December 2022

Master project: Mapping tau seeds to create a spatiotemporal atlas of the tauopathy in the neurodegenerative disorder Progressive Supranuclear Palsy

Research idea and context

Progressive supranuclear palsy (PSP) is a progressive neurodegenerative disorder and is characterized by impairments in motor, cognitive, and behavioral functions. Clinical diagnosis of PSP is challenging due to the lack of decisive biomarkers, and a definitive diagnosis of PSP rests on post-mortem neuropathological analysis. However, we know that neuropathological processes have an onset years before the clinical symptoms, creating a window for possible preventive strategies. Therefore, if we can understand the tempo and the spreading of these pathological events, we can create a map illustrating the process of the progressive disease in humans having PSP and thus when to intervene.

PSP is characterized with abundant tau inclusions in glial and neuronal cells. Neuropathological studies suggest that clinical PSP-subtypes like PSP-parkinsonism (PSP-P), are distinguished not only by tau inclusions but also by the brain regions and cell types affected. How the tau inclusions spreads throughout the brain and/or why some brain regions and cell types are more prone to be affected by this is still unclear. However, there is strong evidence that the tau inclusions are propagated in a prion-like fashion where tau seeds are passed from one neuron to the next. According to this hypothesis, *tau seeds* are the main "building blocks" for tau filaments, and it, is therefore, important to localize tau seeds in tauopathies as this will tell us if seed propagate from region to region or are widely distributed at an early stage of the disease. This will also lead to an establishment of a map illustrating the "migration" of tauopathy in the human PSP brain as well as an establishment of the relationship between the four factors 1) Age, 2) The location of tauopathy, 3) The atrophy of the brain, and 4) The clinical symptoms.

Methods

This project will focus on:

- Isolate tau seeds from human brains
- Establish and optimize a method called seed amplification assay (SAA) to quantify tau seeds and their ability to form filaments *in vitro*.

For these experiments, *we will use samples from donated human brains* which are saved in our brain bank at the Centre for Neuroscience and Stereology, Bispebjerg Hospital.

We are looking for MSc students who would like to conduct their Master project in our lab and who has an interest in neuroscience. Previous experience with immunoassays is an advantage, though not a requirement.

Start date summer 2023 or after agreement.

Please contact Michel Rasmussen if interested at email: Michel.rasmussen@regionh.dk