

PAR-1 Suppression of Toxicity in a *Drosophila* Model of Tauopathy

Abstract

A hallmark of many neurodegenerative diseases including Alzheimer's disease (AD) is the accumulation of intracellular neurofibrillary tangles in brains of diseased patients. These tangles are comprised of aggregated tau, a microtubule associated protein found abundantly in the central nervous system. Over-expression of human tau in *Drosophila* can mimic many of the characteristics of AD, including formation of tau inclusions and progressive neuronal death. Previous work in a genetic screen for modifiers of tau toxicity has identified PAR-1, a *Drosophila* homolog of the mammalian kinase MARK, as a suppressor of toxicity. However, more recent literature has suggested a contrary role for PAR-1 as an initiator of neurodegeneration. In my experiments I examined modification of tau toxicity by PAR-I through both eye and brain morphology. I found a marked suppression of tau toxicity in the retina, and a trend for PAR-1 suppression of toxicity in the brain as revealed through histological examination. In addition, a growing body of literature has suggested tauopathic neurodegeneration is a direct consequence of phosphorylation at certain pathological sites on tau. Using animal lines expressing two artificial tau constructs with mutations at the pathological sites, I was able to probe PAR-1 modification of toxicity within these two lines and propose a general mechanism for PAR-I suppression of toxicity as acting downstream of tau phosphorylation.