Exploring the Effects of Post-Translational Modifications on the Tau Proteins' Stability

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A hallmark of Alzheimer's disease is misfolded tau proteins, driven by hyperphosphorylation. This study investigates the structural stability of tau protein domains—N-terminal, proline-rich domain, microtubule binding domain, and C-terminal—after phosphorylation. By using PyMOL and PyTMs, phosphorylation was modeled on individual amino acid residues and domains, the van der Waal (vdW) strain report was collected. Tyrosine residues had the greatest change (118 kcal/mol from baseline of 97.15 kcal/mol), serine residues had little to no change, and threonine residues consistently increased (~101-103 kcal/mol). There was no significance of protein stability by domain; the vdW strain was dependent on frequency and type of amino acid residues. Results highlight potential future usage of threonine kinase inhibitors as an Alzheimer’s treatment. Future studies would incorporate more tau isoforms and an in vivo experimental design.

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