

AI Discovery of Circuit-Level Mechanisms and Electrophysiological Biomarkers of CDKL5 Deficiency Disorder

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CDKL5 Deficiency Disorder (CDD) is a severe neurodevelopmental condition causing treatment-resistant epilepsy and profound impairments in motor, cognitive, and visual function. While several promising therapies are in development, the field lacks objective, quantitative biomarkers that can track specific symptoms and predict treatment response. In this project, we will apply a novel artificial intelligence (AI) framework—developed by our team and validated in a study recently published in *Nature Neuroscience*¹ — to the largest available collection of research quantitative EEG recordings from individuals with CDD. We will train AI systems to detect CDD-specific brain activity patterns from EEG and link those patterns to specific clinical symptoms such as seizure burden, motor impairment, and visual dysfunction. We will then use these AI systems alongside a computational model of brain circuits to identify which specific neural circuit changes drive the EEG abnormalities seen in CDD. The resulting biomarkers will enable objective tracking of disease severity in future clinical trials, and the circuit-level mechanisms we identify will generate specific targets for future therapeutic testing in patient-derived brain organoids.