The Children's Tumor Foundation is pleased to announce the funding of six Young Investigator Awards (YIA) for the 2021-2023 cycle.

**JORDAN KOHLMeyer**  
The University of Iowa  
*Defining the RABL6A-YAP Axis in MPNST Pathogenesis and Therapy*  
NF1 patients are at increased risk of developing malignant peripheral nerve sheath tumors (MPNSTs) due to the possibility of neurofibroma transformation. This study aims to evaluate two powerful cancer pathways, RABL6A and the Hippo pathway, whose dysregulation promotes MPNST pathogenesis. We will investigate how RABL6A regulates the YAP protein to promote MPNST development, and will develop new combination therapies for MPNSTs that will have reduced toxicity and high efficacy.

**LINDY ZHANG**  
Johns Hopkins University School of Medicine  
*The Effects of RAS Signaling Pathway Inhibitors on Tumor Cells and the Tumor Immune Microenvironment in MPNSTs*  
NF1-associated MPNSTs are resistant to MEK inhibition monotherapy because of activation of alternate cancer signaling pathways. This study will test combinations of MEK inhibitors, SHP2 inhibitors, and CDK inhibitors, which target different signaling pathways, to treat MPNSTs. Additionally, we will investigate the role of the tumor microenvironment and the impact of various inhibitors on immune cells to design trials of drugs.

**SARA PARDEJ**  
University of Wisconsin-Milwaukee  
*Neural Underpinnings of Attention in Children with NF1*  
Attention difficulties are a common cognitive phenotype in children with NF1, yet very little is known about the underlying neural mechanisms. This research will test the feasibility of electroencephalography (EEG) approaches in children with NF1 to identify potential biomarkers of attention problems. By studying differences in neural functioning between children with NF1, their peers, and children with ADHD, we hope to find unique functioning patterns that can effectively track the impact of medical and psychosocial interventions affecting attention in NF1.

**JAMIE GRIT**  
Van Andel Research Institute  
*Targeting inflammatory signaling in cutaneous neurofibromas*  
Cutaneous neurofibromas (CNF) are a major cause of morbidity in NF1 and clinically behave very differently than plexiform neurofibromas (PNF). Since CNFs rely more on inflammation than the strong MEK signaling that typifies PNFs, they may need different treatment approaches. This study will test diclofenac, an anti-inflammatory COX2 inhibitor ointment, on CNFs, and will determine patient experience and tumor response after treatment.

**ISABELLE LOGAN**  
Oregon State University  
*Signaling Pathways Regulated by Nitrated Proteins as Novel Therapeutic Targets for NF2*  
Nitrated proteins are a novel category of NF2 tumor targets as they play a key role in schwannoma growth and are not present in normal cells. The goals of this project are to investigate the regulation of signaling pathways by nitration and to identify the specific nitrated protein(s) that support NF2 tumor cell survival. Besides NF2, these proteins could be new targets in conditions such as glioblastoma, breast cancer, and colon cancer, where protein nitration is involved in proliferation.

**FILIPP KULIKOV**  
Russian National Research Medical University  
*Exploiting Cytotoxic Role of Nuclear Rac1 to Develop Targeted Antitumor Therapy of NF2-Associated Tumor*  
There is no specific treatment for NF2 other than non-specific radiotherapy and surgery, which can sometimes be ineffective due to remote localization of tumor. This proposal will determine the mechanism by which statins and bisphosphonates induce Rac1 translocation into the nucleus, thereby causing cell death. We will also investigate the effectiveness of a statin-bisphosphonate combination therapy for NF2-associated tumors.