
CDKL5 Program of Excellence 2021 Pilot Grant Program

Project Title: “Advancing a mosaic CDKL5 zebrafish model for high-throughput screening approaches”

PI: Christopher McGraw, MD, PhD

Institution: Boston Children’s Hospital

Zebrafish is a powerful organism for modeling neurodevelopmental disorders such as CDKL5 Deficiency Disorder (CDD). In order to make the most authentic models of CDD in zebrafish, we propose a new technique that will recapitulate the mosaic pattern of CDKL5 loss-of-function seen in girls with CDD due to X-chromosome inactivation, despite the fact that zebrafish do not possess X chromosomes. We think this may be an important aspect of the disease, but we will also develop zebrafish with complete CDKL5 loss-of-function to compare. We will assess our *cdkl5* mutant fish for seizures, altered seizure susceptibility, and vision abnormalities to see if they have the same problems we see in patients with CDD. This is a critical first step to validate zebrafish as a model of CDD. If positive, we will immediately pursue a drug screen to identify therapeutic compounds for CDD, which is much easier and faster to do in zebrafish.