The Neuro-Protective Role of Select Transcription Factors in a PINK1 Loss-of-Function Based Model of Neurodegeneration in Drosophila melanogaster

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Mutated PTEN induced kinase 1 (PINK1) is linked to Parkinson's disease, predisposing an individual to neurodegeneration. Interestingly, the FOXO, AOP, PNR, and TOR transcription factors have been postulated to have anti-aging effects in humans. The fruit fly Drosophila melanogaster has homologous versions of PINK1, FOXO, AOP, PNR, and TOR, and it expresses easily-observable indications of neurodegeneration. It was hypothesized that if four experimental groups of PINK1 flies overexpress each of these transcription factors, and a control group of PINK1 flies does not, then the experimental groups will have lower levels of neurodegeneration due to the transcription factors' expected protective properties. To obtain the desired genotypes, five sets of genetic crosses were conducted over five months. Afterwards, PINK1 control flies and PINK1 flies that simultaneously overexpressed the transcription factors were aged and assessed on neural health. Results show that PINK1 control flies suffered serious dopaminergic neuron depletion, severe brain vacuolization, and significantly reduced motor function and lifespan. In contrast, PINK1 flies that overexpressed FOXO and AOP had abundant and healthy dopaminergic neurons, minimal brain vacuolization, three times better motor function, and a 50% increase in lifespan, which supports the hypothesis that overexpression of these transcription factors serves as a protective agent against neurodegeneration. Currently, treatment for neurodegenerative diseases is limited, but because the genes studied in this experiment are highly homologous in humans, it is likely that they prevent human neurodegeneration as well, introducing the promotion of protective genes through gene therapy as a potential solution to a notoriously unsolvable problem.

Awards Won:

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