CDKL5 Program of Excellence
2024 Pilot Grant Program

Project Title: "Integrating Experimental and Computational Approaches to Unravel the Neurophysiological Basis of CDKL5 Deficiency Disorder"

PI: Roy Ben-Shalom, PhD

Institution: University of California, Davis

CDKL5 Deficiency Disorder (CDD) is a rare genetic condition causing early-onset seizures, severe developmental delays, and a range of neurological issues. This project aims to understand how mutations in the CDKL5 gene disrupt brain function at the levels of individual neurons, synapses (connections between neurons), and neural networks. By studying these disruptions in mouse models of CDD, we hope to identify key factors contributing to the disorder's symptoms. Our approach involves three main steps. First, we will use advanced recording techniques to measure the activity of neural networks in brain cells from mice with CDKL5 mutations. This will show us how network function is impaired at different stages of development. Second, we will examine the properties of individual neurons and synapses to pinpoint specific changes caused by CDKL5 mutations. Finally, we will create a detailed computer model that integrates our experimental findings. This model will help us understand how various neural alterations combine to produce the network dysfunctions seen in CDD. By manipulating components within the model, we can predict which changes are most critical for causing CDD symptoms and identify potential targets for treatment. We will also use the model to simulate the effects of different therapeutic strategies, accelerating the development of effective interventions. Ultimately, our goal is to improve the lives of those affected by CDD. By advancing our understanding of the disorder's underlying mechanisms and facilitating the discovery of targeted therapies, this project holds the potential to make a meaningful difference for patients and their families. In the future, we plan to extend our approach to human brain cells derived from CDD patients, ensuring that our findings are relevant to the human condition.