Elucidating the mechanism of mitochondrial quality control in Drosophila

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Research Abstract

? DESCRIPTION (provided by applicant): Neurodegenerative diseases affect a large amount of the population and currently have no cures. Many neurodegenerative diseases, such as Parkinson’s disease, have been linked to mitochondrial malfunction, which may have a causative role in disease onset and progression. Because mitochondria supply most of the chemical energy for the cell, they are critical for the normal function of high-energy tissues such as neurons. Mitochondria can become damaged carrying out their normal role in the cell, and

the cell must be able to subsequently actively target and destroy damaged mitochondria, a process called mitophagy. Elucidating the mechanism of mitophagy will give researchers potential therapeutic targets to alleviate the symptoms and progression of neurodegenerative disease. Two proteins, PTEN induced putative kinase 1 (PINK1) and Parkin, are frequently mutated in early onset inherited forms of Parkinson’s disease. In addition, they have been shown to be involved in mitophagy. While studies of PINK1 and Parkin have been important, there are still many unanswered questions about the molecular mechanisms of mitochondrial quality control. To understand how this process works in vivo, the authors of this proposal have developed Drosophila ovary and larval brain as a model in which to study mitochondria function. Their long term goal is to understand the mechanisms that control mitochondrial quality control in tissues in vivo. To accomplish this, they have characterized the Drosophila gene clueless (clu), and found that it is critical for mitochondria function. clu mutant flies are male and femal sterile, highly uncoordinated and short-lived, and have swollen mitochondria in their flight muscle and germ cells. Their mitochondria suffer oxidative damage, and they make substantially reduced amounts of ATP. Many of these phenotypes are shared with PINK1 and parkin mutant flies and they have found clu genetically interacts with parkin. As a result, the researchers hypothesize that Clu plays a critical role in PINK1 and Parkin-induced mitophagy. Their Aim will determine how lack of Clu alters PINK1 and Parkin function and determine the effect of lack of Clu on the levels of mitophagy. Evidence supporting that Clu is involved in targeted mitochondrial destruction will represent a new member of the pathway. Knowledge gained from the research proposed here will significantly advance our understanding of how mitochondrial quality control is regulated, which is an important process for regulating neuronal health.

Further information available at:

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