

Submission to Lillie's Friends Foundation for consideration for funding support.

Name of project: A Clinical Trial using Molecular-guided therapy for the treatment of patients with refractory or recurrent neuroblastoma

Brief description: Neuroblastoma accounts for 15% of all pediatric cancer deaths in the US with no curative treatment for relapsed patients so there is a clear and urgent need to develop novel strategies to improve patient outcomes. Recent efforts to systematically characterize the molecular basis of neuroblastoma has confirmed biologic differences in this disease. This has revealed major molecular sub-types with varying prognoses, suggesting that different sub-types of neuroblastoma may respond to different therapeutic strategies. This is a pilot study focusing on the patients tumor genetics using a novel method to identify potentially active agents for each patient with relapsed/refractory neuroblastoma. We hypothesize that transcriptome analysis of individual tumor samples can be combined with data concerning molecular pathways and knowledge of drug targets and activity to allow for more rational and individualized selection of potentially active drugs in this population.

Goal of project: **Specific Aims:** *Aim 1:* Determine feasibility of generating genome-wide RNA expression profiles from neuroblastoma cells (derived either from primary tumor specimens or bone marrow samples) and utilizing this data to make real-time treatment decisions. *Aim 2:* To determine the effectiveness of treatments chosen by this method based on Overall Response Rate (ORR) and Progression-Free Survival (PFS). *Aim 3:* To explore in a correlative biologic study the relationship between tumor phenotype and response to therapy.

Study Design: The current proposal will involve 20 patients with neuroblastoma that are either refractory to, or have relapsed following, current front-line combination therapy. Patients will have a biopsy from which genomic analysis will be performed and a report will be generated based on XB-BIS predictive modeling technology. This will be used to design a therapeutic protocol by a committee of up to eight pediatric oncologists and two pharmacists. Patients will be followed for response to therapy and survival. A correlative biology study will establish xenografts from patient tumor samples for subsequent analysis. Should the method prove feasible and efficacious, formal comparative trial designs will be implemented.

Impact: This will be the first study in pediatric oncology evaluating the feasibility of using patient specific genetic information as a predictive tool in personalized therapy. It may bring new options to patients with relapsed/refractory neuroblastoma for whom no curative treatment options exist, and so it has potential to extend survival. This method may provide improved ways to make therapeutic decisions for patients with heterogenic diseases such as neuroblastoma.

