CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP170734

Project Title:
Mitochondrial DNA Instability Engages a Cancer-Related Interferon Program to Modify the Immune Microenvironment and NAD+ Metabolome and Enhance Melanoma Growth

Award Mechanism:
High Impact/High Risk

Principal Investigator:
West, Andrew

Entity:
Texas A&M University System Health Science Center

Lay Summary:

Malignant melanoma is a cancer of specialized skin pigment cells called melanocytes. The incidence of malignant melanoma continues to rise more rapidly than all other malignancies except lung cancer. Although early-stage melanoma can be cured by surgical excision of malignant tissue, the five-year survival rate for patients with advanced melanoma is roughly 39 percent, indicating the aggressive and lethal nature of this disease. Recently, immunotherapies that promote anti-tumor immune responses have opened promising avenues for late stage treatment, and a better understanding of the factors that influence the tumor immune environment will support more effective therapies.

Mitochondria are cellular organelles involved in the generation of energy and other metabolic processes. Consequently, perturbations in mitochondrial function contribute to a wide array of human diseases, and mounting evidence suggests that mitochondrial dysfunction (MD) is a key feature of cancer. Preliminary work from our laboratory has shown that MD can augment tumor cell growth in a mouse model that closely recapitulates human melanoma, and we hypothesize that this enhanced growth is due to a suppressive tumor immune environment that prevents immune-mediated destruction of the tumor by effector cells. The overall goal of the proposed work is to further explore these possibilities, using genetic and therapeutic approaches to comprehensively examine the involvement of MD and its downstream effects in melanoma progression and anti-tumor immunity.

It is becoming increasingly apparent that mitochondria influence many human cancers, although the underlying mechanisms by which these organelles promote tumor growth are just beginning to be explored. This research will provide new insight into unique roles for mitochondria in cancer and anti-tumor immunity and may support the development of novel therapies that target these pathways in melanoma and other human cancers.