2016 Million Dollar Bike Ride
Pilot Grant Program

Application Title: Neurophysiological correlates in CDKL5 syndrome: a supplement to the NIH Natural History Study of Rett syndrome, CDKL5 syndrome, and other Rett syndrome-related disorders; protocol RTT5212

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The overall purpose of this project is to advance our understanding of the neurophysiological features of CDKL5 syndrome to gain insight into disease pathogenesis, with an emphasis on identifying biomarkers of disease evolution and severity. This specific study is intertwined to the core study NIH-funded Natural History of Rett Syndrome and Related Disorders (RTT5211), which characterizes range of clinical involvement and genotype-phenotype correlations and will provide phenotypical data for determining the clinical relevance of the neurophysiologic parameters; study subjects here are co- and primarily enrolled in RTT5211. We postulate that the proposed studies will serve as a basis of future translational investigations, including further refinement of biomarkers, development of outcome measures, and clinical trials per se.

Treating CDKL5 syndrome will require more than just an understanding of the molecular and cellular alterations present in affected subjects. While recent advances in this regard are exciting and could lead to disease modifying therapies, none of these approaches will have a substantial impact unless they rescue the changes in cortical networks for sensory processing. Hence, the primary goal of this proposal is to obtain the first human neurophysiological data in CDKL5 syndrome to begin to understand its cortical pathophysiology and develop a biomarker to be used for future clinical trials. We will measure and analyze auditory and visual evoked potentials. Our central postulate is that the proposed studies will serve as a basis of future translational investigations, including further refinement of biomarkers, development of outcome measures, and clinical trials per se. We desire to symmetrically leverage protocol RTT5212 for greater success by increasing the cohort of patients with CDKL5 syndrome; this will allow for comparisons obtained here with the control cohort obtained by protocol RTT5212.