DANDRITE
Danish Research Institute of Translational Neuroscience
Nordic EMBL Partnership for Molecular Medicine

AARHUS UNIVERSITY

Virtual DANDRITE Lecture

Tuesday 19 May 2020
16.00 – 17.00

Online via Zoom

Please find Zoom link via the Outlook calendar invitation. If you have not received this, please write an e-mail to Kathrine: kh@dandrite.au.dk

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Unraveling the role of alpha-synuclein strains in Parkinson's disease and related disorders

Misfolded protein aggregates are a common feature of several neurodegenerative diseases. The recent discovery of the transmissible nature of amyloidogenic proteins suggests a hypothesis of a pathogenic trigger which might spread throughout the nervous system underlying the progression of the disease. There is emerging evidence that these protein aggregates can adopt distinct conformations or 'strains' characterized by noticeable differences in phenotypic traits. α-Synuclein aggregation is considered to play a central role in multiple neurodegenerative diseases, such as Parkinson's disease (PD), Multiple System Atrophy (MSA) and Dementia with Lewy Bodies (DLB). This has led to the hypothesis that strains might account for the distinct clinico-pathological traits within synucleinopathies. We have first assessed the properties of recombinant structurally well-defined alpha-synuclein assemblies after injection in rat brain and could demonstrate that distinct alpha-synuclein strains display differential seeding capacities, inducing strain-specific pathology and neurotoxic phenotypes (Peelaerts et al., 2015, Nature). More recently, we compared different αSYN assemblies derived from the brain of patients with PD, MSA and DLB and assessed their capacities to amplify, propagate and induce neurodegeneration in vivo. We observed a specific signature for PD, MSA and DLB-derived strains that differs from previously described recombinant strains, with MSA strains provoking the most aggressive phenotype and more similarities with PD compared to DLB strains (Van der Perren, 2020, Acta Neuropathol). The existence of αSYN strains may provide a basis for the heterogeneity observed in synucleinopathies and open new therapeutic opportunities.