CDKL5 Program of Excellence
2024 Pilot Grant Program

Project Title: "CDKL5 in Biomolecular Condensates and its Role in CDD Pathophysiology"

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CDKL5 deficiency disorder (CCD) is a genetic disorder that causes epilepsy and severe neurodevelopmental delays, affecting tens of thousands of patients worldwide. There are currently no approved treatments that address the disorder's neurodevelopmental symptoms. CCD is caused by mutations in the cyclin-dependent kinase-like 5 (CDKL5) gene, which encodes for an under-characterized kinase involved in the regulation of numerous neuronal processes. While several dozen mutations in CDKL5 have been linked to CCD, the functional impact on the disease's pathology is not fully understood. In recent years, we have come to appreciate that cells utilize phase separation of proteins and nucleic acids into membraneless organelles to regulate cellular processes spatially and temporally. Based on our preliminary studies, we proposed that the toxicity of some CDKL5 mutants may be due to the dysregulation of these membraneless organelles, such as those involved in DNA repair and stress response. Therefore, we propose to study CDKL5's pathology from the lens of phase separation and to investigate how its mutations affect cellular organization. The findings from this research will enhance our understanding of the root cause of CCD and lay the groundwork for novel and targeted treatments.