POSTDOC in CELLULAR NEUROPHYSIOLOGY - University of Pavia (Italy)

Project PRRT2: "Experimental and modelling investigation of sodium channel dysfunction in the cerebellum to determine the basis of PRRT2 paroxysmal disorders".

The positions:
Postdoc. Expected start: January-March 2024. Duration: 2 years.

Working environment: the postdoc will work in the Neurophysiology Unit headed by Prof. Egidio D'Angelo in the Department of Brain and Behavioural Sciences (University of Pavia, Italy, https://web.unipv.it/). The Neurophysiology Unit is comprised of three laboratories (Cellular Neurophysiology, Neurocomputation, Neuroimaging and Brain Modelling) and generates state of the art concepts, models and theories about brain functioning, with a special focus on the impact of microscopic mechanisms of the cerebellar circuit on brain processing occurring at higher scales. The laboratory operates on various projects on the front of experimental research in cellular/molecular neuroscience, computational modelling and integrative brain functions in health and disease. An overview of laboratory activities and organization can be found at https://dangelo.unipv.it/ .The postdoc will take part to the PRIN project "Experimental and modelling investigation of sodium channel dysfunction in the cerebellum to determine the basis of PRRT2 paroxysmal disorders" of the Italian Ministry of Research. The project will be carried out in close collaboration with other EU projects (EBRAINS, TEF-Health, PNRR-EBRAINS, PNRR-ICT, CEN, Virtual Brain Twin) running in the research unit.

Research project: The cerebellum is gaining attention for its primary involvement in the physio-pathogenesis of neurological diseases that have been postulated to originate from other brain areas so far. In the motor domain, in addition to ataxia, also forms of dyskinesia and dystonia are now thought to involve the cerebellum. The identification of the molecular and cellular basis of these pathologies can be effectively investigated in animal models bearing mutations imitating those occurring in humans. In this project, we will use PRoline-Rich Transmembrane protein-2 (PRRT2) KO mice showing paroxysmal kinesigenic dyskinesia. The highest expression level of PRRT2 in the brain occurs in cerebellar granule cells (GCs) and cerebellar dysfunctions participate in the dyskinetic phenotype of PRRT2 knockout (KO) mice. In this project we will combine molecular/cellular level and microcircuit level experiments with detailed biophysical computational modeling to understand how PRRT2 KO alters GC firing and reverberates on local microcircuit computation. In our research unit, we will investigate the impact of PPRT2 KO in acute cerebellar slices using high-density multi-electrode arrays (hdMEA) and 2-photon calcium imaging, which allow to map the alteration at the multicellular level. Finally, though internal collaborations, we will simulate the entire cerebellar microcircuit to predict how anomalous network processing alters cerebellar output patterns. This work will provide a deeper understanding on the pathophysiology of PRRT2-related paroxysmal kinesigenic dyskinesia, providing new cues to understand the role of cerebellum in pathology and to ameliorate their course through specific therapeutic interventions.

Evaluation: The evaluation of candidates will include CV, publications, reference letters, oral discussion including English language assessment (details to come).

The call: will appear on the UNIPV website (details to come).