



The Ty Louis Campbell Foundation/St. Baldrick's Scholar Award Progress Report

St. Baldrick's Scholar: Samuel Cheshier, M.D., Ph.D.

Title: Assistant Professor of Neurosurgery and Pediatric Neurosurgery

Title of Research Project: *Pre-clinical evaluation of combination anti-CD47 immunotherapy*

Grant Amount: \$330,000.00

Grant Period: 7/1/14 - 6/30/17

Institution: Stanford University

Sponsor: Irving Weissman, M.D.

Please describe any advance in childhood cancer diagnosis or treatment furthered by your research under this St. Baldrick's Scholar Award.

This work utilizes combinations of immune therapies to target malignant pediatric brain tumors. These treatments allow the immune system cells called macrophages to specifically target and "eat" the cancer cells while leaving normal tissues unharmed. The goal is to develop these treatments in order to replace chemotherapy and irradiation, which are less specific to the cancer and more harmful to the patients than these proposed immune therapies.

The first year focused on combination studies with antibodies called anti-CD47 and anti-CD40. When utilized in combination in our mouse model, there was significant synergistic effect when compared to utilizing either agent alone. The mice with human malignant pediatric brain tumors survived longer when treated with anti-CD47 and anti-CD40 than either agent used alone.

Furthermore, residual tumors treated with both agents, contained significantly more macrophages than either agent used alone. One finding was that anti-CD47 alone caused a large infiltration of macrophages at the periphery of the tumor, but the anti-CD47 with anti-CD40 combination allowed for the entire bulk of the tumor to be infiltrated with macrophages. Understanding the mechanism of this increase in macrophages within the tumor will have important implications. Experiments combining anti-CD47 and anti-Herceptin also yielded favorable survival data over either agent alone, and we will continue to probe the degree of efficacy of this combination as well.

Funding by the St. Baldrick's Foundation has allowed us to take the preliminary steps in being able to provide brain cancer treatments to children that do not induce the severely reduced quality of life implicit in current standards of care. We have shown that through the use of complimentary immunotherapeutic approaches, we can robustly activate the innate immune system to safely and

effectively attack tumor cells within the brain. It is our goal to continue these efforts and to fully realize the potential of immunotherapies by bringing these novel treatments to the clinics.

What would you like to say thank you to the donors who funded this grant?

Funding from the St. Baldrick's Foundation is a major stepping-stone in my development as a pediatric brain cancer researcher. It allows me to wholly dedicate my research efforts to address pediatric CNS tumors, a subset of cancer patients that suffer immeasurable hardships due to the disease and the damage created by the limited clinical treatment strategies we currently employ. Funding from St. Baldrick's allows me to develop a foundation of research from which we can justify the pursuit of clinical trials and expose new avenues of research.

Pediatric cancers afflict some of the most vulnerable and valuable members of our society, yet funding for this class of research is incredibly scarce. I would like to personally thank the donors and volunteers of the St. Baldricks Foundation for their support in the hopes of one day allowing us to return the promise of a healthy and happy childhood to all those afflicted by these devastating diseases.

Please explain your research in lay language to someone who has no medical knowledge.

My work involves utilizing cells that eat and destroy damaged cells to remove cancer cells. Cancer cells have evolved many ways to avoid being removed by this naturally occurring system and we have developed a strategy to shut down one of cancer's evasive techniques. Although this allows cancer-removing cells to recognize the cancer, we could further improve upon this through various methods such as using cancer-specific markers to make cancer more visible to the cancer-removing cells or stimulate the body to recruit more cancer-removing cells to the site of the cancer.

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