

NMR study of the neuronal Tau protein

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Tau pathologies, called ‘tauopathies’, are related to several neurodegenerative diseases including Alzheimer Disease (AD). In AD, Tau protein is observed hyper-phosphorylated and aggregated as Paired Helical Filament (PHF). The molecular mechanisms of Tau-linked neurodegeneration is far however from being elucidated. Tau is a paradigm for the growing class of “intrinsically disordered proteins”, often found associated with pathologies such as neurodegenerative diseases, hence increasing the interest to grasp the molecular parameters underlying their functions.

The fine structural characterization at the molecular level of Tau and its interactions remains challenging due to its highly dynamical character. Additionally, 80 Ser/Thr residues in the longest Tau isoform, potential sites of phosphorylations, can be combined to give a multiphosphorylated Tau, leading to a very complex regulation of Tau interactions. Nuclear Magnetic Resonance (NMR) Spectroscopy is used to define the phosphorylation pattern of Tau samples, to investigate the impact of specific patterns of phosphorylation on structural determinants of Tau and to characterize Tau interaction with its molecular partners and its regulation.

Comprehension of the dynamic combination of these aspects represents a huge task but will probably be the key to therapeutic intervention on Tau pathway.