CDKL5 Program of Excellence
Pilot Grant Program

Application Title: Development of biomarkers for CDKL5 activity

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CDKL5 is an X linked gene, which when mutated causes a neurodevelopmental disorder termed CDKL5 deficiency disorder. Despite intial observation of limited overlap with some symptoms of Rett syndrome, early onset seizures, typical of CDKL5 deficiency disorder, are not observed in Rett syndrome. CDKL5 mutations are often loss of function alleles resulting in a mosaic expression of CDKL5 in female patients. Missense mutations are also identified in the kinase domain, indicating that the kinase function is critical. Male CDKL5 deficiency disorder patients are also found, albeit less often. Several treatment options are being evaluated at the moment ranging from protein/ gene replacement to stop codon read-through therapies. Biomarkers which could be used to measure recovery of CDKL5 activity would be helpful in evaluating the outcomes in animal models and as well as in patients. We propose in this study to test if phospho-specific antibodies raised against CDKL5 substrates that we have discovered could be used as biomarkers in CDKL5 knockout mice, patient neuronal cell lines and patient samples.