RUHR-UNIVERSITÄT BOCHUM

RUB

# IGSN - SYMPOSIUM

**Monday, June 19th 2023 • 15.00 (3 pm)** **FNO – 01 / 117**

# Towards magnetic nanoparticle-assisted brain repair


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## Targeting Tauopathies: From Identifying New Aggregation Inhibitors to Magnetic Shaking to Remove Aggregates


Tauopathies such as Alzheimer's disease are characterized by the aggregation of the microtubule-associated protein tau into neurofibrillary tangles composed of paired helical filaments (PHFs). The pathological changes in tau are closely linked to neurodegeneration, making tau a prime candidate for intervention. We have developed an approach to monitor pathological changes in aggregation-prone human tau and to screen for novel aggregation inhibitors in living neurons. Through chemoinformatic analysis, we identified 2-phenyloxazole (PHOX) derivatives as putative polypharmacological small molecules that interact with tau, inhibit tau aggregation, and restore physiological microtubule interaction of tau in neurons. Molecular dynamics simulations highlight cryptic channel-like pockets crossing tau protofilaments and show that the binding of PHOX reduces the protofilament's ability to adopt a PHF-like conformation. We disucss how compounds that bind to tau aggregates and inhibit tau aggregation could be used to remove pathologic aggregates in order to restore tau's physiological function in disease.


**Host**:

ROLF HEUMANN

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