Title: Biomarkers and Genetics of Brain Injury Risk in Diabetic Ketoacidosis (BIGBIRD)

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Synopsis:

Diabetic ketoacidosis (DKA) remains the most common and catastrophic presentation of previously undiagnosed or poorly controlled type 1 diabetes mellitus (T1DM) in children. Cerebral edema is the most devastating form of cerebral injury in DKA (CIDKA) and occurs overtly in approximately 0.5 to 1% of DKA cases. Cerebral edema accounts for a large proportion of the deaths (24-90%) in pediatric patients with DKA, and 20% of all deaths attributable to diabetes. At Children’s Hospital and Research Center Oakland (CHRCO), of 304 patients treated for DKA, 42 had clinical evidence of CIDKA. The long-term effects of this less severe presentation are completely unknown. Some authors indicate that one third of survivors of CIDKA will have significant long-term disability, but the majority of data on pediatric DKA and CIDKA consist of small observational studies, animal data and case reports.

This spring, an NICHD-funded Fluid Therapy in DKA trial (aka FLUID) began enrollment across 10 Pediatric Emergency Departments across the US. The FLUID trial anticipates enrolling over 1500 children over the next 5 years. FLUID is aimed at studying differences in pediatric patient outcomes with variation in fluid treatment after presentation in DKA. It is not funded to explore mechanistic aspects of the treatment algorithms being tested. Our goal is to establish our concept protocol at our 3 institutions first, enabling an RO1 application, such as PAR-09-247 Ancillary Studies to Major Ongoing Clinical Research Studies to Advance Areas of Scientific Interest within the Mission of the NIDDK (R01), to prospectively co-enroll pediatric patients to determine the clinical, genetic and biological marker profile of pediatric DKA, with specific focus on CIDKA.

The overall hypothesis of this study is that clinical, genetic and biological marker profiles vary and these profiles can identify children with DKA at risk for CIDKA. Whereas the majority of DKA research to date has focused around fluid volume and composition, such as is being tested in the ongoing FLUID trial, this study will offer novel hypotheses in pediatric DKA monitoring, diagnosis and treatment to be tested.