Postdoctoral proposal

Molecular basis for perturbed spliceosome homeostasis in Alzheimer's disease

Project description: Tauopathies, including Alzheimer's Disease (AD), are characterized by a cytoplasmic accumulation of abnormal deposits enriched in the protein tau. In these deposits, tau is aggregated into so-called amyloid filaments, which are highly ordered protein aggregates. Although tauopathies are characterized by complex and global dysregulations, it is now clear that tau aggregation is central to their development.

Altered RNA metabolism is a hallmark of neurodegenerative diseases. Among the common alterations are aberrant mRNA splicing and 3'-end processing, both processes in which U1 small ribonucleoprotein (U1 snRNP) plays a major role. In other neurodegenerative diseases (SMA, PCH7 and FUS-induced ALS), impairment in U1 snRNP biogenesis has been described as the basis for the neuronal aberrant function (Campagne S., Chembiochem 2024). Interestingly, mRNA splicing disfunction was also linked to neuronal hyperexcitability and cognitive impairment observed during AD. However, the molecular determinants of the interaction between tau aggregates and biogenesis intermediates of spliceosomal subunits remain elusive. In this context, we are seeking for a postdoctoral candidate to investigate the molecular mechanisms of perturbed spliceosomal homeostasis during the development of AD. The postdoctoral candidate will reassemble biogenesis intermediates of spliceosomal subunits, test their interactions with tau and identify the interface driving the toxic function of tau during the development of AD. This project will be performed in two labs located at the European Institute of Chemistry and Biology in Bordeaux and has been funded by the Alzheimer Foundation.

Expected candidate's profile: We are seeking for an excellent candidate who is willing to work at the interface between biochemistry, structural biology and cell biology in two young and dynamic groups of research. Previous experience in biochemistry and structural biology/biophysics is essential. Skills in NMR spectroscopy would be a nice add-on.

Working environment: The project will be performed in the European Institute for Chemistry and Biology (IECB, Bordeaux; https://www.iecb.u-bordeaux.fr/) under the supervision of Dr. Sébastien Campagne (https://rna-smart.com) and Dr. Yann Fichou (https://www.fichou-lab.cnrs.fr/home). Both labs are located 30 meters away from each other in the IECB building. The IECB provided access to large array of biophysical methods including NMR spectroscopy, EPR spectroscopy and electron microscopy.

Start date: September 2025; Duration: 18 months. The candidate will be strongly encouraged and supported to ask for additional funding to extend the duration of the postdoctoral period.

How to apply: Send your CV, a cover letter and one or two reference letter(s) to sebastien.campagne@inserm.fr and y.fichou@iecb.u-bordeaux.fr