

## IBEC-SJD INTERNATIONAL PhD PROGRAMME

### Position

1. Project Title/ Job Position title:

**Testing orphan drugs for Rett syndrome: combining neurometabolism and neuronal circuit function**

2. Research project/ Research Group description:

Rett syndrome affects 1 in 10,000 people, mostly girls, and is usually caused by *de novo* mutations in the transcriptional regulator *Mecp2*. Patients develop normally for the first 6–18 months of life, then lose acquired milestones—such as crawling, walking and speech—and develop neurological symptoms including epilepsy, stereotypes, and social dysfunction. Effective treatment for Rett is still lacking.

With this project, two IBEC and SJD research groups aim at jointly developing a more comprehensive preclinical testing platform for drugs to treat Rett syndrome.

Previous work in *Mecp2*<sup>+/-</sup> mice from the group of Ángeles García Cazorla and Alfonso Oyarzabal at the SJD Children’s Hospital demonstrated that mitochondrial dysfunction and neuroinflammation are central to Rett syndrome, and that pharmacological regulation of metabolism improves the disease phenotype. This preclinical evidence supported a clinical trial for the treatment of Rett syndrome that started in September 2024 at SJD. However, Rett is a complex disorder, and other mouse phenotypes highly relevant to the human disease, such as epilepsy and limited social functioning, were not tested.

This project, co-led by IBEC’s researcher Silvia Pittolo with expertise in brain recordings in freely moving mice, builds on an existing collaboration between IBEC and SJD funded by the Torrons Vicens/RAC1 call, and aims at understanding whether pharmacological treatment that corrects metabolic and inflammatory endpoints can also correct other Rett’s phenotypes, including unbalanced excitatory and inhibitory circuit activity, propensity to epileptic seizures, and social deficits.

This PhD fellowship will allow our groups to establish solid methods for linking the neurometabolic and inflammatory state of the animal with real-time recordings from specific brain regions and cell types during a social task. We expect this will allow us to screen drugs with higher translational validity and relevance for the human condition.

### 3. Job position description:

The ‘Nanoprobes & Nanoswitches’ group at IBEC is looking for a PhD candidate to work on a Neuroscience project in close collaboration with the ‘Paediatric Neurometabolic Disorders’ group at the Sant Joan de Deu Children’s Hospital (HSJD). The project focuses on Rett syndrome, which is a devastating neurodevelopmental disorder that affects toddlers and causes loss of acquired milestones, as well as epilepsy and impaired social functioning. The successful candidate will test whether and how novel drugs which are in clinical trial at HSJD can effectively rescue a range of phenotypes observed in the Rett mouse model, including impaired metabolism, neuroinflammation, neuronal circuit imbalance, propensity to seizures, and impaired sociability.

Main responsibilities for this position include molecular biology, cell-based assays, mouse surgery, behavior, fiber photometry, electrophysiology, brain histology, confocal and multiphoton microscopy, data analysis and interpretation, and dissemination of results also to patient organizations.

The successful candidate will have a Master in Neuroscience, Biology, Biotechnology, Biomedical Engineering or related fields, excellent interpersonal skills and English fluency. Hands-on experience in a neuroscience laboratory working with Rett syndrome or related disorders will be a plus. FELASA accreditation to work with laboratory mice, prior experience with animal surgery and ability to code in Matlab or Python will be highly valued.

Our labs at IBEC and HSJD offer outstanding training opportunities and international and dynamic environments. Our research is highly multidisciplinary, spanning biology, chemistry, physics, medicine, and genetics, which, combined with the wide-ranging techniques and animal models used in the two host labs, ensures exposure to a range of experimental procedures, laboratory equipment, animal models, and in general to the opportunity of maturing scientific ideas with great potential for future career prospects.

### **Group Leader at IBEC**

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### **Group Leader at SJD**

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