CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100644

Project Title:
Impact of GBM-Specific Oncogenic Events on DNA Repair Pathways: Implications for Therapy

Award Mechanism:
Individual Investigator

Principal Investigator:
Burma, Sandeep

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Glioblastoma multiforme (GBM) is the most common and aggressive primary brain tumor in adults and is universally fatal due to a great degree of therapeutic resistance. Currently, the combination of radiation and the chemotherapy drug temozolomide is the only treatment regimen that has shown some therapeutic promise. In order to improve GBM therapy further, it is very important to understand how tumor cells respond to radiation and temozolomide. Both radiation and temozolomide kill tumor cells by inducing DNA double-strand breaks. Depending upon the DNA-damaging agent, DNA breaks are preferentially repaired by one of two major DNA repair pathways: non-homologous end joining or homologous recombination repair. We find that key genetic changes that promote the development of glioblastoma impact the proficiency of these two DNA repair pathways in very specific ways. These effects can have significant impact on how tumors respond to treatment. We propose to dissect these connections between GBM-specific oncogenic events and DNA repair pathways as this might uncover vulnerable nodes that can be targeted for therapy. Moreover, a more complete understanding of these relationships will help develop personalized treatment options based upon the status of these two DNA repair pathways in brain tumor cells.