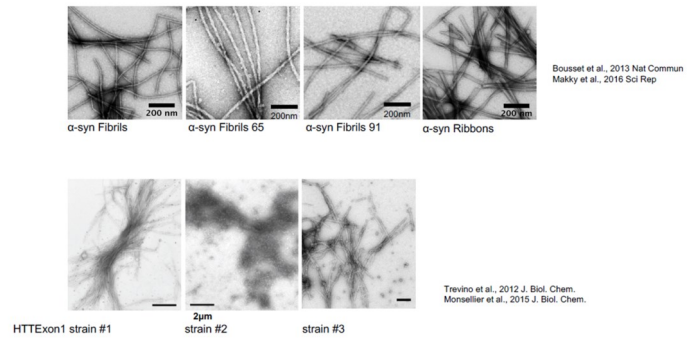
TransPathND

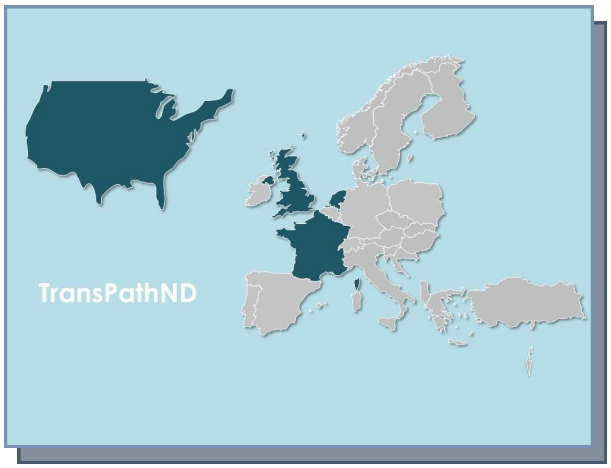
Intraneuronal transport-related pathways across neurodegenerative diseases

The overall goal of this project is to identify pathways/protein networks underlying the spread of distinct aggregates of Aβ1-42, tau, α-synuclein or HTTExon 1 involved in Alzheimer's disease, Parkinson's disease, and Huntington's disease, respectively. The spread of lesions is a common feature of all of these diseases, but strikingly starts and progresses in different brain sub-regions for each pathology. According to recent observations, distinct aggregate conformers could be responsible for different clinical subtypes.

Here we aim to reveal the specific mechanisms by which distinct fibrillary protein polymorphs of Aβ1-42, tau, α-synuclein and HTTExon 1 are taken up and transported by neurons. We will use different types of mouse neurons maintained in primary culture to establish a structure-function relationship for distinct pathogenic protein assemblies and their conformers by analyzing their binding, uptake and cellular trafficking after extracellular application.

Our novel approaches, including (i) the preparation of fibrillary protein strains, (ii) the quantification of their intraneuronal transport, and (iii) the analysis of their interactomes by mass spectrometry and systems biology will drastically improve the chance of unraveling new mechanisms and will provide new targets for the development of specific treatment strategies.





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