Identification of genes and molecular pathways involved in a *C. elegans* model of neuroborreliosis

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Background and Hypothesis: Lyme disease is caused by the spirochaete bacteria from the *Borrelia* species. Recent studies suggest that Lyme disease may be associated with dementia, brain atrophy, and protein aggregates that may be associated with the development of neurodegenerative diseases such as Parkinson's disease (PD) and Alzheimers disease (AD). The molecular basis of the *Borrelia*-associated innate immune response and associated neuropathology is poorly defined. A significant hindrance in dissecting these molecular components is the lack of facile in vivo genetic models to explore the mechanisms involved in the neuropathology. Here we hypothesize that the nematode *C. elegans* will be a useful model for *Borrelia*-associated innate immunity and neuropathology.

Project Methods: We utilized transcriptional reporters, transgenic animals, neuronal morphology analysis, RNAi, host defense pathways, AD- and PD-associated pathologies, and behavior assays to determine the effect that *Borrelia* has on *C. elegans* viability.

Results: *C. elegans* can be infected and survive using *Borrelia* as a food source, and the bacteria can induce highly conserved innate immune response pathways, and exacerbate PD-associated dopamine neuronal death in human A53T α-synuclein-expressing animals. *C. elegans* models expressing AD-associated human Aβ 1-42 also show significant movement defects and increased protein aggregates when exposed to *Borrelia*.

Conclusions and Potential Impact: This study further characterizes a novel genetic model for *Borrelia*-associated innate immunity and neuropathology. Incorporating *C. elegans* genetic screens, this model should allow us to identify mediators of the *Borrelia*-associated pathologies that should facilitate the identification of molecular pathways and potential therapeutic targets.