



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180848

Project Title:
Autoimmune-Prone Mouse Models for Studying Immune-Related Adverse
Events Associated With Cancer Immunotherapy

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Yan, Nan

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Recent advance in cancer immunotherapy has demonstrated exciting potential. These drugs that are known as immune checkpoint inhibitors (or ICIs) remove breaks from immune cells and unleash maximum power to attack tumors. Despite tremendous successes with this approach in controlling tumor growth, these unleashed immune cells also attack normal organs resulting in conditions known as immune-related adverse events (or irAEs). The incidence of irAE is reported to range from 15-60% in single drug clinical trials, with even higher occurrence and more severe outcome in combination therapy. irAE affects multiple organs, and in severe cases becoming irreversible and fatal. Poor understanding of irAE and lack of small animal models severely limit our ability to use the powerful cancer immunotherapy in the most effective way possible. The high genetic diversity in the human population likely causes some to becoming more susceptible to developing irAE or other autoimmune diseases. We propose to use genetically engineered mice called autoimmune-prone mice to mimic the susceptible human population. We hypothesize that autoimmune-prone mice treated with cancer immunotherapy will develop symptoms similar to irAE observed in humans. The goal of this high-risk/high-impact proposal is to evaluate cancer immunotherapy in a wide variety of autoimmune-prone mouse models. We hope to identify valuable preclinical animal models and establish an experimental system for predicting individual or synthetic toxicity of cancer immunotherapy drugs due to irAE and for studying irAE-related biology.