CDKL5 Program of Excellence
2021 Pilot Grant Program

Project Title: "Comparison of Brain Biodistribution of Two CDKL5 Gene Therapy Vector Leads"

PI: Dolan Sondhi, PhD

Institution: Weill Cornell Medical College

Mutations in cyclin-dependent kinase-like 5 (CDKL5) cause CDKL5 deficiency disorder (CDD), a developmental encephalopathy which is a relatively common and devastating genetic cause of early-life epilepsy. Other common symptoms are developmental problems, loss of language skills, and repeated stereotypic hand movements. Delivery of the CDKL5 gene mediated by an adeno-associated viral vector to the brain of mouse models of CDD has shown to be therapeutically efficacious in murine models. As a next step in clinical translation, we propose to assess CDKL5 expression in a nonhuman primate brain using a viral vector that has been radiolabeled, such that we can track it non-invasively in vivo using positron emission tomography in realtime and compare the distribution pattern we observe, to CDKL5 transgene expression at the time the animal is sacrificed. This will allow us to gain critical insight into capsid spreading throughout brain and other tissues, as well as information regarding persistence of vector genomes and CDKL5 transgene expression.