

Mechanisms of tau self-aggregation and neurotoxicity

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Pathological tau protein aggregates can be found in brain of patients with some of the neurodegenerative diseases collectively known as tauopathies, which include Alzheimer's disease (AD). Since tau post-translational modifications including phosphorylations, glycosylations, truncation and the subsequent aggregation in oligomers, paired helical filaments (PHFs) and neurofibrillary tangles (NFTs), correlate with cognitive impairment and neurodegeneration in AD, a pathogenic role for tau and its modifications has been raised. Here we summarize the current status of knowledge about tau modifications under pathologic conditions and the evidence supporting neurotoxic - or neuroprotective - roles of the diverse forms of modified and aggregated tau. Finally, we analyze the structural and functional tau alterations found in different tauopathies and how these modifications are related to the pathophysiologic mechanisms of neurodegeneration. © 2011

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