Investigating the Interaction of Tau and Aβ Proteinopathy in Novel Mouse Models

Giavanna Paterno1,2 , Kimberly-Marie Gorion1,2 , Brach M. Bell1,2 , Yuxing Xia3 , Benoit I. Giasson1,2,4

1. 2. 3. 4. Department of Neuroscience, College of Medicine, University of Florida, Gainesville, FL 32610, USA.
Center for Translational Research in Neurodegenerative Disease, College of Medicine, University of Florida, Gainesville, FL 32610, USA. Department of Neurology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA 90095, USA. McKnight Brain Institute, College of Medicine, University of Florida, Gainesville, FL 32610, USA.

Alzheimer's disease (AD) is a progressive neurodegenerative disease which clinically presents as significant impairment in cognitive domains. AD falls under the group of diseases termed proteinopathies, where normal proteins misfold into specific conformations which are thought to contribute to disease progression. In the context of AD, the defining neuropathological hallmarks include the aggregation of hyperphosphorylated tau protein in the form of neurofibrillary tangles (NFTs) as well as amyloid-beta (Aβ) peptides which accumulate extracellularly into plaques. While significant efforts have been made to further define individual and synergistic contributions of both tau and Aβ towards disease severity, it is still unclear how these proteins amplify each other under a pathological state. To investigate tau accumulation, we generated novel mouse models of tauopathy termed SPAM (S320F P301S aggregating mutations). Previously characterized TgBy as well as the TgDy mouse models both develop NFT-like pathology throughout the neuroaxis despite human tau expression being below that of murine tau. While the TgDy line can live beyond 20 months of age, the TgBy line exhibits a predictable lethal phenotype around 6 months of age due to enteric neuron loss. Both tauopathy mouse models were crossed with the TgCRND8 transgenic mouse model of amyloidosis, which contain the amyloid precursor protein (APP) with Indiana (V717F) and Swedish (K670N/M671L) mutations. These studies will collectively determine the extent to which co-deposition of tau and Aβ pathologies enhance authentic disease-specific biochemical and neuropathological signatures and provide further information on potential targets for disease-modifying therapies.

Presenter Name and contact information:

Giavanna Paterno
Department of Neuroscience, College of Medicine, University of Florida, Gainesville, FL 32603
Email: giavanna@ufl.edu