

Master student project proposal

Disruption of the blood-brain-barrier in Parkinson and Atypical Parkinsonism: crosstalk signaling between the central and peripheral system?

BBB leakage is increased in Parkinson's Disease (PD), as well as in other less-known atypical parkinsonism, such as Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP). This may have important implications for the disease course, as increased BBB permeability exposes the brain to unwanted insults from the periphery. BBB opening may be a consequence of the neuroinflammation that accompanies these diseases, and the signaling to the peripheral immune system for recruiting immune cells components into the brain parenchyma. We know from our own studies on postmortem brain material, as well as from cerebrospinal fluid from these patients, that the neuroinflammatory response is more extensive in MSA and PSP patients than in PD patients. These diseases have a more severe disease course indicating neuroinflammation to be an aggravating factor. As such, BBB leakage is also more pronounced in MSA and PSP patients. Here we want to see whether the crosstalk with the peripheral blood circulation induces the BBB leakage. For that we will expose BBB organoids, prepared from primary human cells, to serum from PD, MSA, PSP patients, as well as from a control group and monitor BBB leakage by use of a fluorescence dye. We expect serum from MSA and PSP to have a stronger effect on BBB permeability. In a second experiment, we will expose BBB organoids to serum from the same MSA and PSP patients, taken at different time-points during the disease course, in order to measure whether the impact on the BBB depends on the disease state.

This will be a collaborative project between the laboratory of Ass. Prof. Yvonne Adams, at the Department of Immunology and Microbiology, KU, and the Centre for Neuroscience and Stereology at Bispebjerg-Frederiksberg Hospital.

The techniques/methods the project involve are:

- Elaboration of BBB organoids (3D cell culture and confocal microscopy)
- Biobanking of serum samples
- Multiplex protein measurements (Meso scale discovery platform)
- Western blotting and RT-qPCR techniques

If interested contact Yvonne Adams (tlf 35337675/Email: yadams@ku.dk) or Susana Aznar (tlf 38635811/Email: susana.aznar.kleijn@regionh.dk)