CDKL5 Program of Excellence
2018 Pilot Grant Program

Project Title: "Testing functional and structural connectivity in CDKL5 deficiency disorder as novel biomarkers"

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The CDKL5 gene is expressed from late gestation and early postnatal life, likely contributing to the assembly of neuronal circuits and their experience-dependent refinement during critical neurodevelopmental periods. Whether and how CDKL5 affects the development and refinement of neuronal circuits, however, is largely unknown. Our goal is to elucidate the role of CDKL5 in the establishment of functional and structural neuronal connectivity and to identify novel quantitative biomarkers of CDKL5 deficiency disorder in patients. Here, we propose testing the working hypothesis that CDKL5 regulates the refinement of posterior connections across hemispheres. We will combine in vitro and in vivo electrophysiological analysis with functional and structural imaging in both animal models of CDKL5 deficiency disorder and patients. Our preliminary data collected in CDKL5 KO mice indicate statistically significant functional posterior interhemispheric over-connectivity as revealed by in vitro recordings and rsfMRI imaging. Leveraging advances in translational neuroimaging, our studies will allow us to elucidate how disruption of CDKL5 expression derails the early refinement of neuronal circuits and significantly impact downstream function and behavior. Furthermore, our project may help establish DTI, rs-fMRI and VEP as novel structural and functional quantitative biomarkers of CDKL5 deficiency disorder to be employed to predict progression of the disorder and response to treatment.