CDKL5 Program of Excellence
2023 Pilot Grant Program

Project Title: "New Drosophila models of CDD"

PI: Máximo Ibo Galindo, PhD

Institution: Centro de Investigación Príncipe Felipe

CDKL5 deficiency disorder (CDD) is a rare epileptic encephalopathy caused by X-linked loss-of-function mutations in the CDKL5 (cyclin-dependent kinase-like 5) gene. Seizures, mainly of the myoclonic type, start within a few months of life, and subsequently other very severe comorbidities appear, such as cognitive and developmental delay, mobility problems, gastrointestinal problems and sleep disturbance. Our research group has extensive experience in the development and analysis of models of rare neurological diseases in the fruit fly Drosophila melanogaster. The current project will apply a biotechnological approach to develop new disease models of CDD. We have identified the Drosophila gene that would be the equivalent of the human gene and we have preliminary data that it would be a relevant model. We will use two types of techniques to try to reproduce the phenotype of patients, silencing of the gene by RNA interference and gene editing using CRISPR-Cas9 technology. Male patients, less common as this is an X-chromosome-linked disease, are probably genetic mosaics. By using CRISPR-Cas9 editing somatically we could also simulate this situation. We will characterize and compare the different models generated, to determine which of them would be suitable for each one of the projects aims and for future research. We intend to use these models to understand the effect of the mutations found in the patients, and to discover other genes that can modify the disease, including other CDKL gene family members. An important aspect is that we have a close relationship with the CDKL5 Spanish association, which will be involved in the development of the research and will contribute to the dissemination of the results to the community at the national level, and also through its contacts with international associations.