PhD position for 2017

Title of the project: Endoplasmic reticulum-mitochondria axis in Alzheimer's disease

Scientific context:

Alzheimer's disease (AD) is a devastating age-related neurodegenerative disorder affecting more than 35 million people worldwide, and characterized by a progressive cognitive decline with impairments in learning and memory.

Extensive literature, including findings from our group, supports the role for mitochondrial dysfunction as an early and preponderant feature of AD pathogenesis. Endoplasmic reticulum (ER) stress is also a common feature of AD, but whether it is a causative factor or a consequence of AD pathology is still under debate. ER and mitochondria are tightly connected via the mitochondria-associated ER membranes (MAMs), and this interaction plays a key role in the regulation of metabolic function as well as Ca²⁺ homeostasis.

Recent findings highlight damage to the ER-mitochondria association in AD. However, the mechanisms leading to these alterations are not clear. Thus, there is an urgent need to firstly identify more clearly, the mechanisms involved in damage. This information will facilitate any therapeutic targeting of the ER-mitochondria axis for AD with the aim of correcting the ER-mitochondria-related damage.

PhD project:

We propose to dissect a novel fundamental mechanism and identifies how the two key molecules in AD, A β and Tau, interact on the ER-mitochondria axis using state-of-the-art technology and functional readouts. Moreover, by different pharmacological approaches we will study the ERmitochondria axis as a potential therapeutic 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, and the identification of new therapeutic targets for the treatment of AD.

<u>Contract length:</u> 3 years (PhD student salary according to the guidelines of the Swiss National Science Foundation SNF)

Contact:

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Application guideline:

- Please send your:
- CV
- Letter of motivation
- Copies of grades of Bachelor and Master studies to Prof. Anne Eckert (<u>anne.eckert@upkbs.ch</u>)