CDKL5 Program of Excellence
2020 Pilot Grant Program

Project Title: "Assessing peripheral sensory neuron dysfunction in animal models for CDKL5 deficiency disorder"

PI: Lauren Orefice, PhD

Institution: Massachusetts General Hospital

Autism spectrum disorders (ASDs) are thought to arise exclusively from aberrant brain function. Our research proposes a surprising revision of this view. We established an emerging theory, which states that peripheral sensory neuron dysfunction contributes to major ASD-related phenotypes including tactile overreactivity, anxiety and social impairments in three different ASD mouse models. Further, we found that peripheral sensory neurons may be targeted to improve ASD outcomes. The idea that peripheral sensory neurons contribute to ASD phenotypes is a paradigm shift for the field. A major question is whether peripheral sensory neurons are abnormal and contribute to phenotypes in other forms of ASDs including CDKL5 deficiency disorder (CDD). Patients with CDD exhibit severe sensory abnormalities, including touch over-reactivity and gastrointestinal (GI) dysfunction. We hypothesize that loss of Cdkl5 in peripheral sensory neurons causes abnormal tactile and GI function, and this contributes to some related phenotypes such as anxiety and social impairments. We will also test whether methods that reduce peripheral sensory neuron dysfunction improve tactile and GI-related phenotypes in mouse models for CDD.