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Analysis of photoactivatable tau proteins in living cells

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Tau is a cytoskeletal protein that is mainly enriched in axons where it is thought to regulate microtubule dynamics. Tau is also involved in many diseases referred to as "tauopathies" which includes Alzheimer's disease (AD). In AD, tau is redistributed to the somato-dendritic compartment and becomes aggregated.

To study the effect of tau proteins (a wild type tau and a R406W mutation present in cases of Frontotemporal dementia and parkinsonism linked to chromosome 17, FTDP-17) in living cells, different PC12 cell lines expressing the proteins were created. With the purpose of studying their mobility, the proteins were fused to a photoactivatable molecule.

The stable lines showed differences in their state of phosphorylation as analyzed by western blots, where mutant tau exhibited a hypophosphorylated state. The development of neurites after NGF treatment showed differences in the kinetics in that mutant-tau-expressing cells developed processes earlier, which also became longer throughout time.

Finally, photoactivation experiments revealed that the mutant tau line shows a higher proportion of stationary tau proteins over time suggesting a potential mechanism for the different distribution of mutant proteins or differently phosphorylated proteins in tauopathies. This finding was not related to an effect on microtubule stability as could be seen in western blots by analyzing the degree of tubulin acetylation.

Taken together, the data demonstrate that photoactivatable tau proteins provide a useful tool to analyze dynamic properties (with a supportive biochemical correlate) in a living neuronal cell model scenario to help determine the effects of different tau mutations in neurodegenerative diseases.