



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP170317

Project Title:
Developing Effective Immunotherapeutic Strategies for Advanced Uveal
Melanoma

Award Mechanism:
Individual Investigator

Principal Investigator:
Woodman, Scott

Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Uveal melanoma (UM) is the most common eye tumor in adults. Although the tumor in the eye can be effectively treated, in half of cases, UM cells will have already traveled to other organs well before the initial diagnosis and later develop into lethal metastases. Metastatic UM patients have only a 10% one-year survival. No effective therapy exists. We aim to develop rational, more effective therapies for metastatic UM. Immune checkpoint blockade therapy (e.g., anti-CTLA-4, anti-PD-1) is revolutionizing cancer treatment. By taking off the "brakes" that immune cells naturally apply when confronting cancer cells, checkpoint blockade drugs enable the immune system to fight cancer cells. These agents can provide long-term clinical benefit rarely achieved previously. Rapid clinical advances have been observed in cutaneous melanoma (CM) using anti-PD-1 (nivolumab "Nivo") and anti-CTLA-4 (ipilimumab "Ipi"). These drugs gained FDA-approval in CM, but UM patients were excluded from these studies. We, and others, have shown that therapeutic benefit in CM from single-agent therapy correlates with the presence of inflammation in the tumor. A striking observation, however, is that combination Nivo + Ipi treatment shows efficacy even in "less inflamed" CM tumors, and we have observed efficacy in UM tumors (which are "less inflamed") using combination Nivo + Ipi. We have also shown in CM that the genetic alterations within cancer cells can promote an environment that suppresses the function of cancer killing immune cells. Our early data indicates that genetic alterations within UM, which are distinct from CM, may also suppress immune function. Thus, in this proposal we aim to 1) determine the relationship between the hallmark genetic and immune features in UM metastases to identify mechanisms by which UM cells promote a "pro-tumor" microenvironment and evade immune cell killing, 2) determine the unique molecular/immunological changes induced by combination therapy in metastatic UM