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**“Genetic Evaluation of Methotrexate Treatment in Pediatric Cancer Patients”**

Cancer is one of the number one cause of death among children. Leukemia comprises approximately 30% of all pediatric cancers, with acute lymphocytic leukemia (ALL) and acute myeloid leukemia (AML) as the most common. ALL is seen among patients from ages 2-5 years of age, whereas AML may present throughout childhood. One of the most common types of pediatric cancer treatments is the chemotherapy agent methotrexate. Based on our preliminary results in collaboration with Children's Hospital of New Orleans, LA (CHNOLA) and data from the literature, treatment with methotrexate in pediatric patients has been implicated with long-lasting development of detrimental neurological and psychosocial sequela following cancer survival. These deficits which persist after the methotrexate exposure, termed “late effects”, may include memory loss, and abnormal behavior such as unusual aggression, problems with executive functioning and processing speed as well as mental disorders like ADHD, depression, and anxiety.

The goal of our project is to elucidate gene-environment interactions caused by methotrexate treatment. We hypothesize that gene expression changes occur in neuroinflammation genes due to methotrexate treatment. To prove this hypothesis, we are conducting 1.) retrospective neurological and psychosocial analysis of living cancer survivors who have completed cancer treatment with methotrexate as their chemotherapy agent, and 2.) genetic analysis of white matter brain tissue samples obtained from autopsies of deceased patients who have previously undergone chemotherapy. RNA is isolated from the formalin-fixed paraffin embedded (FFPE) brain autopsy tissue samples of patients and age-matched controls. A Nanostring neuroinflammation gene microarray panel of more than 94 genes is followed by bioinformatics and ingenuity pathway analysis (IPA). This project will reveal pathways contributing to neurocognitive and psychiatric late effects secondary to methotrexate therapy.