CDKL5 Program of Excellence
2018 Pilot Grant Program

Project Title: "Systems Level Analysis of CDKL5 Astrocytes to Identify Novel Markers and Pathways in CDKL5 Deficiency Disorder (CDD)"

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Patients with CDKL5 deficiency disorder (CDD) suffer from a range of neurological conditions that include seizures, motor dysfunction, and intellectual impairment. Recently generated mouse models of CDD also exhibit neurological impairments, and neurons within critical regions of their brains are often underdeveloped. We study the roles played by astrocytes (the main non-neuronal cell type in the central nervous system) in brain development, and have shown that neurons grown in the absence of astrocytes are functionally compromised. Furthermore, we have isolated astrocytes from a range of neurodevelopmental disorders (NDs), including Rett syndrome (RTT), Fragile X syndrome (FXS), and Down syndrome (DS), and shown that these astrocytes are incapable of supporting normal neuronal development. Here, we will isolate astrocytes from a mouse model of CDD and characterize their effect on neuronal development. We will then use a range of molecular analyses to compare CDD astrocytes to wild type astrocytes, an approach that will potentially identify astrocyte-specific targets for developing new therapies against CDD. Because we have performed similar analyses in a number of NDs, both CDD-specific targets, and targets that are shared across NDs, will be revealed.