

# Investigating Diversity of DNA Elements that Threaten and Preserve Genome Integrity



Nneamaka Okolo<sup>1,2</sup>, Sophia Mohammed<sup>2</sup>, Mia T. Levine<sup>2</sup>

<sup>1</sup>College of Arts and Sciences, University of Pennsylvania <sup>2</sup>Department of Biology, University of Pennsylvania  
nokolo@sas.upenn.edu (COL 2027)



## Introduction

- Selfish genetic elements are stretches of DNA that act to enhance their transmission to the next generation, irrespective of their impact on individual fitness.<sup>2,7</sup>
- Satellite DNA is a type of selfish genetic element. Characterized by highly repetitive non-coding sequences, they compose the majority of compact DNA in many eukaryotic genomes.<sup>3,8</sup>
- Satellite DNA represents some of the fastest evolving sequences in eukaryotic genomes.<sup>1,2</sup>
- Despite initially being labeled "junk DNA", studies have shown that DNA satellites both support and threaten important cellular processes.<sup>1,6</sup>
- Existing research suggests that satellite-interacting proteins can coevolve with DNA satellites to mitigate deleterious effects on the host organism.<sup>1</sup>

## Can variation in the *D. melanogaster* 359bp sequence inform strain of origin?

### Fragment of 30858 *D. Melanogaster* 359bp Sequence Alignment

```
ACAGACTCTGCAAAAATGTTGATATTTACAAACGAAATT
ACAGACTCTGCAAAAATGTTGATATTTACAAACGAAATT
ACAGACTCTGCAAAAATGTTGATATTTACAAACGAAATT
ACAGACTCTGCAAAAATGTTGATATTTACAAACGAAATT
```

■ = same nucleotide

### Fragment of B2 *D. Melanogaster* 359bp Sequence Alignment

```
TTGCATAGTCTGTTTTTCCAAAATTCGGTCATCAAAAT
TGCCAAAATCCGTTTTTCCAAAGATTCGGTCATCAAAAC
TGCCAAAATCCGTTTTTCCAAAGTTCGGTCATCAAAAC
TTGCAGAGTCTGTTTTTCCAAAATTCGGTCATCAAAAC
CGGCAGAATCTGTTTTTCCAAAATTCGGTCATCAAAAT
```

Multi-sequence alignment shows a greater degree of similarity in the nucleotide sequences of 359bp copies from 30858 strain flies compared to those within the B2 strain

## Positive selection in *Drosophila* helicase proteins

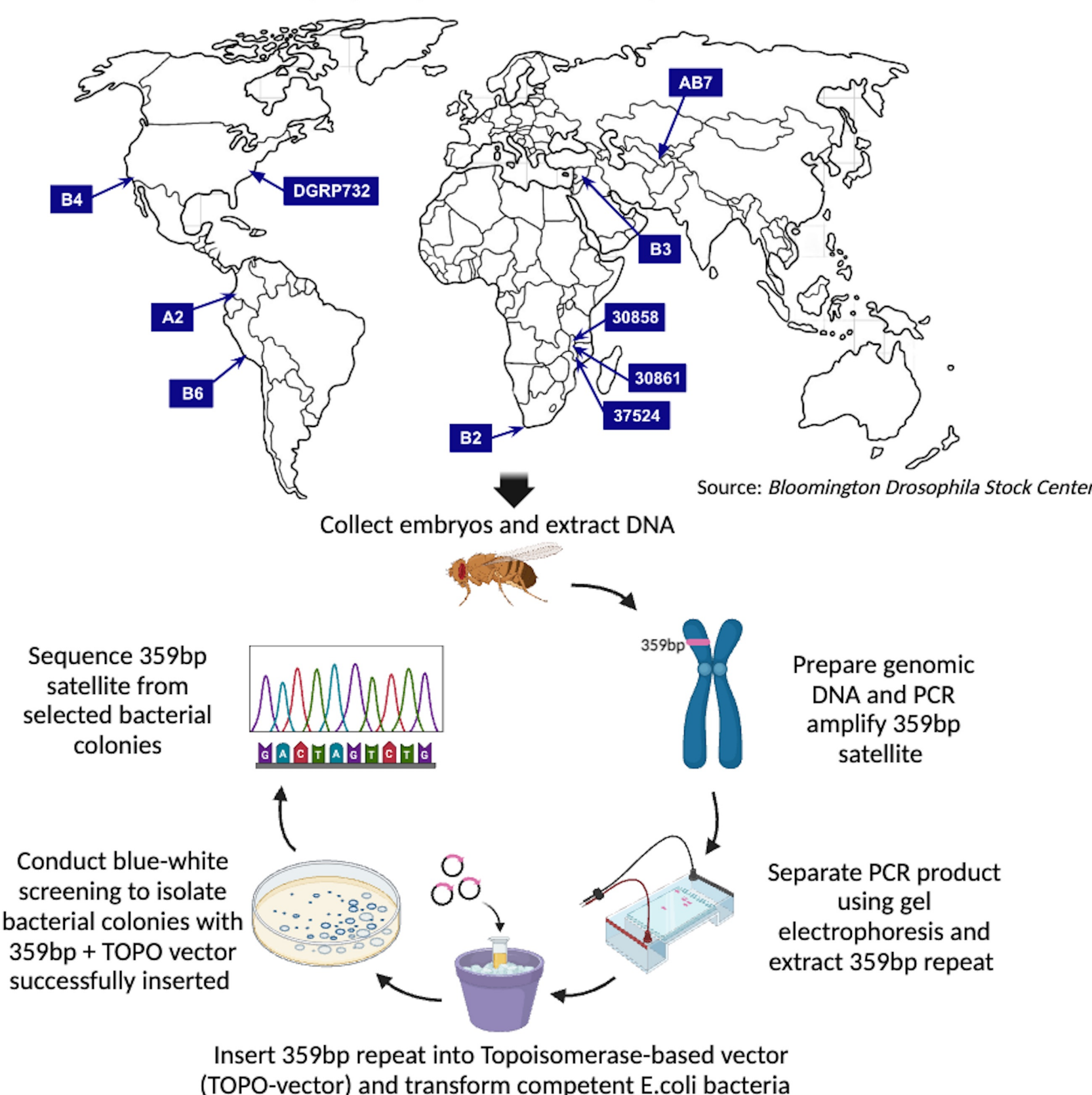
- Rapid evolution of satellite DNA, like the 359bp, challenge DNA functions such as DNA replication, which are necessary for maintaining genome integrity.<sup>1</sup>
- Helicases are crucial enzymes in DNA replication and other metabolic processes. Using ATP to bind and remodel nucleic acids, helicases perform a wide range of functions on chromosomal DNA and are essential to supporting cellular processes.<sup>5</sup>
- By comparing the ratio of synonymous (dN) to non-synonymous (dS) amino acid changes in the helicase protein sequences of *D. melanogaster* and its most closely related species *D. simulans*, I investigated the rates of molecular evolution of helicase genes. I discovered that many helicase proteins have signatures of positive selection (dN/dS > 1)

## Investigating variation in 359bp within the *melanogaster* genome

- 359bp is an 11Mb satellite array on the X chromosome of *D. melanogaster*. Its entire length is composed of repetitive 359-bp units of nucleotide sequence.<sup>4</sup>
- The 359bp satellite accounts for over 4% of the *D. melanogaster* genome, however it is not present in its most closely related species *D. simulans*. This suggests that changes in satellite DNA occur rapidly over evolutionary timespans.<sup>1</sup>
- Though previous studies have established the evolutionary and functional importance of 359bp, variation between and among individuals hasn't been well characterized.<sup>8</sup>
- This study aims to explore the possibility of variation in 359bp both within individual strains of *D. melanogaster* and across the species globally.

## Sequencing 359bp across worldwide strains of *D. melanogaster*

Within the *D. melanogaster* species there exists a wide variety of strains originating in various locations around the globe. I sequenced 10 worldwide strains of *D. melanogaster* to analyze within and between strain polymorphism of the 359bp locus.



## Constructing a Phylogenetic Tree

Input FASTA file containing multi-sequence alignment of all 359bp satellite sequences

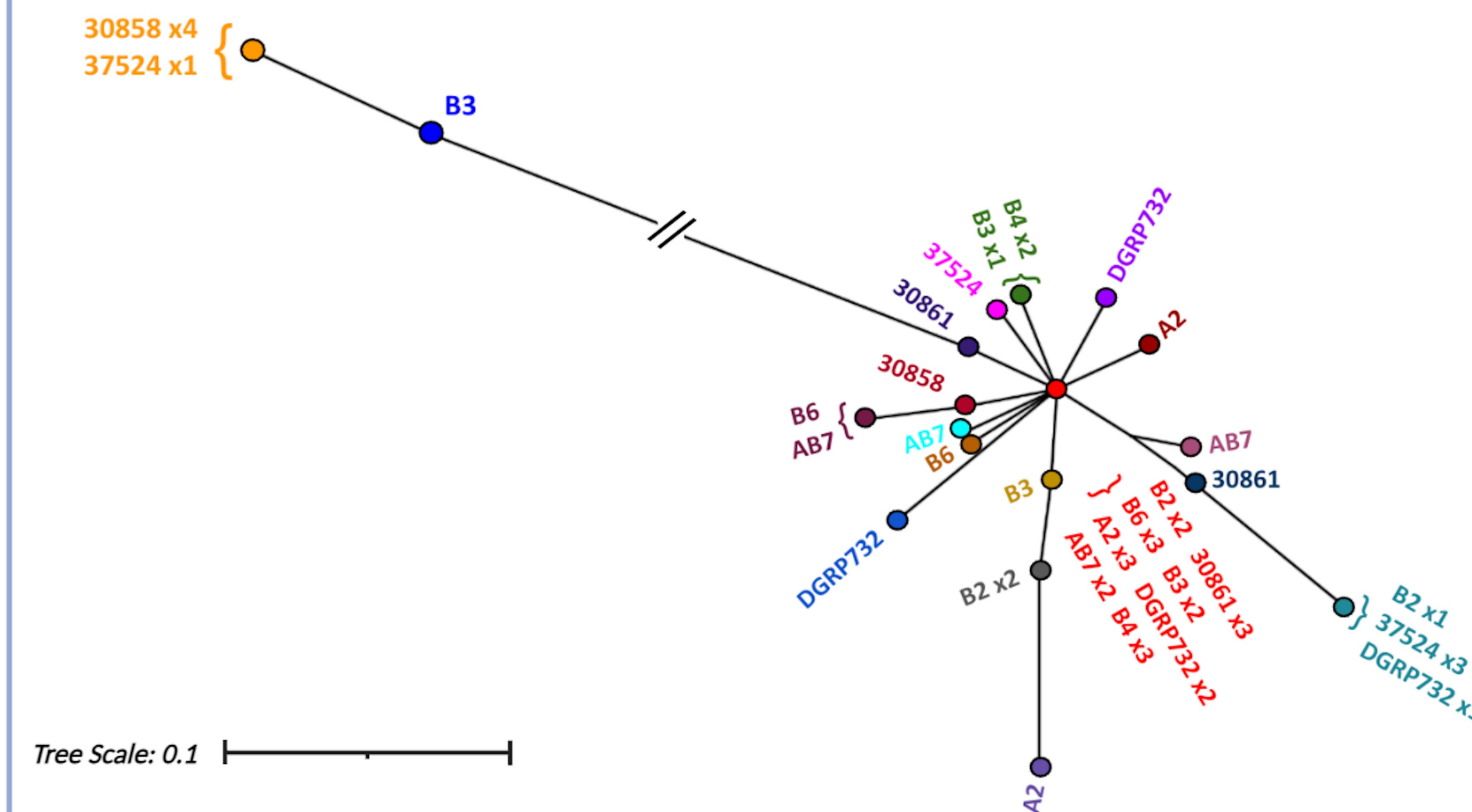
Conduct high accuracy alignment using MUSCLE

Curate alignment with Gblocks software

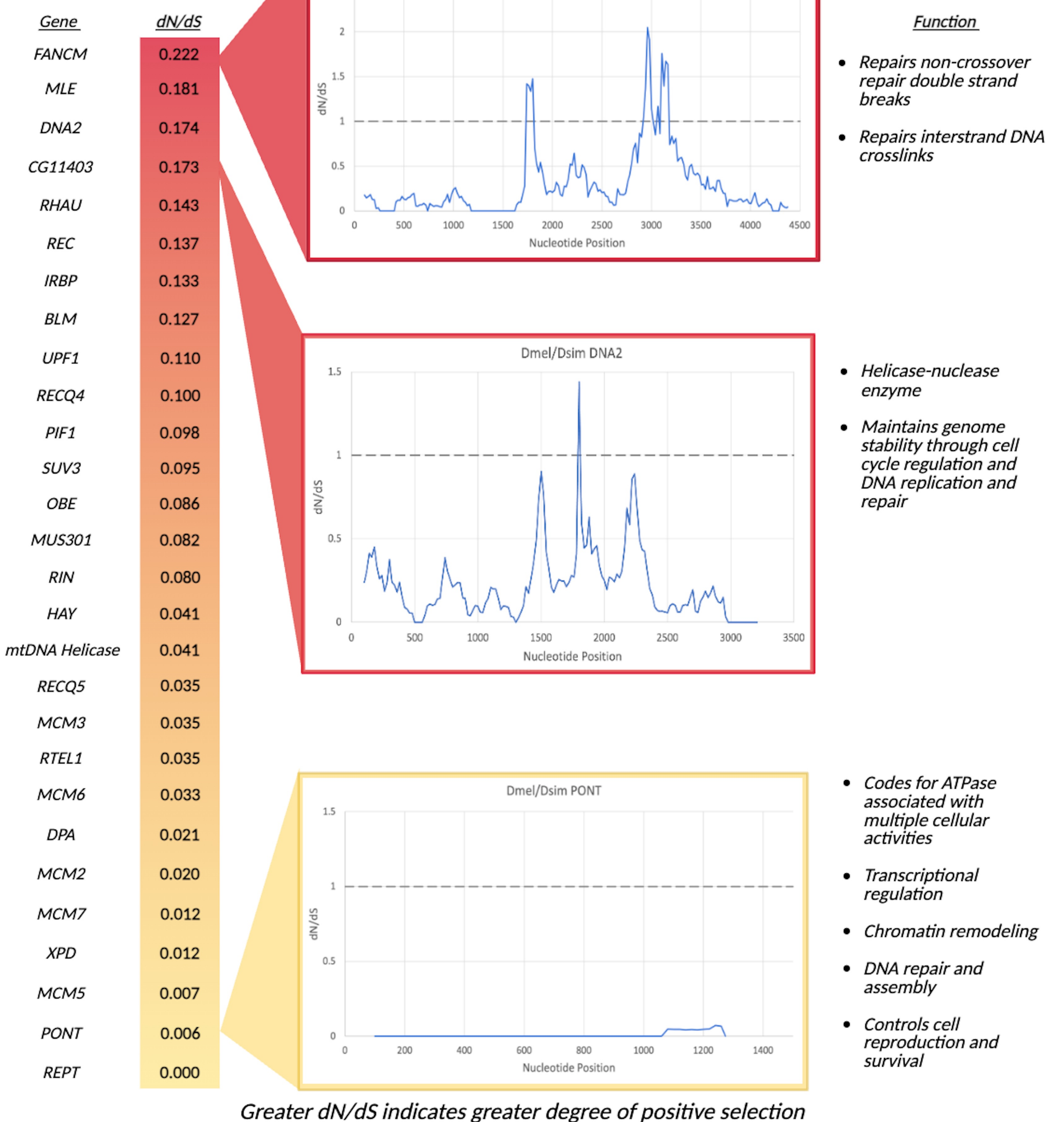
Construct phylogenetic tree using PhyML program

Render graphical representation of phylogenetic tree with TreeDyn

## Phylogenetic relationships among 359bp copies suggest similar variation among copies within individuals and among copies between strains.



- Phylogenetic analysis indicates that there is minimal strain-specific genetic difference between *D. melanogaster* 359bp satellite sequences.
- Longer branch length and high degree of similarity between strains of fly from Malawi (e.g. 30858) show that this strain lacks polymorphism compared to other strains of *D. melanogaster*. This data suggests that gene conversion is occurring within this strain of *D. melanogaster*.



## References

- Brand, C. L., & Levine, M. T. (2022). Cross-species incompatibility between a DNA satellite and the *Drosophila* Spartan homolog poisons germline genome integrity. *Current biology*, *32*(13), 2962-2971.e4.
- Burt, A., & Trivers, R. (2006). Selfish Genetic Elements. In *Genes in Conflict: The Biology of Selfish Genetic Elements* (pp. 1-18). Harvard University Press.
- Cechova, M., Harris, R. S., Tomaszewicz, M., Arbeituber, B., Chiaromonte, F., & Makova, K. D. (2019). High Satellite Repeat Turnover in Great Apes Studied with Short- and Long-Read Technologies. *Molecular biology and evolution*, *36*(11), 2415-2431.
- Lohe AR, Hilliker AJ, and Roberts PA (1993). Mapping simple repeated DNA sequences in heterochromatin of *Drosophila melanogaster*. *Genetics* 134, 1149-1174.
- Fairman-Williams, M. E., Guenther, U. P., & Jankowsky, E. (2010). SF1 and SF2 helicases: family matters. *Current opinion in structural biology*, *20*(3), 313-324.
- Ferree, P. M., & Barbash, D. A. (2009). Species-specific heterochromatin prevents mitotic chromosome segregation to cause hybrid lethality in *Drosophila*. *PLoS biology*, *7*(10), e1000234.
- Griffiths, University Anthony J F, Wessler, University Susan R, Carroll, D. S. B., & Doebley, J. (2015). *Introduction to genetic analysis* (11th ed.). W.H. Freeman.
- Jagannathan, M., Warsinger-Pepe, N., Watase, G. J., & Yamashita, Y. M. (2017). Comparative Analysis of Satellite DNA in the *Drosophila melanogaster* Species Complex. *G3 (Bethesda, Md.)*, *7*(2), 693-704.