Modeling Neurodegeneration in vitro: A Dynamic Study of Tau in a Microfluidic Chamber System via Quantum Dot Labeling

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Current research suggests that toxic tau aggregates propagate from neuron to neuron in a prion-like manner. However, no dynamic proof exists to trace tau's transmission and traffic in neurodegeneration. To dynamically image tau's propagation, an in vitro system must be created by 1. constructing biologically functional quantum dot (Qdot) conjugated tau filaments (wild type (WT) and P301L mutation causing tauopathy) and 2. performing the propagation and transport experiments in vitro with a specially designed microfluidic chamber system. I developed a protocol to synthesize tau proteins that could be uptaken by neurons and could conjugate to the Qdot tags for visualization. A staining study was conducted for the biotinylated tau's uptake in neurons with Texas Red-Streptavidin. Not only were WT and P301L tau filaments both uptaken, but P301L tau induced aggregation of native tau inside the neuron, suggesting my system accurately reflected tau's clinical behavior. Finally, a live neuronal transport of tau filaments with Qdot-Streptavidin was conducted in the microfluidic chamber which serves as a unique transport environment by isolating neuron axons from soma. This setup allows for clear imaging of tau proteins propagating retrogradely from axon to soma: the first time tau's transport in primary neuron culture has been virtually observed. I successfully developed this system to model neurodegeneration and propose that tau filaments (both WT and P301L) were uptaken and traffic from terminal to soma in neurons. My in vitro system may service as a platform for detailed mechanism studies and for drug screening tests to further understand and potentially find cures for tauopathies such as Alzheimer's Disease.

Awards Won:

Intel ISEF Best of Category Award of $5,000

First Award of $3,000

Intel Foundation Young Scientist Award