Journal of Alzheimer's Disease & Parkinsonism

Tales, J Alzheimers Dis Parkinsonism 2021, 11:S8

Opinion Article Open Access

Significance of Tau Proteins in Dementia Therapy

Andrea Tales*

Department of Experimental Psychology, University of Bristol, Bristol, UK

***Corresponding author**: Andrea Tales, Department of Experimental Psychology, University of Bristol, Bristol, UK, E-mail: Andrea.Tales@bristol.ac.uk

Received: November 12, 2021; **Accepted**: November 26, 2021; **Published**: December 03, 2021

Citation: Tales A (2021) Significance of Tau Proteins in Dementia Therapy. J Alzheimers Dis Parkinsonism S8: 033.

Description

Tau is primarily a microtubule-associated protein regulated by its phosphorylation state but has functions in chromatin structure, signal transduction and nucleic acid protection. Alternative splicing and tau expression are also new aspects of its biology. Tau monomers belong to the family of intrinsically disordered proteins that upon ordered assembly, form structured amyloid fialments. Their expression is largerly confined to central and peripheral nerve cells, where they are highly enriched in axons. Ordered assembly of a small number of proteins into filaments characterises the majority of case of age-related neurodegenrative diseases including Alzheimer's and Parkinson's. Finally, its new functions, its other post-translational modifications that phosphorylation, its half-life, its secretion and degeneration recently aroused new interests, as you could discover it in the various relevant researches of this field. In the 1980s, tau was considered the constituent of neurofibrillary degeneration but the notion of phosphorylation was not clear.

In the mid-1990s, the notion of pathological phosphorylation is physiological and disappears in healthy subjects due to post-mortem dephosphorylation, there is also a pathological phosphorylation. Various researches on a therapeutic potential around the tau protein and its gene, MAPT. Some have fallen into oblivion and other has appeared. This reflects the different streams of ideas about tau protein and neurofibrillary degeneration. Currently MAPT is considered to encode a pleiotropic protein but this was not always the case. The hypothesis of the amyloid cascade made of tau a secondary actor. However, there have been some pre-clinical and clinical therapeutic approaches. Investigations on tau silencing, tau alternative splicing, post translational tau modifications, tau metabolism, microtubular tau function, tau aggregation, tau immunotherapy and brain homeostasis have enhanced the overall understanding and contributed to the contemporary research.

To stop tau toxicity, one of the most obvious approaches is probably to modulate the expression of tau protein. Indeed there is some evidence that decreasing tau expression is beneficial in reducing the electrophysiological and/or behavioral disturbances found in models of Alzheimer's disease. This positive side should not obscure the fact that tau protein is essential for synaptic plasticity, signal transduction and nucleic acid protection. Alternative splicing of tau has quickly emerged as a therapeutic target. Indeed, some mutations on the MAPT gene in frontotemporal lobar degeneration are responsible for misplacing. Thus, the intron mutations around exon 10 favor its default insertion within tau transcripts leading to overexpression of isoforms with four microtubule binding domains. Similar approaches are also investigated to modulate tau alternative splicing. Correcting the alternative splicing of tau thus seems to be an excellent strategy for some tauopathies like frontotemporal lobar degeneration and myotonic dystrophies. In addition, some works have suggested that hyperphosphorylated tau proteins may serve as nucleation agents for tau aggregation. Thus, inhibition of tau phosphorylation is clearly considered as a therapeutic approach, other post translational modifications such as acetylation may also be of interest. Other studies have shown the opposite effect where Tau protein nonacetylated aggregates more rapidly *in vitro* than acetylated Tau protein.