A Novel Genomic Framework for Personalized Medicine: Optimizing LMTX for Tau Proteins in Alzheimer's

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Tau protein aggregation is a hallmark of Alzheimer's disease (AD), disrupting neuronal function and impairing synaptic signaling. The clinical efficacy of tau aggregation inhibitors like TRx0237 (LMTX) has been inconsistent, mainly due to patient-specific genetic variations in tau protein that alter its structure, binding affinity, and drug metabolism. This project employs novel custom-built Large Language Model Systems (LLMs) each equipped with Drug-Target Interaction (DTI) prediction tools to rapidly design, test, and optimize new LMTX derivatives with enhanced binding affinity for genetically diverse tau proteins. In silico validation was conducted using molecular docking simulations, deep learning-based binding site predictions, and molecular dynamics modeling to assess drug stability, interaction strength, and potential off-target effects. These simulations confirmed that the newly designed LMTX analogs exhibit significantly increased tau-binding stability, reduced aggregation propensity, and improved microtubule stabilization. Furthermore, predictive cognitive modeling, based on established correlations between tau pathology and cognitive decline, projects measurable improvements in MMSE scores, suggesting enhanced therapeutic efficacy. The significance of this in silico validation lies in its ability to rapidly and systematically evaluate drug candidates before costly in vitro or clinical trials, accelerating the discovery of effective, patient-specific therapeutics. These findings have broad implications for precision medicine, offering a scalable computational framework for designing genetically tailored neuroprotective treatments that could improve drug efficacy, minimize side effects, and support early intervention strategies in AD.

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