Cancer Prevention & Research Institute of Texas (CPRIT) + Carson Leslie Foundation (CLF) =

$3,200,000.00 Childhood Brain Cancer Research Collaboration

Grant	Researcher	Institution	Cancer Type
Non-Toxic Therapeutic Strategies For Pediatric Brain Cancers **The Carson Leslie Award**	Dr. Kalkunte Srivenugopal	Texas Tech University Health Sciences Center	Childhood Brain
Proton Beam Radiation vs. Conventional Beam Radiation Toxicities During & After Craniospinal Radiation Therapy in Children **The Carson Leslie Award**	Dr. Douglas Ris	Baylor College of Medicine	Childhood Brain
Genotype and Metabolic Phenotype in Pediatric Brain Cancer **The Carson Leslie Award**	Dr. Elizabeth Maher	The University of Texas Southwestern Medical Center	Childhood Brain

Annette Leslie is part of CPRIT's Advisory Council on Childhood Cancer, and the two organizations have established a close relationship to help pediatric cancer patients. One of the most recent initiatives was the awarding of a joint $3,200,000.00 grant to fund research for less toxic childhood brain cancer treatments. - Wayne Roberts, CEO CPRIT

Key Accomplishments and Impact of Funding
CPRIT/ Carson Leslie Awards for Pediatric Brain Cancer Research

RP130629
PI: Dr. Elizabeth Maher
Organization: The University of Texas Southwestern Medical Center at Dallas
Title: Genotype and Metabolic Phenotype in Pediatric Brain Cancer

Question #1 What did you learn through your project?
First, we learned that it is safe to infuse 13C-labeled substrates in pediatric patients during resection of their brain tumor and that the tumor samples provide an unprecedented level of information about the metabolic pathways being used by the tumors as they exist within the brain microenvironment. Second, we learned that pediatric gliomas have very different metabolic profiles than adult gliomas, with almost no oxidation of glucose in the citric acid cycle. Third, we determined that the metabolic profile of medulloblastoma is similar to the adult gliomas, despite the profound differences in cell of origin and development stage of tumor development.

Question #2 How does what you learned advance knowledge about cancer?
We have advanced the field in two ways. First by providing a new way to study pediatric cancer metabolism in vivo and providing an avenue to obtain significantly more relevant basic information about tumors than can be obtained in cell culture. Second, the data provides a metabolic framework for further investigation of the pediatric brain tumors, which may lead to identification of key metabolic vulnerabilities in the tumors that may differ depending on the histological subtype and may be potential targets for treatment development.

Question #3 What is the significance of your findings for people with or at risk for cancer?
For patients with cancer, the study improves basic knowledge, which can lead to better understanding of complex pathways driving cancer and ultimately lead to more targeted therapies.

Question #4 What role did CPRIT funding play in your success?
First, CPRIT was critical in galvanizing our adult and pediatric brain tumor groups to work together. Second, without the CPRIT funding we would not have had the resources either in terms of personnel or funds to purchase 13C-glucose for infusion and analysis.

*Data extracted from Final Progress Reports
8/21/2018

Key Accomplishments and Impact of Funding
CPRIT/ Carson Leslie Awards for Pediatric Brain Cancer Research

RP130368
PI: Dr. M Douglas Ris
Organization: Baylor College of Medicine
Title: Proton Beam Radiation Therapy vs. Conventional Beam Radiation Therapy: Toxicities During & After Craniospinal Radiation Therapy in Children

Question #1 What did you learn through your project?
Statistical analyses are in process and so conclusions are pending. The adoption of proton beam radiation therapy (PBRT) in the field has advanced so rapidly that we were unable to enroll the anticipated number of patients in conventional radiation therapy arm of the study. Nevertheless, we have acquired unprecedented detail in side-effects, toxicities, and outcomes during the first year of treatment on a sizable sample of pediatric brain tumor patients.

Question #2 How does what you learned advance knowledge about cancer?
Knowledge gained through this study will provide important information as to anticipated side effects and toxicities associated with PBRT and how these relate to quality of life and short-term neurobehavioral outcome. Such information will contribute to treatment planning, preparation of patient and family, and, to a more limited extent, differences across types of radiation therapy (PBRT vs convention x-ray).

Question #3 What is the significance of your findings for people with or at risk for cancer?
This study will add important information to the cost-benefit analysis inherent in treatment planning for pediatric brain tumors.

Question #4 What role did CPRIT funding play in your success?
Funding through CPRIT allowed us to build a sophisticated, web-based data capture system supported by collaborators at 5 different sites in which highly uniform side-effects/toxicity, quality of life, neurocognitive effects, and neurobehavioral outcome data at a level of granularity that is unprecedented.

*Data extracted from Final Progress Reports
8/21/2018

Key Accomplishments and Impact of Funding
CPRIT/ Carson Leslie Awards for Pediatric Brain Cancer Research

RP130266
PI: Dr. Kalkunte Srivenugopal
Organization: Texas Tech University Health Sciences Center
Title: RATIONAL REDOX-DRIVEN NON-TOXIC THERAPEUTIC STRATEGIES FOR PEDIATRIC BRAIN CANCERS

Question #1 What did you learn through your project?
Currently, temozolomide is the sole chemotherapy drug for brain tumors, used with or without radiation. The DNA repair protein MGMT is a major stumbling block for temozolomide therapy. Our research showed that there are many ways to inhibit MGMT and sensitize gliomas to drug therapy. Along the way, we have discovered that MGMT has non-repair functions in cell cycle and DNA replication. We have already begun to exploit these findings for brain cancer therapy.

Question #2 How does what you learned advance knowledge about cancer?
Our translational research efforts create new drugs for better treatment of gliomas and medulloblastomas. By suppressing the MGMT activity and inducing oxidative stress in brain cancers, one will be able to design superior therapeutic regimens for this cancer type. Furthermore, the knowledge gained will be helpful in the treatment of other cancer types (colon cancer, melanoma, leukemia etc.) as well.

Question #3 What is the significance of your findings for people with or at risk for cancer?
The DNA repair protein MGMT is a double-edged sword. It prevents oncogenic mutations due to endogenous and exogenous alkylating agents in normal tissues. MGMT is overexpressed in cancers and its anti-mutagenic action makes tumors resistant to alkylating drugs. Previously, we showed that MGMT in normal tissues can be induced in normal tissues and peripheral blood lymphocytes by antioxidants. Such an upregulation can significantly reduce cancer risk. On the other hand, for cancer patients, our findings will help with treatment.

Question #4 What role did CPRIT funding play in your success?
CPRIT funding played a great role in furthering our research. Because NIH funding has become scarce and difficult to obtain, CPRIT grants have really helped with our drug discovery research. Because of this grant, I was able to obtain another major CPRIT grant (RP170207) and continue our translational efforts.

*Data extracted from Final Progress Reports
8/21/2018