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A Batten disease model in *Drosophila*

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Batten disease comprises a group of genetic neurodegenerative diseases which primarily affect children and are characterized by the accumulation of autofluorescent inclusions and the death of CNS neurons. Infantile neuronal ceroid lipofuscinosis (INCL), the most severe form of Batten disease, is caused by mutations in *PPT1*, which encodes lysosomal palmitoyl-protein thioesterase 1 (PPT1). It is not known how mutations in *PPT1* result in neuronal death or in accumulation of inclusions. The goal of this research is to develop *Drosophila melanogaster* as a model system to investigate the etiology of this disease. *Drosophila* has a putative PPT1 homolog that shares 55% identity and 77% similarity with human PPT1. Northern-blot analysis demonstrated that *Drosophila Ppt1* is expressed during all stages of *Drosophila* development and in all adult tissues tested. PPT1 enzyme activity was quantitated using a fluorogenic substrate and was detected in all tissues tested. *Df(1)446-20* is a deletion that removes *Ppt1* in addition to three unrelated neighboring genes. Less than 3% of wildtype levels of PPT1 enzyme activity were detected in homozygous *Df(1)446-20* flies, demonstrating that *Drosophila Ppt1* is the functional ortholog of human *PPT1*. Although *Df(1)446-20* flies live long enough to reproduce, preliminary data suggests that their viability is reduced. Autofluorescent inclusions were detected by light microscopy and membranous whorls were detected by electron microscopy in brain tissue from *Df(1)446-20* flies. Further phenotypic characterization is in progress, including proving that these phenotypes are due specifically to the absence of *Ppt1*.