

### **C3 / Padres Pedal the Cause 2018**

"Responses of Melanoma Patients to Checkpoint Immunotherapy"

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#### **SCIENTIFIC ABSTRACT**

Advances in immunotherapy for cancer have yielded tremendous optimism that even aggressive cancers, including metastatic melanoma, can one day be cured in the most patients. Melanoma tumor eradication depends on responses of CD8 T cells, but the tumors can evade the immune system by eliciting functionally “exhausted” T cells. Although therapies that block the immune checkpoint receptors, PD-1 and CTLA-4, can greatly improve anti-tumor responses, their efficacy, individually or in combination remains limited. Moreover, recent studies indicate that both treatments act by inhibiting costimulation of T cells through CD28, and elicit T cells that are refractory to treatment. Thus, there is a critical need to better understand the extent of T cell exhaustion in patients and to develop new targets for immune modulation by distinct mechanisms. This pilot project is a collaboration between Dr. Linda Bradley in the Tumor Microenvironment and Cancer Immunology program at the Sanford Burnham Prebys Research Institute (SBP) and Dr. Gregory Daniels in the Solid Therapeutics program at Moore’s Cancer Center (MCC). We seek to evaluate the responses of melanoma patient T cells to immune checkpoint blockade, the frequencies of progenitor vs terminally exhausted T cells, and the potential for targeting PSGL-1, a novel T cell inhibitory receptor discovered by the Bradley lab. Dr. Bradley’s lab will perform all tests on patient samples. Dr. Daniels will provide melanoma patient PBMCs and clinical history for data evaluation. We will also analyze patient samples from the MCC Biorepository and will use the MCC Biostatistics core for data analysis.

#### **LAY ABSTRACT**

Advances in immunotherapy for cancer have yielded tremendous optimism that even aggressive cancers, including metastatic melanoma, can one day be cured in the majority of patients. However, many patients fail to respond to current treatments, or their tumors become resistant to treatment. It has been proposed that the T cells that are necessary for tumor eradication become refractory to treatment, by the development of progressive loss of function. Thus, there is a critical need to better understand the loss of T cell function in patients and to develop new targets for immune modulation by distinct immune mechanisms. This pilot project is a collaboration between Dr. Linda Bradley in the Tumor Microenvironment and Cancer Immunology program at the Sanford Burnham Prebys Medical Discovery Institute (SBP) and Dr. Gregory Daniels in the Solid Therapeutics program at Moore’s Cancer Center (MCC). We seek to evaluate the responses of melanoma patient T cells to anti-PD-1 blockade, the frequencies of responsive vs non-responsive subsets

of T cells, and the potential for blocking a new T cell inhibitory receptor that we discovered, designated PSGL-1, as a new immunotherapy for metastatic melanoma and other cancers.