Evolution rate of insulin component *Pten* gene in *Drosophila* species

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BACKGROUND

The insulin signaling pathway is involved in regulating growth and metabolic homeostasis. The components are encoded by many genes, such as *Pten* (phosphatase and tensin homolog), which are evolutionarily conserved across animals. This study examined whether there is a direct relationship between the evolution rate of *Pten* and the phylogenetic distance of three divergent *Drosophila* species from the model species, *Drosophila melanogaster*. Furthermore, this study compared the evolutionary rates of two insulin pathway genes, *Pten* and *Foxo*, to identify whether genes evolve at rates with respect to their position in the pathway.

Pten - lipid and protein phosphatase that functions as a tumor suppressor and regulates many cellular processes involved in metabolism, cellular structure, growth, and survival (Song et al. 2012). PIP-3 is the lipid substrate of Pten (Chen et al. 2018).

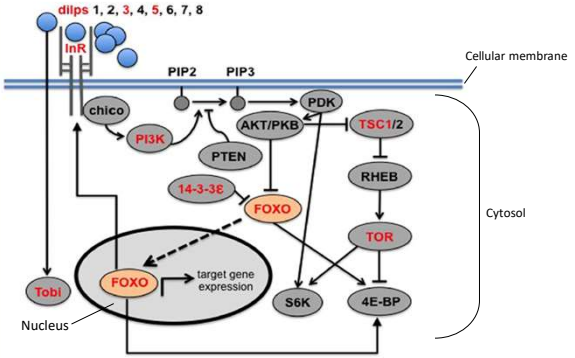

Figure 1: Overview of the insulin pathway components in cell (Durmaz et al. 2015).

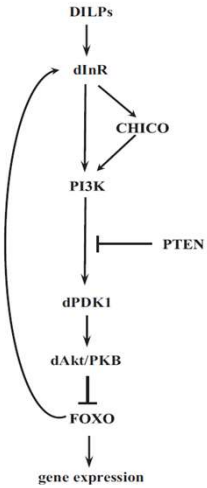

Figure 2. Brief overview of the *Drosophila* insulin/insulin-like growth factors (IGF) pathway. This schematic illustrates the general positions of Pten (phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase) and Foxo (transcription factor Forkhead box O) in the insulin pathway. Other proteins included in the figure: DILPs, Drosophila insulin-like peptides; dInR, insulin-like receptor; CHICO, insulin receptor substrate; PI3K, phosphatidylinositol 3-kinase; dPDK1, 3-phosphoinositide-dependent protein kinase 1; dAkt/PKB, protein kinase B. (Eremina et al. 2021).

HYPOTHESES

1. Evolution rates of genes within the insulin pathway have a direct relationship to the phylogenetic distance of the target species from the model species, *D. melanogaster*.
2. Genes of insulin pathway components evolve at rates that depend on their location in the pathway.

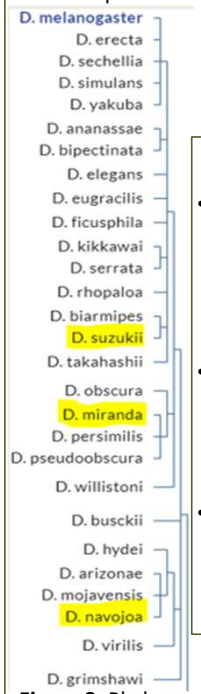

Figure 3. Phylogenetic tree of *Drosophila* species

OBJECTIVES

- Analyze the evolution of the *D. melanogaster* phosphatase and tensin homolog (*Pten*) in three *Drosophila* species of increasing divergence, *D. suzukii, D. miranda, and D. navajoa* (Figure 3).
- Compare the evolutionary rates of two insulin pathway genes, *Pten* and *Foxo* (transcription factor Forkead, box O), with respect to their position in the pathway (Figure 2).
- Compare the evolution rates calculations of *Pten* and *Foxo* within similar *Drosophila* species, *D. miranda* and *D. navojoa*.

METHODS

1. Annotate *Pten* gene in each species following the GEP Pathways project walkthrough protocol
2. Obtain encoded protein sequence from annotations
3. Use Molecular Evolutionary Genetic Analysis (MEGA) program to calculate evolutionary genetic distance through analysis of amino acid substitution per site in target species compared to *D. melanogaster*
4. Compare findings with other insulin pathway component gene, *Foxo* (transcription factor Forkead, box O)

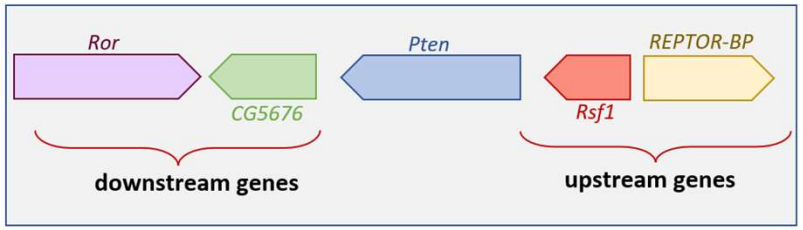

Figure 4. Genomic neighborhood of *Pten* in *D. melanogaster*

RESULTS

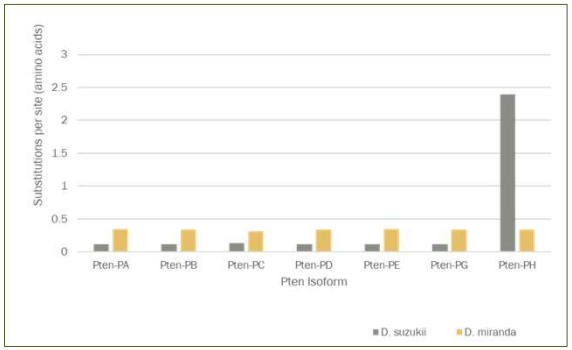

Figure 5. Comparison of number of amino acid substitutions per site of *Pten* between target species (*D. suzukii* and *D. miranda*) and *D. melanogaster.*

Summary

- Evolution rates of *Pten* was greater in the more phylogenetically distant species *D. miranda* for most isoforms
  - *D. miranda* had a greater amount of amino acid substitutions per site in all isoforms except Pten-PH than *D. suzukii*
  - Pten-PH in *D. suzukii* had a significant amount of amino acid substitutions per site compared to *D. miranda*
- *Pten* ortholog in *D. navojoa* and *Foxo* ortholog in *D. miranda* was not completed to the likelihood they have not been sequenced or catalogued yet or these orthologs do not exists in the respective species, which is unlikely.
  - Comparison between *Pten* and *Foxo* was not performed
  - *D. navojoa* genetic distance data not obtained

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