CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP170071

Project Title:
Genetic Epidemiology and Molecular Basis of Cancer Predisposition in Pediatric Rhabdomyosarcoma

Award Mechanism:
Individual Investigator Research Awards for Prevention and Early Detection

Principal Investigator:
Lupo, Philip

Entity:
Baylor College of Medicine

Lay Summary:

Compared to other pediatric cancers, the outlook for children with rhabdomyosarcoma (RMS) remains poor. In particular, for those with high-risk disease, fewer than 43% of patients survive for more than 5 years. Currently, there are no genetic testing and counseling strategies for children with RMS; there are no clinical surveillance or prevention protocols; and there are few therapeutic targets for this highly fatal tumor. One of the strongest risk factors for RMS is having a genetic cancer predisposition syndrome. While it is believed that about 7% of RMS patients have changes (or mutations) in the genes responsible for these syndromes, there have been: 1) no population-based assessments to support this estimate, and 2) no family-based studies to determine how many patients develop RMS due to new mutations (de novo mutations) in cancer predisposition genes. Furthermore, it is not clear how these gene mutations lead to RMS. Because of this, we will leverage the resources of the Children's Oncology Group, which is supported by the National Cancer Institute and has more than 200 participating institutions throughout the United States and Canada, to obtain over 1,000 samples from children newly diagnosed with RMS. We will also create the first family-based study of RMS for genomic analyses. We will then utilize state-of-the-art techniques in DNA sequencing available at Baylor College of Medicine to thoroughly study cancer predisposition genes in these individuals. We will also work with leading sarcoma experts at the University of Texas Southwestern Medical Center to understand the functional consequences of mutations in these genes on RMS using a novel zebrafish model. Our overall goal is to fully explain the role of cancer predisposition genes on the risk of RMS. This study represents an important step toward a better understanding of the causes of pediatric RMS by combining population-based research strategies with innovative molecular biological approaches.