The Children’s Tumor Foundation is pleased to announce the funding of nine Young Investigator Awards (YIA) for the 2022-2024 cycle.

**SIMGE ACAR**  
Washington University  
*Global Protein Changes Associated with Chr8 Gain in MPNST*  
Malignant peripheral nerve sheath tumors (MPNST) are one of the common malignancies in individuals with NF1 and are associated with poor overall survival. Unlike plexiform neurofibromas, MPNSTs have an extra copy of chromosome 8 (Chr8q gain), which is hypothesized to induce genome-wide perturbations that specifically promote cancer progression. This study will analyze cells with Chr8q gain along MPNST samples from patients to test the above hypothesis and to characterize the molecular changes caused by this phenomenon.

**HALEY HARDIN**  
University of Central Florida  
*Evaluation of BRD4 Inhibitors for Use in Combination with Kinase Inhibitors for NF2 Schwannomas*  
NF2 tumors respond to treatment with MEK inhibitors but eventually develop drug resistance. This study will evaluate a MEK-BRD4 inhibitor combination therapy for drug response in NF2 compared to MEK inhibitor monotherapy. Specifically, this study will investigate the drug resistance mechanism by examining the role of BRD4 in regulating the expression of resistance-mediating genes and will test various MEK-BRD4 inhibitor combinations to identify new drug combinations for NF2.

**CHARLENE ILTIS**  
Memorial Sloan Kettering Cancer Center  
*Characterization of the Molecular Mechanisms Conferring Resistance to Treatment on NF1-associated MPNST*  
MPNSTs in the context of NF1 are often the result of malignant transformation of benign precursor lesions including plexiform neurofibromas. The proposed project will characterize a rare MPNST population with stem-cell like properties that is essential for tumor initiation and relapse, and elimination of which promotes tumor shrinkage and abolishes tumor relapse. This study can provide deeper insights into MPNST development and new therapies for targeting them.

**TONCI IVANISEVIC**  
Vlaams Instituut voor Biotechnologie, Belgium  
*The Role of LZTR1 in Schwannomatosis Development and Progression*  
Pathogenic variants in the LZTR1 gene account for up to 40% of the cases of familial schwannomatosis. However, the molecular mechanisms by which these variants predispose to schwannomas are still unknown. This project will perform multi-omic analyses of an LZTR1-deleted schwannoma model to identify the interactions between the RAS/MAPK and Hippo pathways during schwannoma development and progression. It will also develop clinically relevant 3D models of schwannomatosis to assess candidate drugs as monotherapy or in combination with Hippo pathway inhibitors.
PAUL JONES
Washington University

*Early Detection and Model Development of NF1-MPNST Using Liquid Biopsy of cfDNA*

MPNSTs are the leading cause of death in NF1 patients but current methods to detect them, especially the early-stage ones, and track their progression are insufficient. This project aims to develop an assay based on cell-free DNA analysis that will more sensitively detect early-stage MPNST formation. It will further apply this assay in mouse models to understand tumor evolution, treatment response, and resistance mechanisms.

ERICA LEIF
Alliant International University

*The Impact of Self-Determination Theory on Increasing Health-Promoting Behaviors in Adults with NF1*

NF1 is a complex health condition with multiple clinical manifestations including debilitating chronic pain. By applying the self-determination theory, which suggests autonomy, competence, and relatedness as main psychological needs for growth and change, this study will investigate NF1-associated pain and the contribution of a wide range of factors to successful self-management of pain.

NAMRATA RAUT
Cincinnati Children’s Hospital Medical Center

*The Role of Schwann Cells in the Onset of Pain due to NF1*

The majority of NF1 patients experience moderate to severe neuropathic pain. However, the underlying mechanisms of pain development are not fully understood. The proposed study will examine the specific cell types and mechanisms involved in neuropathic pain development in NF1. Using preclinical mouse models, this study will test whether growth factors produced by Schwann cells together with select immune cell populations that infiltrate the affected peripheral nerves contribute to neuropathic pain-like behaviors.

NIPUNIKA SOMATILAKA
The University of Texas Southwestern Medical Center

*From Cold to Hot: Reprogramming Tumor Microenvironment to Target NF1 Malignancies*

MPNSTs associated with NF1 respond poorly to chemotherapy and radiotherapy. Immunotherapy drugs are also not effective against MPNSTs because these tumors are ‘cold,’ lacking T cells and other immune cells near or within the tumor. The present study aims to reprogram the MPNST microenvironment such that they are converted from non-T cell ‘cold’ tumors into T cell-rich ‘hot’ tumors. This will be achieved by activating the STING-IFN pathway using known small molecule agonists. This study will then test various combinations of STING agonists and immune checkpoint blockers to determine their efficacy in treating MPNST.

DEREK WONG
University Health Network, Canada

*Integrated Analysis of Plasma Whole Genome Sequencing for the Early Detection of Malignant Tumours in Patients with NF1*

The clinical manifestations of NF1 are diverse and range in severity from mild (e.g., skin discoloration) to very serious (e.g., cancer). Clinicians need new ways to identify NF1 patients requiring heightened surveillance or treatment. The objective of this study is to develop an assay that utilizes cell-free DNA (cfDNA) to monitor NF1 disease severity and identify tumors with malignant potential. This assay will integrate two technologies that enable more thorough genetic and epigenetic profiling of cfDNA and will potentially allow physicians to deliver personalized, risk-adapted care to NF1 patients.