tumor capacity to sense DNA damage can provide a clinician with two pieces of information critical to personalizing breast cancer radiation or chemotherapy. Knowing the DNA damage sensing ability of a tumor before treatment begins would allow the clinician to make informed decisions about the specific treatment that would best suit the individual patient, as some therapies are more effective in patients with high DNA damage sensing capacity, while others suit patients with a poor ability to sense DNA damage. This first piece of information, then, would allow the tailoring of therapy to the specific breast cancer of the individual. The second piece of information obtainable from monitoring DNA damage sensing is a positive therapeutic response of the tumor. Many common breast cancer therapies, including radiation and some of the most common chemotherapies, kill tumor cells by damaging their DNA. Once therapy is administered, detection of an increased amount of tumor DNA damage sensing can signal effective therapy. A single piece of cellular machinery is responsible for this DNA damage sensing, and we are proposing to develop two new imaging agents for application in MRI and in fluorescence imaging (i.e. the detection of light produced by the imaging agent) that can tell the clinician when the particular piece of cellular machinery becomes active. The strength of our proposal in relation to current clinical methods of monitoring therapeutic response by measuring changes in tumor size is that the cellular machinery targeted by our imaging agents becomes activated with successful therapy at a much earlier stage (i.e. on the time scale of a day) than changes in tumor size (i.e. weeks to months). So by combining both the capability to tailor therapy to an individual and to monitor the efficacy of the therapy in real time, the goal of pushing clinical breast cancer therapy into an era of personalized medicine could be realized.