CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP170722

Project Title:
Identification of Critical Dependencies and Actionable Therapeutic Options in Smarcb1-Deficient Pediatric Tumors

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Draetta, Giulio

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

Lay Summary:

Cells have special enzymes that control how genes are expressed. Because of this, even when two people may share the same genes, these enzymes can impact how those genes are expressed and influence physiological processes. Increasingly, we are understanding that these enzymes controlling gene expression may significantly impact the development and progression of cancer. The function of one of these enzymes, Smarcb1, has been documented to be lost in a group of very aggressive pediatric tumors, malignant rhabdoid tumors (MRTs) and renal medullary carcinomas (RMCs). Although very rare, patients with these tumors suffer an overall dismal prognosis, especially very young patients under one year of age. It has proven very challenging to study the biology MRTs and RMCs for a number of reasons. For one, the tumors are very rare, making tumor specimens very difficult to obtain. Other approaches to model the disease are difficult because the deletion of SMARCB1 causes myriad negative effects on cells and tissues that are not directly related to the reasons SMARCB1 deficiency causes cancer. To address these problems, we have established collaborations with The Departments of Genitourinary Oncology at the MD Anderson Cancer Center and Memorial Sloan Kettering Cancer Center to obtain these rare tissue samples, and we have developed a novel mouse model of the disease that will allow us to study Smarcb1-deficient tumors. We will employ these models to screen for unknown dependencies within these tumors that may lend themselves to therapeutic intervention, including potentially the use of drugs that are currently available for patients with cancer, but that are not yet proven to be effective for these pediatric indications. If successful, our research may illuminate novel approaches to treat the young patients who present with these devastating diagnoses.