SFB 1286 Quantitative Synaptology

UNIVERSITÄTSMEDIZIN GÖTTINGEN UMG

"Transmission of Proteins in the Brain: Pathological Implications for Huntington Disease"

Speaker

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Time

Thursday, 30th March 2023
12 o´clock

Location

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

Abstract
Huntington disease (HD) is caused by the CAG/CAA expansion encoding polyQ huntingtin (mutant huntingtin [mHTT]) and striatal medium spiny neuron (MSN) atrophy and loss, preceded by cortical neuropathology. mHTT spreads in the brain, but the processes that cause stereotyped degeneration and malfunctioning of neurons from the striatum to the cortex are unknown. We found, mHTT expression initially localized to the striatum extended to the cortical areas. Such transmission is diminished in mice lacking the striatal-enriched protein Ras-homolog reduced transmission (Rhes). Rhes protein confined to MSNs was also discovered in brain cortical layers, suggesting a new Rhes protein transmission route to the brain. We found Rhes utilizes tunneling nanotubes (TNTs), membrane protrusions that self-transport Rhes, transmit mHTT, and other vesicular payloads via direct cell-to-cell contact. These transmission patterns indicate Rhes via TNT-like cell-to-cell connections spread mHTT in the brain. This presentation offers a perspective on these recent findings: Rhes may start striatal mHTT transmission, which may overlap with HD development and progression through an anatomically related striato-cortical retrograde route involving TNT-like cell-cell communications.

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