

Research Project

The role of the endoplasmic reticulum-mitochondria coupling in Tau-related neurodegenerative diseases

Third-party funded project

Project title The role of the endoplasmic reticulum-mitochondria coupling in Tau-related neurodegenerative diseases

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Tau protein aggregation is a hallmark of Alzheimer's disease (AD) brains and additional tauopathies including frontotemporal lobar degeneration (FTLD). Substantial evidence has been linking Tau to neurodegeneration, but the mechanisms are still incompletely understood. Tau impacts mitochondrial function and dynamics by impairing **mitochondrial shaping proteins**, leading to neurotoxicity. These proteins are also involved in the **endoplasmic reticulum-mitochondria coupling** via the **mitochondria-associated ER membranes or MAMs**. An upregulation of MAMs function is observed in A β -related AD models, impairing calcium homeostasis as well as phospholipid and cholesterol metabolism, leading to neuronal death. Interestingly, the influence of Tau on the ER-mitochondria axis remain elusive until today. Thus, we **hypothesize** that abnormal Tau protein disturbs the ER-mitochondria interaction by affecting the MAMs in a process involving the mitochondrial shaping proteins. **The specific aims** of this project are to prove this concept and to elucidate in detail the impact of abnormal Tau protein on the ER-mitochondria coupling. We aim to dissect a novel fundamental mechanism using state-of-the-art technology (confocal microscopy, structure illumination microscopy, proximity ligation assay) and functional readouts. Moreover, by different molecular and CRISPR approaches, we will study the ER-mitochondria axis as a potential target in AD. The project has ramifications for additional neurodegenerative diseases such as Parkinson's disease as well as amyotrophic lateral sclerosis with associated temporal dementia (ALS/FTD) that also have been linked with damaged ER-mitochondria associations.

Financed by

Foundations and Associations

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Published results

4624212, Szabo, Leonora; Eckert, Anne; Grimm, Amandine, Insights into disease-associated tau impact on mitochondria, 1661-6596 ; 1422-0067, International journal of molecular sciences, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

4624215, Grimm, Amandine; Lejri, Imane; Hallé, François; Schmitt, Martine; Götz, Jürgen; Eckert, Anne; Bihel, Frederic, Mitochondria modulatory effects of new TSPO ligands in a cellular model of tauopathies, 0953-8194 ; 1365-2826, Journal of Neuroendocrinology, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

4624217, Witzig, Melissa; Grimm, Amandine; Schmitt, Karen; Lejri, Imane; Frank, Stephan; Brown, Steven A.; Eckert, Anne, Clock-Controlled Mitochondrial Dynamics Correlates with Cyclic Pregnenolone Synthesis, 2073-4409, Cells, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

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