SFB 1286 Quantitative Synaptology

UNIVERSITÄTSMEDIZIN GÖTTINGEN : UMG

"Protein aggregates and their involvement in neurodegenerative diseases"

Speaker

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Time

Thursday, 5th October 2023
12 o´clock

Location

Center for Biostructural Imaging of Neurodegeneration (BIN)
Von-Siebold-Straße 3a, 37075 Göttingen
Seminar Room

Abstract
Several neurodegenerative diseases are characterized by the presence of intracellular protein aggregates in neurons and glial cells. Alpha-synuclein is the main component of the Lewy pathology of Parkinson's disease and Lewy body dementia and of the glial cytoplasmic inclusions of multiple system atrophy. In Alzheimer's disease, Pick's disease and number of other diseases, the abnormal filamentous intracellular inclusions are made instead of the microtubule-associated protein tau. The relevance of tau and alpha-synuclein in neurodegenerative diseases is supported by findings that mutations in their genes cause neurodegeneration. Recently, cryo-EM studies have allowed a new classification of neurodegenerative diseases based on how tau or alpha-synuclein specifically fold in the aggregates in the various conditions. The cryo-EM studies have also led to the identification of the novel TMEM106B aggregates of yet unclear function but that are associated with aging. Study on the distribution of Lewy bodies have suggested that alpha-synuclein aggregation starts at the periphery and spreads to the brain leading on the way to pre-motor and motor symptoms. In the brain of Parkinson's patients, besides the large Lewy body inclusions in the substantia nigra, alpha-synuclein forms smaller aggregates at the synapse that by impairing neurotransmitter release they contribute to the early stages of neurodegeneration. We have reproduced the alpha-synuclein pathology observed in Parkinson's disease in transgenic models where progressive neurodegeneration can be investigated. Similarly, transgenic mice reproducing tau aggregation reveal that not only neurons are involved in the pathological process but that glial cells also greatly contribute to tau-related neurodegeneration. The link between protein inclusions and neurodegeneration supports them as a target for the treatment of neurodegenerative diseases.

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