CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP130573

Project Title:
Blocking TNFR1 increases tumor radiosensitivity and ameliorates radiation-induced cognitive impairments

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

Brain tumors are the most common solid tumors in childhood and while different treatments achieve increased rates of survival in cases such as medulloblastoma in other brain tumors such as gliomas the survival rates are unacceptably low. Radiation therapy is one of the most successful treatments for brain tumors. However, brain radiotherapy elicits an acute and long-term inflammatory response, which is a hallmark of radiation toxicity. Further, radiation therapy for some tumors is associated with declines in intelligence on the order of 15 IQ points over 4 years. This irreversible change in cognitive functioning ultimately impacts educational and occupational success, and could be prevented by improved treatments, such as those investigated in this proposal. We intend to investigate the strategy of blocking part of the action of one of the main inflammatory molecules secreted in the brain in response to radiation. We contend that this will abrogate the observed inflammatory cascade initiated by the radiation treatment and hence protect the vasculature (in the tumor as well as in normal tissue) from radiation damage. This will in turn increase the oxygen levels in the tumor rendering the tumor more sensitive to radiation damage and at the same time protect the normal tissue from the propagation of damage over time fuelled by the inflammatory cascade. We have designed experiments to test if blocking such inflammatory molecule will: (1) increase tumor vascular perfusion, increasing the amount of oxygen available to the tumor and hence enhancing tumor radiosensitivity, (2) protect the blood brain barrier (which controls the entrance of substance to the brain tissue) from radiation-induced damage restoring the controlled environment of the brain tissue and reducing late radiation sequelae, and (3) attenuates radiation-induced cognitive impairments.