Using CRISPRi to Analyze the Role of Caveolae-Mediated Endocytosis in Tau Uptake of Central Nervous System Culture

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Alzheimer’s is a neurodegenerative disease characterized by Tau protein aggregation and amyloid beta plaque presence on neurons. Past Alzheimer’s research failed to find definitive links between these plaques and disease progression, suggesting that Tau aggregation could be the underlying factor. Tau, a microtubule-associated protein (MAP), is located in nerve cells. However, pathogenic Tau can create neurofibrillary tangles (NFTs) that cause subsequent neuron degeneration. Although current research has investigated Tau pathology, the specifics of how Tau enters neurons remain unknown. This project presents the role of the Polymerase I and transcript release factor (PTRF) protein and the Insulin-like growth factor 1 (IGF-1) receptor in Tau uptake of neuroglioma cells. CRISPRi knocks down the target genes, which are crucial for caveolae-mediated endocytosis. Analyzing the modified extent of Tau uptake shows a significant decrease in intracellular Tau levels. This association contributes to novel therapeutics that may lower PTRF/IGF-1 expression and inhibit Tau propagation, thus preventing neurodegeneration advancement.

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