Neurodegenerative proteinopathies & genomic vulnerability

Initiative: "Experiment!" (beendet)

Ausschreibung: Explorative Phase

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Laufzeit: 1 Jahre 6 Monate

Neurodegenerative diseases like Alzheimer's Disease, Frontotemporal Dementia, and Amyotrophic Lateral Sclerosis are characterized by pathological aggregation of neuronal proteins in the brain, but the loss of neuronal function seems to occur independent of protein aggregates and is caused by unknown mechanisms. As a novel concept to explain neurotoxicity in proteinopathies, this project proposes that proteinopathy proteins are directly linked to DNA damage and therefore contribute to genomic instability and neuronal death in these diseases. To test this hypothesis, a combination of genetic approaches and newly designed tools will be used to investigate if and how neurodegenerative proteinopathies (driven by Tau and TDP-43, representative of many age-related neurodegenerative conditions) directly trigger genomic instability. Moreover it will be tested if the formation of breaks in the genome can sensitize neurons for aggregation or missorting of proteinopathic proteins in or out of the nucleus. If true, this new concept will impact not only our understanding about neurophysiological and pathological processes in the brain, but also change therapeutic strategies for a panel of neurodegenerative diseases, for which, so far, no successful treatment is available.

Projektbeteiligte

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