



**Susan G. Komen
Research Grants – Fiscal Year 2014**

This research grant was approved by Komen's national board of directors for FY2014 Research Programs funding. This grant will be funded upon the execution of grant agreements between Komen and the grantee institutions.

A nanoparticle-based HER2 breast cancer vaccine

Investigator(s): Nicole Steinmetz, Ph.D.

Lead Organization: Case Western Reserve University

Grant Mechanism: CCR Basic and Translational

Grant ID: CCR14298962

Public Abstract:

We propose the development of a cancer vaccine for treatment of patients with HER2+ cancers. HER2+ means that the cancer cells in these patients up-regulate the protein human epidermal growth factor receptor 2 (HER2). HER2+ cancers are aggressive, and a patient with this diagnosis has a higher risk of relapse, development of metastasis and death. The treatment of their HER2+ cancers typically involves chemotherapy combined with an antibody known as trastuzumab. Nevertheless, not all patients benefit from trastuzumab therapy. Also patients suffer from undesired side effects from the chemotherapy. To overcome this clinical challenge, we propose a HER2 cancer vaccine. The administration of a prophylactic vaccine for high-risk patients and those diagnosed with HER2+ cancer holds the potential to prevent the development of the disease before doctors would be able to diagnose its onset. While treatment and diagnosis can reduce the disease burden and improve outcome, the prevention of cancer would be an important milestone, especially to protect high-risk patients. Further, the vaccination approach holds the promise to reduce relapse and prevent metastasis and therefore reduce mortality rates. The proposed vaccine is expected to be safer compared to current antibody therapy, and therefore administration is expected to be associated with fewer side effects; this would increase the quality of life of the cancer patient. Furthermore, we propose the development of the vaccine in edible plant tissue for oral administration. The potential exists to produce the vaccine 'in the region for the region' in underdeveloped countries and therefore could be applied globally. Specifically, we will develop a plant-produced HER2 vaccine: HER2 epitopes (peptides that elicit protective immunity against the cancer) will be linked to potato virus X. Potato virus X is a plant virus, present in the food chain. Potato virus X is a non-toxic nanoparticle that naturally targets antigen-presenting cells (cells of the immune system involved in the production of protective antibodies, that will protect and treat the disease). The idea pursued is that potato virus X will serve as a platform to present HER2 epitopes to the patient's immune system to elicit a long-lasting, protective immunity. We hypothesize that patients immunized with the vaccine, have reduced risk of disease progression, recurrence, and metastasis development; therefore the vaccine could reduce mortality rates associated with HER2+ cancer. The proposed vaccine will be evaluated in preclinical studies, an important milestone in the development of novel therapies. The platform would provide a novel technology that could be widely implemented in the clinic for vaccination strategies; for example, a combination of epitopes and molecular targets could be considered.