“Tau Proteostasis Imbalance and Toxicity in Neurodegeneration"
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Abstract

Alzheimer’s disease is characterized by accumulation of amyloid β (Aβ) and microtubule binding protein tau. Toxic forms of tau have emerged as a major therapeutic target in AD and other tauopathies. Over the past decade, most of studies have been focused on how hyperphosphorylation affects tau accumulation and aggregation. We discovered that acetylation of tau is a critical posttranslational mechanism and represents a novel therapeutic direction. We developed highly specific antibodies against acetylated-tau and identified aberrant tau acetylation sites that are elevated in AD brains. Our recent finding revealed a novel mechanism by which acetylated tau impairs synaptic plasticity. Using small molecule inhibitor of p300/CBP, acetyltransferases for tau, we provided proof-of-principle that inhibition of tau acetylation could reduce pathogenic accumulation of tau and protect against tau-mediated cognitive deficits and neurodegeneration. Immunotherapy targeting pathogenic acetylated tau species will also be discussed.

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