

Project Name: Pathogenic tau disrupts local translation required for synaptic plasticity

Project Description: Alzheimer's disease is characterized by severe loss of cognitive function. Pathological tau contributes to the cognitive decline and neurodegeneration associated with Alzheimer's disease and other tauopathies. Tau protein accumulates in the brain in AD. Growing evidence supports that under disease conditions tau protein becomes toxic to neurons in the brain. Synapse dysfunction precedes neurodegeneration and cognitive loss, however, the underlying mechanisms that disrupt synapse function remain unclear. We are using human induced pluripotent stem cell (iPSC)-derived neurons that carry the frontotemporal dementia (FTD)-causing V337M tau mutation to study how pathogenic tau disrupts synapse function. We found that human neurons expressing the tau V337M mutation have impaired synaptic plasticity and inhibited local translation in neuronal dendrites. We are currently investigating possible translation mechanisms disrupted by pathogenic tau in human neurons using immunostaining and Western blot analyses. In addition, we are exploring how pathogenic tau impairs activity-dependent translation in the PS19 tauopathy mouse model.

Desired Skills or Experience: Completed coursework in a molecular biology course and lab. Neuroscience coursework desired but not necessary. Familiarity and proficiency with the following techniques desired but not necessary: PCR, Western blot, and immunostaining

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