Research Project Title:
Mical is a novel Tau interactor that regulates its aggregation propensity
Mical is a novel Tau interactor that regulates its toxicity

Scientific Field:
Neurobiology

Host Institution:
BSRC Alexander Fleming
Microtubule-associated Tau is a protein that performs essential functions in healthy neurons, but forms insoluble deposits characteristic of diseases now known collectively as Tauopathies. Tauopathies encompass more than 20 clinicopathological entities, including Alzheimer’s disease (AD), Progressive Supranuclear Palsy (PSP), Pick’s disease, Corticobasal Degeneration (CBD) and Frontotemporal Dementia with Parkinsonism linked to chromosome 17 (FTDP-17) among others. Using the Drosophila adult brain as a model, we are trying to probe molecular interactions that induce Tau to become neurotoxic and possibly involved in specific intracellular signaling pathways. A series of proteomics experiments led to the unexpected identification of Drosophila MICAL (Mical) as a Tau cellular partner. The present study aims to study the Tau protein and Mical interaction, focusing mainly on how this interaction affects Tau's tendency to aggregate in vivo. The proposed work can provide mechanistic insights into the process by which Tau self-assembles into fibrillar inclusions in vivo and improve our knowledge on the role of Tau aggregation propensity, on its function as a cytoskeletal protein and on Tau-associated brain toxicity and dysfunction.
Tauopathies encompass more than 20 clinicopathological entities, including Alzheimer’s disease (AD), Progressive Supranuclear Palsy (PSP), Pick’s disease, Corticobasal Degeneration (CBD) and Frontotemporal Dementia with Parkinsonism linked to chromosome 17 (FTDP-17) among others. AD is the most common Tauopathy and the most widespread neurodegenerative disease globally. It affects nearly 2% of the population in industrialized countries and the number of patients is expected to increase threefold within the next 50 years, which poses a tremendous public health burden in terms of patient care, lost wages, and responsibilities of caregivers. Progress towards amelioration and eventual cure of such diseases requires a thorough understanding of the molecular mechanisms that when dysfunctional precipitate Tau pathology. The proposed research proposal will contribute to the establishment of an internationally pioneering and innovative research area for Greece related to the design of diagnostic and therapeutic tools for neurodegenerative diseases with widespread impact.
Through H.F.R.I. funding, I will be able to develop the necessary basic research infrastructure in order to be productive in my research work. In addition, funding will support my participation in international conferences, workshops and seminars, where I'll have the opportunity to present my research results. Finally, it offers me the opportunity to become competitive by publishing in various international scientific journals and thus be able to claim international funding.

The Principal Investigator,
Katerina Papanikolopoulou

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