CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140430

Project Title:
Synaptic Mechanisms of Cognitive Decline After Cranial Radiation

Award Mechanism:
Individual Investigator

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

Lay Summary:

Cure rates for childhood brain tumors have greatly improved over the past few decades; indeed, for some brain tumors nearly 8 of 10 children are cured. Combined treatment approaches using surgery, chemotherapy, and radiation are largely responsible for these improved outcomes. Unfortunately, many survivors live with lifelong side effects from the treatment itself. Radiation therapy to the brain is particularly damaging for young children. When large regions of the brain are treated with radiation, the patients' intelligence and quality of life decline. Despite attempts to reduce radiation doses or even omit radiation, this therapy remains essential—without radiation therapy, tumors recur and patients have poor survival. Historically, radiation-induced side effects have been attributed to DNA damage and gradual declines in cells that reproduce. Because neurons do not reproduce, few studies have looked at how radiation affects neurons. However, neurons are ultimately responsible for brain function. Departing from historical theory, we have found that radiation leads to early changes in the function of neurons. We now seek to understand how these changes relate to long-term brain dysfunction. As part of this proposal we will study the molecular mechanisms of radiation-induced changes in excitatory neuronal transmission. In doing so, we will generate new theories as to how neurons are involved in radiation-induced cognitive declines, and we will provide a rationale for developing pharmacologic strategies to prevent or even reverse this devastating side effect. This work will contribute to our ultimate goal of improving functional outcomes and quality of life for survivors of childhood brain tumors.