CDKL5 Program of Excellence
2020 Pilot Grant Program

Project Title: "CDKL5 regulation of ciliary assembly and signaling"

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CDKL5-deficiency disorder (CDD) and diseases caused by ciliary dysfunction (ciliopathies) share common phenotypes. This phenotypic overlap combined with observations that CDKL5 localizes to cilia suggest that CDD is a ciliopathy. This proposal will use *Chlamydomonas* and mammalian cells to test this hypothesis. In *Chlamydomonas,* CDKL5 is known to control ciliary length. This organism has unique advantages for proteomic and genetic studies of cilia that we will leverage to uncover the mechanisms regulating CDKL5 activity and the effects of CDKL5 deficiency on ciliary structure and function. Findings from *Chlamydomonas* will inform studies in mammalian cells to understand the regulation and function of mammalian CDKL5. In addition, we will use mammalian cells to explore the function of CDKL5 and its substrates on the dynamics of primary cilia assembly and in ciliary signaling. It is expected that these studies will uncover the mechanisms controlling CDKL5 activity and the role of CDKL5 in regulating ciliary signaling processes. Discovery of these mechanisms has the potential to identify new therapeutic targets.