CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP130297

Project Title:
Inhibition of DNA polymerase theta (POLQ) for radiosensitization of breast cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
Wood, Richard D

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

Lay Summary:

Radiation therapy is very effective in some phases of breast cancer therapy. For others, particularly triple-negative breast cancer, radiation is not currently effective. An drug that increases sensitivity to radiation in tumors would be most valuable. The purpose of this proposal is to explore and develop a new target for improved therapy of breast cancer. This target is DNA polymerase theta (POLQ), a protein first isolated and studied in our laboratory. The goals of the research outlined here are to test the principle that reduction of POLQ in breast cancer cells is beneficial for therapy with radiation and to set up and test an assay suitable for high-throughput screening. We have discovered that cells that don't have any POLQ are more sensitive than normal cells to radiation. This is because POLQ helps cells repair breaks in DNA caused by radiation. Studies have also shown that breast cancers that have larger amounts of POLQ are more likely to kill the patient. Untreated cells and organisms can survive without any POLQ, yet become very sensitive to radiation when treated with POLQ inhibitors. This makes POLQ a preferable target, because some other potential targets for radiosensitization cause toxicity if removed from normal cells. The goals of the research outlined here are to test the principle that reduction of POLQ in breast cancer cells makes the cells more likely to be killed by radiation, and to identify chemicals that inhibit POLQ. We propose to determine which types of breast cancer cells can be made more sensitive to radiation by inhibition of POLQ. We will also begin isolating chemicals that inhibit POLQ. The pre-clinical research proposed here will set the stage for work with POLQ inhibitors in mouse models. If successful, this research will provide opportunities for better treatment of breast cancer patients.