Annotation of *Thor* in *Drosophila albomicans*: Detangling the Insulin Signaling Pathway of Drosophila

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Introduction

- The insulin signaling pathway is well-conserved across animals, playing a critical role in growth and metabolic homeostasis.[1]
- This pathway is studied in *Drosophila* to understand how metabolic diseases, such as obesity and diabetes, develop in humans.[1]
- However, many genes of this pathway remain unannotated in multiple *Drosophila* species.
- We annotated *Thor* (also called 4E-BP1), which contributes to translation regulation, response to environmental stress, and cell growth regulation (**Fig. 1**),[2] in *D. albomicans*.

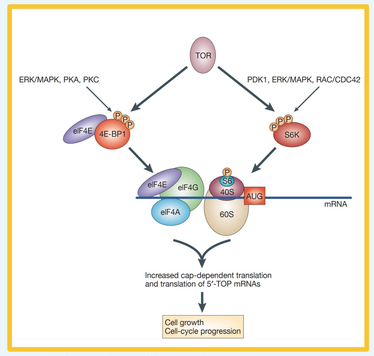
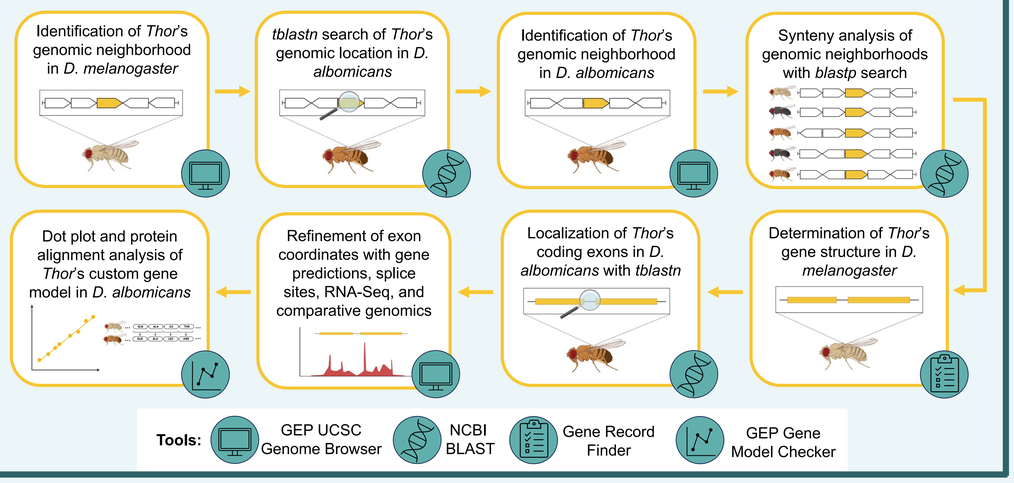


Fig. 1: Regulation of translation, cell growth, and cell-cycle progression by the TOR protein.[3] The Eukaryotic initiation factor 4E-binding protein 1 (4E-BP1), which is encoded by *Thor*, is inhibited in this process.

Objective & Approach

- As part of the Pathways Project of the Genomics Education Partnership (GEP), *Thor* in *D. albomicans* was annotated to:
  - Expand the number of annotated genes in the insulin signaling pathway in *Drosophila*
  - Provide insight into the evolution and function of this pathway
  - Assess *Thor*'s conservation in the pathway
- Following the GEP's protocol[4], annotation was based on local synteny conservation and parsimony with *D. melanogaster*.

Methods



Results

Identification of *Thor* in *D. melanogaster*

Genomic Neighborhood

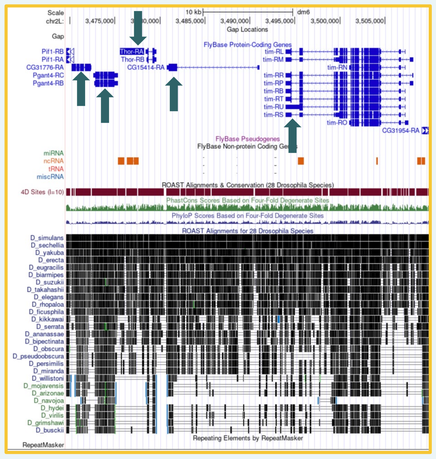


Fig. 2: Observed genomic neighborhood of *Thor* in *D. melanogaster* from the GEP USCS Genome Browser.

Gene Structure

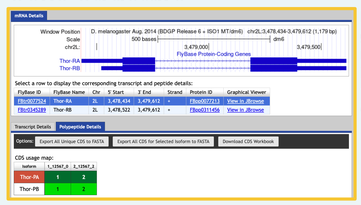


Fig. 3: Observed genomic neighborhood of *Thor* in *D. melanogaster* from the GEP USCS Genome Browser.

The conservation of *Thor* across *Drosophila sp.*, despite changes in local synteny, suggests an essential role in the insulin signaling pathway.

Localization of *Thor* in *D. albomicans*

Genomic Neighborhood

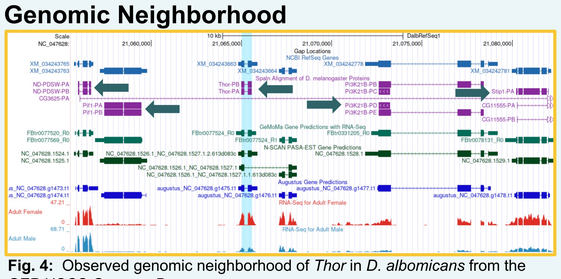


Fig. 4: Observed genomic neighborhood of *Thor* in *D. albomicans* from the GEP USCS Genome Browser.

Coordinates

Gene	Coding Exon	Coordinates (bp.)	
		Start	End
Thor (PA & PB)	1	21,064,996	21,065,149
	2	21,065,363	21,065,568
Thor Duplicate	1	21,067,256	21,067,409
	2	21,067,605	21,067,810

Table 1: Gene model for *Thor*'s isoforms (PA & PB) and its duplicate in chromosome 2L of *D. albomicans*.

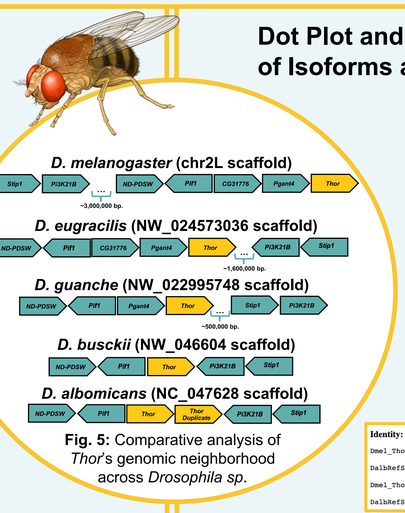


Fig. 5: Comparative analysis of *Thor*'s genomic neighborhood across *Drosophila sp.*

Dot Plot and Protein Alignment of Isoforms and Duplicate

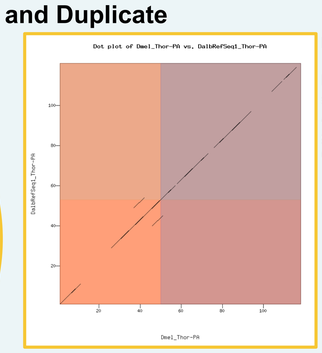


Fig. 8: Dot plot of *Thor*'s isoforms (PA & PB) in *D. albomicans* against the putative *D. melanogaster* ortholog generated by the Gene Model Checker.

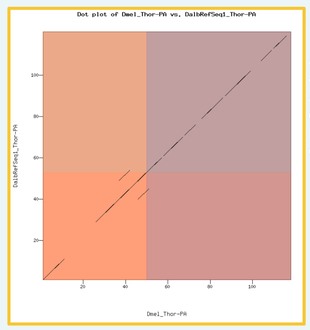


Fig. 9: Dot plot of *Thor*'s duplicate in *D. albomicans* against the putative *D. melanogaster* ortholog generated by the Gene Model Checker.

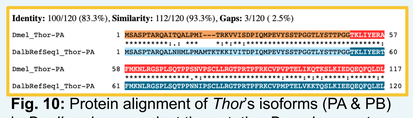


Fig. 10: Protein alignment of *Thor*'s isoforms (PA & PB) in *D. albomicans* against the putative *D. melanogaster* ortholog generated by the Gene Model Checker.

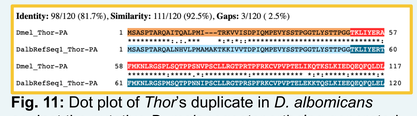


Fig. 11: Dot plot of *Thor*'s duplicate in *D. albomicans* against the putative *D. melanogaster* ortholog generated by the Gene Model Checker.

Gene Model of *Thor* in *D. albomicans*

Gene Structure of Isoforms and Duplicate

Fig. 6: Gene model for *Thor*'s isoforms (PA & PB) in *D. albomicans* as shown on the GEP USCS Genome Browser.

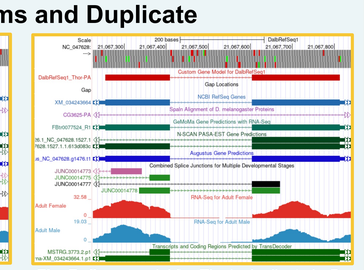


Fig. 7: Gene model for *Thor*'s duplicate in *D. albomicans* as shown on the GEP USCS Genome Browser.

Discussion

- *Thor* has two coding exons at 21,064,996-21,067,810 bp. in *D. albomicans*.
- While *Thor* conserved its structure, its genomic neighborhood in *D. albomicans* does not share synteny with *D. melanogaster*.
- The comparative analysis of *Thor*'s genomic neighborhood across *Drosophila* species (**Fig. 5**) revealed recombination during speciation within the genera.
- This analysis and the annotation also revealed a *Thor* gene duplicate in *D. albomicans*, which has been observed in other basal *Drosophila*.

Conclusion

- A putative ortholog (and duplicate) of *Thor* in *D. albomicans* was supported via its annotation and the comparative analysis of its genomic neighborhood across *Drosophila* species.
- Despite local synteny changes, *Thor's* conservation in *Drosophila* likely stems from its critical role in the insulin signaling pathway.
- Future gene annotations across *Drosophila* species could provide insight into the evolution, function, and disease relevancy of this pathway, including its role in diabetes.

References

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Acknowledgments

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