Expression and localization of NUB1 in Tauopathy and Alzheimer's disease mouse models.

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Alzheimer's disease (AD) is characterized at a subcellular level by intracellular neurofibrillary tangles (NFTs), aggregates of hyperphosphorylated Tau, and by senile plaques, extracellular aggregates of amyloid beta peptides. Previous data revealed that Nedd8 ultimate buster 1 (NUB1) plays a role in reducing the aggregation and phosphorylation of Tau in an in vitro model.

To clarify the role of NUB1 in AD, the spatiotemporal expression and localization of NUB1 was analyzed in T301L, a mouse model for Tauopathy characterized by NFTs, and in TASTPM mice, characterized by early development of senile plaques.

The analysis revealed no change in the level of NUB1 expression in T301L mice and a significant decrease at 12 months in TASTPM mice. In brain cryosections, NUB1 expression was detected in the hippocampus and entorhinal cortex. Subcellularly, NUB1 was localized predominantly in the neuronal nuclei, but also in neuronal processes. In both mouse models at 12 months, NUB1 signal was observed to co-localize with AT8 positive cytoplasmic aggregates. Moreover in TASTPM mice, a NUB1 cytoplasmic signal was observed in non-neuronal cells.

Our data confirm that NUB1 could be a therapeutic target in AD and also help to establish the appropriate window of opportunity for therapeutic intervention.