

Human Alzheimer's Disease Tau Seeds Increase Tau Seeding and Uptake in Different *In Vitro* Models

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BACKGROUND

Tau aggregation and its cellular propagation plays a crucial role in the pathology of several neurodegenerative diseases, especially Alzheimer's disease (AD). The process of propagation is mediated by extracellular tau, which is taken up by cells and serve as seeds for tau aggregation. The development of new compounds to block tau seeding or uptake activity is currently an active field of research. Consequently, reliable *in vitro* models mirroring this tau pathology are needed.

MATERIAL & METHODS

To monitor tau seeding and uptake, we established *in vitro* assays in different cell types: (1) stably transfected tau overexpressing SH-SY5Y cells (2) mouse primary neurons isolated from wild type mice (3) mouse primary neurons isolated from Tau P301S (PS19) mice. Cells were treated with tau seeds isolated from human AD brains (AD-Tau seeds) in the presence of lipofectamine to induce tau seeding or in the absence of lipofectamine to monitor tau uptake. As positive control, the anti-tau antibody HT7 was co-incubated with AD-tau seeds, to counteract tau seeding and uptake. Tau aggregation was assessed using the HTRF-based Tau Aggregation Kit from Cisbio.

RESULTS

Tau seeding and uptake was detectable as increased HTRF signal after incubation of all cell types with human AD-tau seeds compared to vehicle control. The HT7 antibody significantly reversed the AD seed-associated tau aggregation in the seeding and uptake assay.

