



Susan G. Komen

Research Grants – Fiscal Year 2015

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Improving MUC1-targeted immunotherapy to eliminate established breast cancer

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Lead Organization: Medical University of South Carolina

Grant Mechanism: CCR Basic and Translational

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Public Abstract:

The protective effect of anti-tumor immunity has long been appreciated in the treatment of breast cancer. Patients with high level immune responses targeting the tumor-associated protein MUC1, present in over 90% of mammary tumors, have a favorable prognosis and increased survival. Yet, patient immunity against MUC1 is predominantly present at low frequencies and unable to prevent disease progression. Therapeutic vaccination provides a strategy to enhance the anti-tumor immune response and eliminate established mammary tumors. Regrettably, conventional vaccinations have failed to fulfill their potential due to two crucial factors; the inability to generate effective and long-lasting anti-tumor immunity, and the direct suppression of the immune response by the tumors themselves. Our proposal seeks to improve immune-based therapy for the treatment of breast cancer by 1) delivering a novel vaccine that induces unique, highly-specialized immune cells, termed T cells, capable of producing the inflammatory factor IL-17 to destroy tumors and, 2) combining vaccination with a new investigational drug, anti-PD-L1, which blocks the ability of cancer cells to hide from the immune system. We will test the ability of experimental vaccination to promote qualitatively superior immunity against the MUC1 target in mice which express MUC1 in a similar manner to humans. We will then compare our novel immunotherapy regimen with one using a conventional vaccination to treat disease in a clinically relevant mouse model which spontaneously develops breast cancer. We believe that our improved vaccination strategy will induce superior T cell-mediated immunity against MUC1 which will be capable of increased tumor killing and long-term persistence following treatment. We predict that a treatment



regimen combining novel vaccination in the presence of anti-PD-L1 drug to render tumor cells susceptible to immune-mediated killing will completely eliminate both early and late stage mammary tumors and, importantly, prevent disease metastasis. Due to the high specificity of immune-based therapy, therapeutic vaccination will result in minimal toxicity, enhancing the quality of life of breast cancer patients. Notably, successful immunotherapy will establish long-lived immune memory capable of preventing disease recurrence in breast cancer Survivors. The present study represents the first demonstration that IL-17-mediated responses can be induced through vaccination and will provide an innovative method to improve immune-based therapy to eradicate breast cancer.

