# CDKL5 Program of Excellence
# 2020 Pilot Grant Program

**Project Title:** "Visualizing the effect of CDKL5 Deficiency Disorder on ciliary core structures"

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**Institution:** Harvard Medical School

Children born with a lack of functional protein kinase CDKL5 often develop a severe neurological disorder characterized by early-life epilepsy and cognitive disabilities. Recently, CDKL5 has been found to be located inside cilia, the small hair-like projections on the surface of many cells in the human body including those in the brain. CDKL5 modifies by phosphorylation a number of proteins associated with microtubules and CDKL5 deficiency has been shown to affect the overall shape of cilia. We propose that CDKL5 binds the unusual doublet microtubules of the ciliary cytoskeleton and that this interaction is important for its function. Using a combination of biochemistry and electron microscopy we aim to test this hypothesis. These biochemical and structural experiments will help to explain the function of CDKL5 in cilia and childhood epilepsy. A better understanding of the causes of CDKL5 deficiency disorder will ultimately improve therapies to treat it.