



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180634

Project Title:
Understanding metabolic regulation of pediatric glioma through mouse modeling and patient tumor interrogation in vivo.

Award Mechanism:
Individual Investigator Research Awards for Cancer in Children and Adolescents

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

Lay Summary:

Pediatric brain cancer is among the most challenging tumors to treat, with short survival times despite intense multi-modality treatment. Progress has been made in identifying the genetic changes in these aggressive tumors and making the link between the mutations and processes that lead to malignant growth in the brain. Some genetic changes are well known to be important for reprogramming normal cellular metabolism to enable the cancer cells to generate energy and the building blocks of new cells. Targeting these processes is a potential new way to attack the cancer cells. Recent observations in adult brain cancers from our laboratory have challenged the longstanding view that the tumors are fueled solely by glucose. We have demonstrated that the tumors can burn acetate in addition to glucose, a property that seems to be common among rapidly growing tumors like glioblastoma as well as the slow growing grade 1 pilocytic astrocytomas. In order to fully understand and potentially exploit this finding for therapeutic benefit, we have proposed a study that infuses non-radioactively glucose and acetate in pediatric glioma patients while they are having their tumors removed during surgery. The tumors become labeled and the specific pathways being used to generate energy and building blocks in the cell can be traced directly. This provides a virtual road map from which potential targets can be identified that may be potentially useful for targeting. In addition, we have generated mice that have been genetically engineered with the important pediatric brain cancer genes. These mice develop high-grade gliomas which are very similar to the pediatric tumors and, as such, are highly valuable for studying the metabolism mechanisms in depth. The overarching goal is to understand the processes involved in pediatric brain tumor development, identify the substances that are being used for fuel and investigate ways to essentially cut off the fuel supply and kill the cells.