



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180725

Project Title:
Targeting Tumor Tissues Increases DNA Sensing to Bridge Innate and Adaptive Immunity

Award Mechanism:
Multi-Investigator Research Awards (Version 2)

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Cancer cells' ability to develop resistance to conventional therapies poses one of the most daunting challenges to effective treatment. Strategic combinations of different therapies represent the future of cancer treatment, as they hold the greatest promise for overcoming therapeutic resistance. Radiation therapy's primary aim is to kill cancer cells by damaging their DNA, but it has also been shown to stimulate the body's immune system to attack cancer cells. For this reason, therapeutic combinations that pair radiation with immunotherapy, which also uses the immune system to fight cancer, are especially promising. The clinical usefulness of these combinations is currently limited, however, as the mechanisms by which DNA damage caused by radiation activates the immune system are still poorly understood. Uncovering these mechanisms is crucial to designing more effective therapeutic combinations and advancing cancer treatment. We have recently discovered the molecular and cellular pathway that links DNA damage to immune responses, but further study is needed to understand precisely how damaging tumor DNA triggers the immune system to fight cancer. We propose three research projects, each of which will closely investigate a portion of this pathway to understand how it works and how it can be stimulated or suppressed for therapeutic purposes. Understanding, at the molecular level, how DNA damage leads to anti-tumor immune responses will allow us to more effectively design therapeutic combinations of radiation and immunotherapy, as well as combinations of immunotherapy and other therapies or drugs that damage tumor DNA. If successful, our studies will develop innovative therapeutic strategies that could challenge current standard clinical practice to greatly improve treatment outcomes for patients with cancer.