Identifying potential *PARIS* homologs in *D. melanogaster*

E.M. Merzetti and B.E. Staveley

Department of Biology, Memorial University of Newfoundland, St. John's, Newfoundland and Labrador, Canada

Corresponding author: B.E. Staveley
E-mail: bestave@mun.ca

Genet. Mol. Res. 15 (4): gmr15048934
Received July 1, 2016
Accepted September 15, 2016
Published November 3, 2016
DOI http://dx.doi.org/10.4238/gmr15048934

ABSTRACT. Mitochondrial destruction leads to the formation of reactive oxygen species, increases cellular stress, causes apoptotic cell death, and involves a cascade of proteins including PARKIN, PINK1, and Mitofusin2. Mitochondrial biogenesis pathways depend upon the activity of the protein PGC-1α. These two processes are coordinated by the activity of a transcriptional repressor, Parkin interacting substrate (PARIS). The PARIS protein is degraded through the activity of the PARKIN protein, which in turn eliminates the transcriptional repression that PARIS imposes upon a downstream target, PGC-1α. Genes in this pathway have been implicated in Parkinson's disease, and there is a strong relationship between mitochondrial dysfunction and pre-mature neuron death. The identification of a PARIS homolog in *Drosophila melanogaster* would increase our understanding of the roles that PARIS and interacting genes play in higher organisms. We identified three potential PARIS homologs in *D. melanogaster*, one of which encodes a protein with similar domains to the *Homo sapiens* PARIS protein, CG15436. The *Drosophila* eye is formed from neuronal

precursors, making it an ideal system to assay the effects of altered gene expression on neuronal tissue formation. The eye-specific expression of RNAi constructs for these genes revealed that both *CG15269* and *Crol* caused neurodegenerative phenotypes, whereas *CG15436* produced a phenotype similar to *srl-EY*. *Crol-RNAi* expression reduced mean lifespan when expressed in dopaminergic neurons, whereas *CG15436-RNAi* significantly increased lifespan. *CG15436* was PARIS-like in both structure and function, and we characterized the effects of decreased gene expression in both the neuron-rich *D. melanogaster* eye and in dopaminergic neurons.

Key words: *PGC-1α*; *Spargel*; *PARIS*; *CG15436*; *CG15269*; *Crol*