

Tauopathies are a collection of dementia disorders characterized by the aggregation of tau proteins in the brain, leading to the death of brain cells. Among these disorders, frontotemporal dementias specifically affect executive functioning, planning, and behavior, in addition to the typical memory problems associated with Alzheimer's Disease. Anti-IgLON5 disease, discovered in 2014, is also classified as a tauopathy. In this condition, the immune system produces antibodies against IgLON5 (protein responsible for neuronal connections), leading to an autoimmune attack on the brain. The precise mechanism by which this process results in tau protein aggregation and neuronal loss is still not fully understood, but it is known that the antibodies and immune system play significant role.

The goal of this project is to investigate the malfunctioning components of the immune system that contribute to the development of anti-IgLON5 disease. To achieve this, we will leverage the knowledge and expertise of seven international teams. These teams will employ a range of techniques, including single-cell sequencing and mass cytometry, to analyze samples from patients. This collaborative approach will enable us to address important scientific inquiries. The study will examine the immune system's involvement across all stages of the disease, including early onset, progression, and in the brains of deceased patients. We will analyze the composition of cells present in the cerebrospinal fluid and blood of individuals affected by this disorder.

In neurodegenerative dementias, such as tauopathies, the pathological changes occurring in tau proteins are observed. However, the underlying mechanisms by which these changes lead to dementia remain unclear. It is highly likely that the immune system plays a role in determining when and how rapidly patients develop dementia. Thus, our project aims to unravel the pathological alterations in tau proteins and their impact on the formation of tau clusters in the brain, shedding light on disease progression.

Understanding the role of the immune system in tauopathies is crucial for comprehending the mechanisms behind neuronal death and tau protein aggregation. Furthermore, this knowledge could pave the way for the development of novel therapeutic approaches targeting the immune system. Additionally, it may provide biomarkers that can better predict disease progression and the rate of cognitive decline in affected individuals.