
CDKL5 Program of Excellence 2023 Pilot Grant Program

Project Title: “Assessment of the therapeutic potential of TATk-hCDKL5 isoforms 1 and 2 produced in recombinant Antarctic *Pseudoalteromonas haloplanktis* TAC125”

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Enzyme Replacement Therapy (ERT) is a consolidated therapeutic approach to cure monogenic-based disorders caused by loss-of-function protein mutations. It consists of the supply of the active enzyme produced and purified from suitable cell factories. The potential of ERT for CDKL5 Deficiency Disorder (CDD) treatment in KO mice was demonstrated in 2018, but the lack of an efficient manufacturing processes for the therapeutic biologic, i.e. TATk-hCDKL5, stopped the progression toward the clinic. Recently, new possibilities were opened by the setup of the first ever reported efficient genetic system for the recombinant production of the full-length TATk-hCDKL5 isoform 1 in an unconventional marine bacterium. Therefore, this application aims:

- i) To establish an efficient manufacturing process for the large-scale production and purification of the two main cerebral hCDKL5 isoforms (1 and 2)
- ii) To explore for the first time the possibility to carry out a CDKL5-based ERT with the two main cerebral isoforms (1 and 2) and suitable combinations thereof in the CDD preclinical mouse model.