PURIFICATION AND CHARACTERIZATION OF TAU AGGREGATION INTERMEDIATES

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Tau protein is a microtubule-associated protein and located mainly in the axonal part of neurons. Tau proteins regulate stability of microtubules, which are essential for neurite extension and axonal transport. In Alzheimer's disease highly phosphorylated tau protein no longer binds to microtubules but exists in an aggregated, beta sheet containing, filamentous form in the cytoplasm. The fibrillization of monomeric tau to tau filaments is a multistep process proceeding via intermediate states. These tau aggregation intermediates may be involved in the pathogenic cascade leading to neuronal loss.

By analysing cellular viability of SH-SY5Y cells and integrity of artificial phospholipid vesicles after extracellular treatment with tau protein pre-aggregated for different periods of time we have found that early tau aggregation products containing tau oligomers decrease the viability of SH-SY5Y cells and increase the leakage of artificial phospholipid vesicles. So our results point out that tau oligomers which arise during tau fibrillization are a toxic species in contrast to tau monomers and tau fibrils.

The aim of our present study was to purify different tau aggregation products from tau protein pre-aggregated for different periods of time by gel filtration and to characterize the obtained fractions with regard to size, beta-sheet content and toxic effects on cell lines.