

Identification and Functional Characterization of the Axolotl (*Ambystoma mexicanum*) Tau Protein

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Tauopathies are characterized by abnormal aggregation of the tau protein that results in neuronal dysfunction and neurodegeneration. Developing strategies to preserve existing neuronal function, prevent neurodegeneration, or restore lost neurons may have the most potential to combat human tauopathy; however, the adult human brain possesses limited capacity to replace lost neurons. Interestingly, some vertebrate species such as axolotls (*Ambystoma mexicanum*) possess the capacity to regenerate the brain and spinal cord. We previously compared the degree of tau protein homology between human and axolotl sequences and reported that axolotls express a tau protein with regions of high similarity to human tau. Utilizing *in vitro* tau self-aggregation assays and tau-microtubule binding assays, we will determine axolotl tau's ability to aggregate and bind microtubules. Missense mutations of the human *MAPT* gene at the Proline-301 residue to a lysine (P301L) or serine (P301S) increase the self-aggregation ability of tau and are causal for tauopathy. Axolotl tau possesses an equivalent site (Proline-387), so we will explore how P387S/P387L mutations change the aggregation potential and microtubule binding ability of axolotl tau. We will report the first ever characterization of axolotl tau's ability to bind to microtubules and potential for self-aggregation and how axolotl mutations equivalent to human mutations modulate these abilities. These results will further elucidate our understanding of tau-microtubule interactions in the axolotl, unveil axolotl tau's capacity for aggregation, and position the axolotl as a novel model system in which to investigate how a regenerative organism might respond to an attempt to induce tauopathy.

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