CDKL5 Program of Excellence
2022 Pilot Grant Program

Project Title: "Rescuing functional defects in a zebrafish model of CDKL5 deficiency: Contribution to the identification of therapeutic targets"

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We have previously validated the cdkl5^{sa21938} zebrafish mutant line as a suitable model to analyze the functional and molecular defects associated to CDKL5 deficiency disorder (CDD). As a follow up, we propose to exploit this model to screen commercial compound libraries for the identification of molecules capable of treating or relieving symptoms of CDD and thus become potential candidates for therapeutic applications. Our data supports the hypothesis that zebrafish can mimic human behavior phenotypes associated with expression of mutant CDKL5. In the present proposal, we will use transgenic zebrafish lines expressing fluorescent reporters in neuronal and skeletal cells, previously crossed with the mutant line cdkl5^{sa21938}, to screen for molecules capable of rescuing CDD phenotypes based on the automatic analysis of fish behavior and identification of changes in the expression of marker genes using confocal imaging. Our final output will be the identification of compounds capable to rescue the mutant phenotype of zebrafish larvae and thus become suitable candidates for further studies towards the discovery of novel therapeutic applications.