



Department of
Biology and Biochemistry
College of Natural Sciences
and Mathematics

Mapping Irradiation Sensitivity in *Drosophila melanogaster*

Lillian Pennington, Dr. Llewellyn Green, Dr. Erin Kelleher

ABSTRACT

Organisms are constantly bombarded by various mutagens present in their surroundings. These mutagens have the potential to cause damage to an organism's DNA, resulting in mutations and even death at high concentrations. Therefore, for an organism to maintain its fitness, it is crucial to possess a certain degree of mutagen tolerance. Additionally, since the level of exposure to mutagens varies widely over time, organisms experience diverse selection pressures that are predicted to increase the number of organisms with a higher mutagen tolerance. Despite this, the genetic factors responsible for natural variations in mutagen tolerance remain poorly understood. To address this gap, we utilized an X-QTL, pooled-sequencing method using the DSPR to identify the genetic determinants of mutagen tolerance.

BACKGROUND

The *Drosophila* Synthetic Population resource (DSPR) is a recently developed collection of more than 1700 recombinant inbred lines of *Drosophila melanogaster*. These lines were generated from two synthetic populations that were highly recombined by interbreeding eight founder lines in each population. The DSPR panel serves as an intermediate approach between conventional QTL mapping and genome-wide association mapping and offers a few advantages over these methods. As a result, the DSPR is widely used to map certain traits in the *Drosophila melanogaster* genome, including irradiation sensitivity.

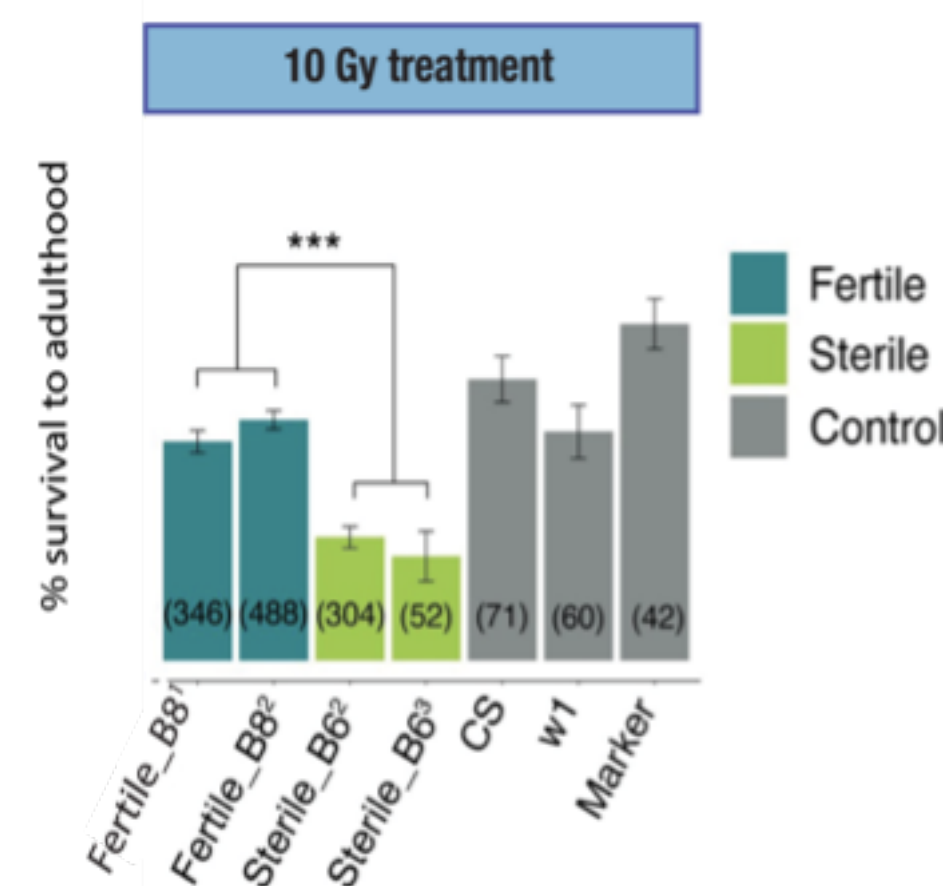


Figure 1: One of the eight genetic backgrounds that make up the DSPR (B6) has been associated with a greater sensitivity to x-ray irradiation when compared to other genetic backgrounds (B8).

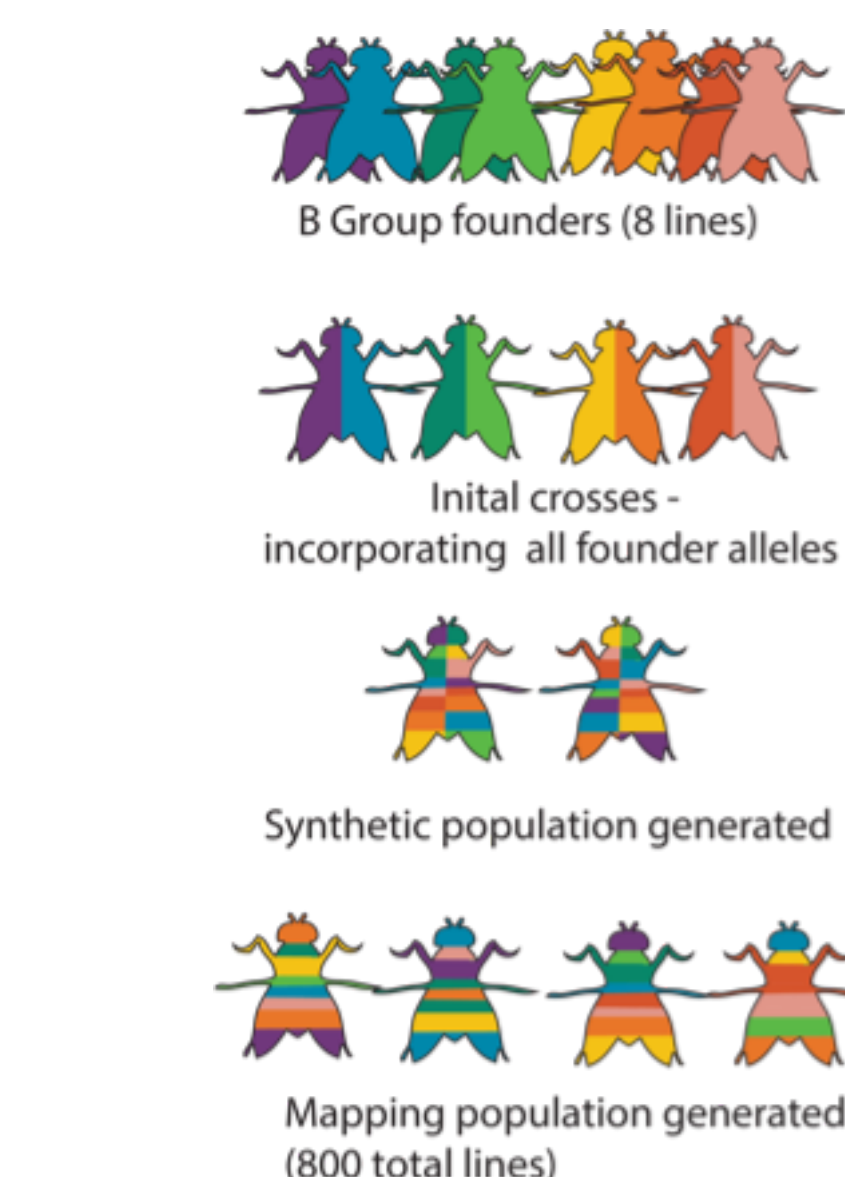


Figure 2: The *Drosophila* Synthetic Population Resource (DSPR) includes a panel of ~800 recombinant inbred lines (RILs) that are derived from the same 8 founder backgrounds.

METHODS



Figure 3: To enable precise X-QTL mapping without individual screening, a population of *Drosophila melanogaster* was created by breeding a large number of inbred lines. 700 RILs, each containing the same 8 founder genetic backgrounds, were randomly selected. 10 eggs from each RIL were collected and pooled for several generations until approximately 7,000-20,000 *Drosophila melanogaster* resided in the population. Irradiation screening was deferred until the fifth generation to ensure high-resolution mapping.

Use your smartphone to scan the QR code and get a more detailed view of the cages that house the population utilized for X-QTL mapping.

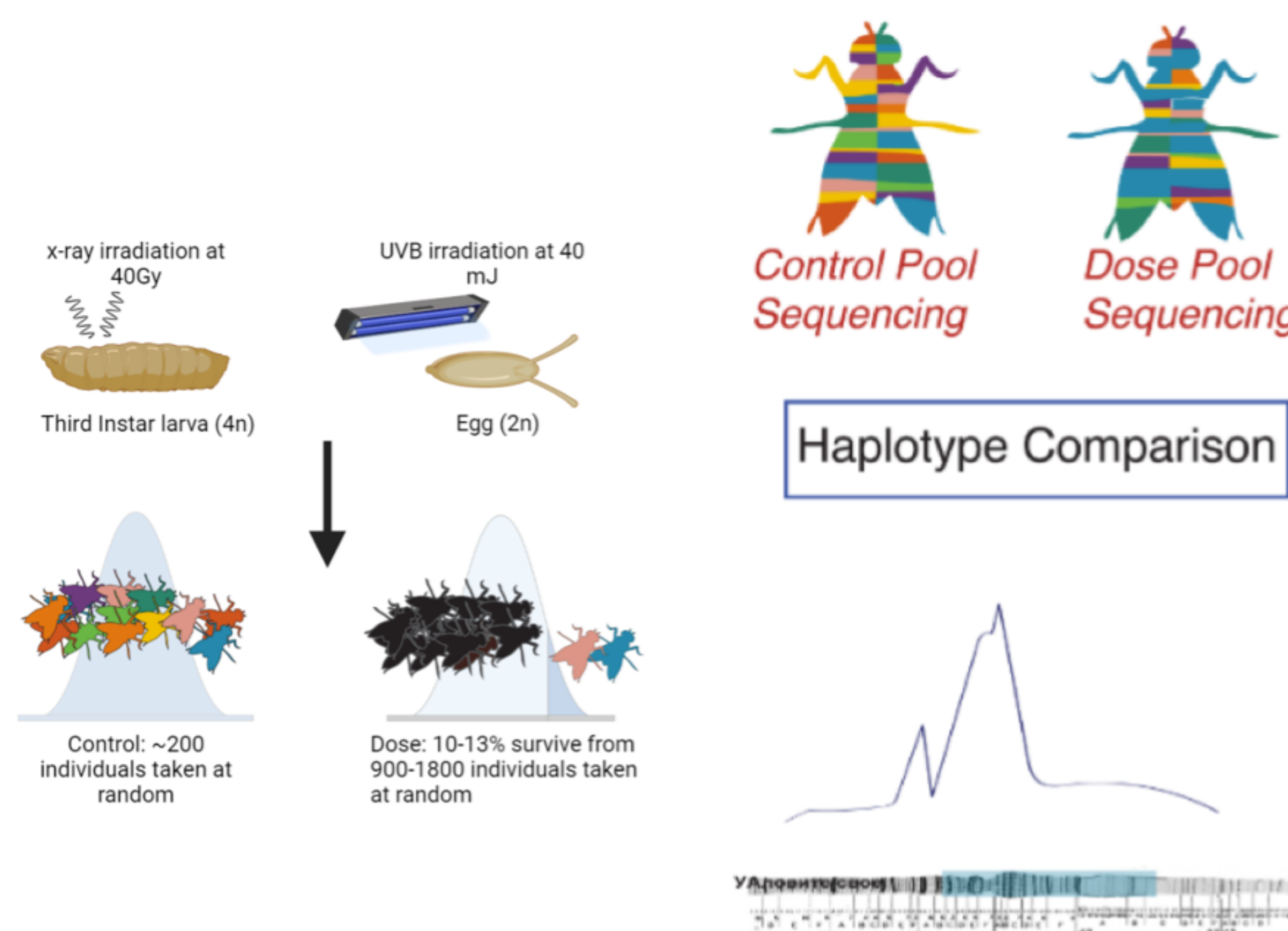


Figure 4: The goal for this study is to screen for a dose close to the ED_{50} for both X-ray and UVB irradiation. Third instar larvae were subject to x-ray irradiation while *Drosophila melanogaster* eggs were irradiated with UVB light.

Figure 5: A sequencing coverage that is relatively low should be enough to determine the frequencies of haplotypes in both the treated and control samples.

FURTHER RESEARCH

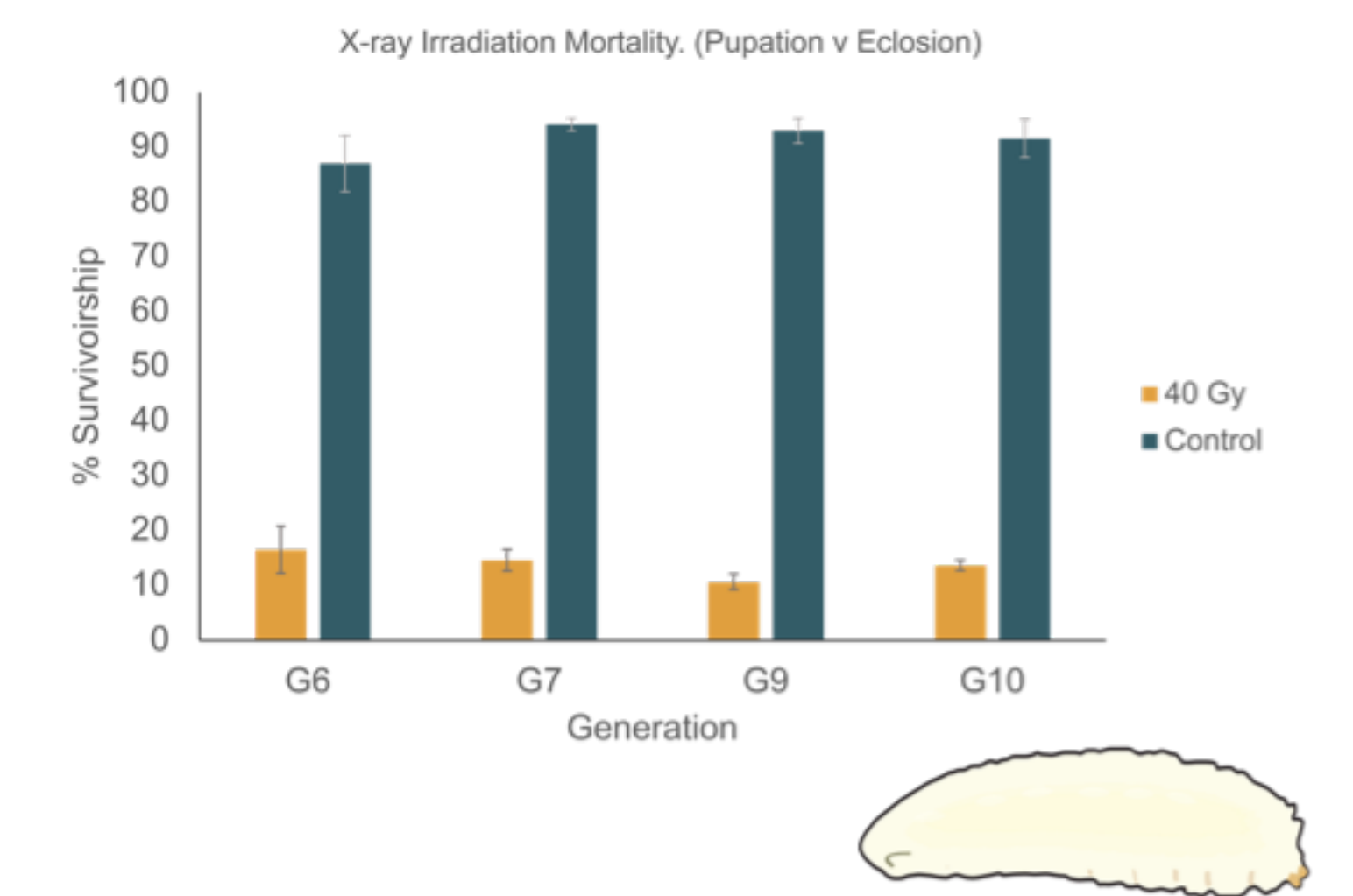


Figure 6: An X-ray irradiation mortality assay was performed between G6 and G10. Mortality was quantified as a percentage of pupae cases vs. emergent adults. Future research will include sequencing the above samples.

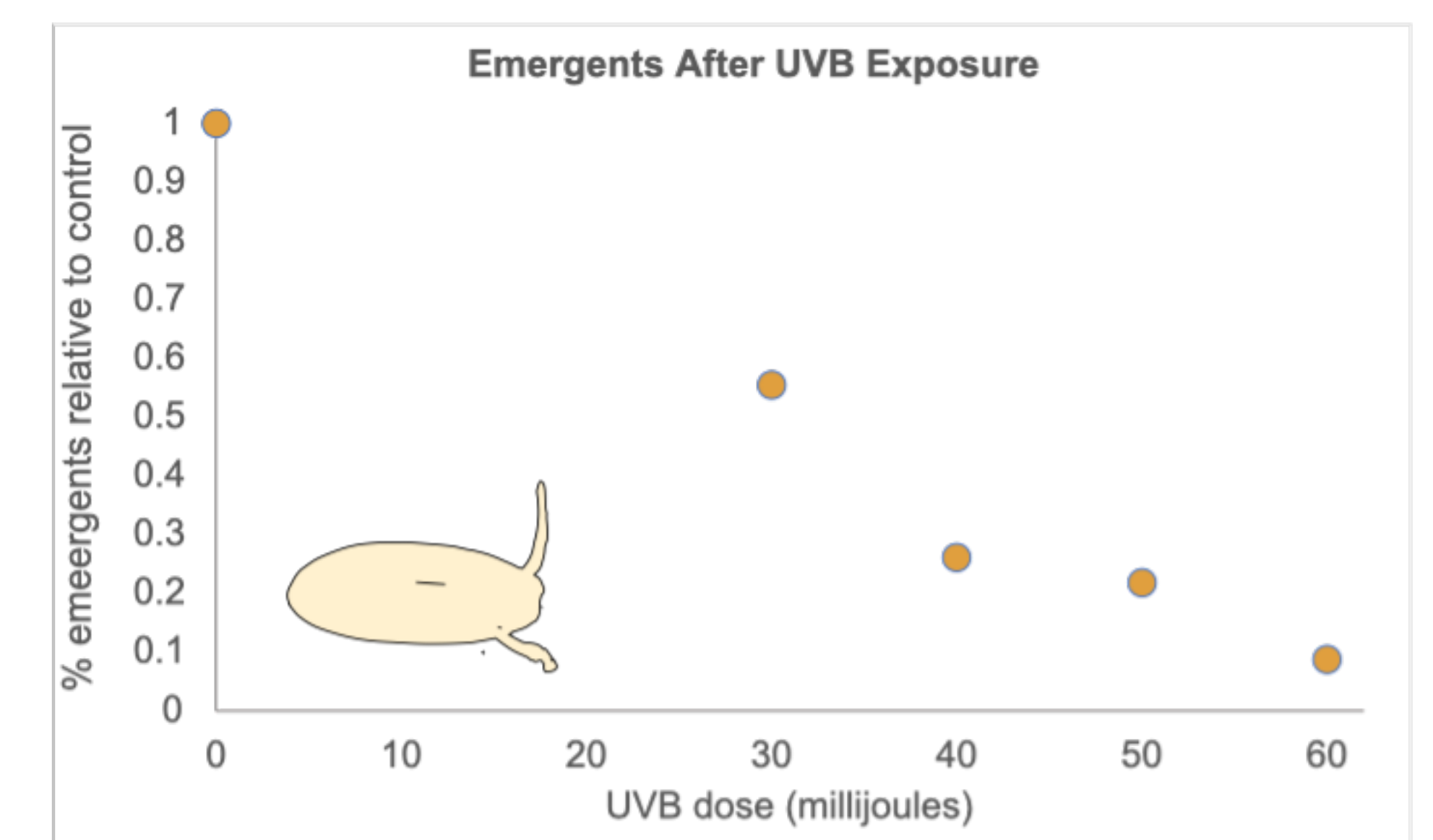


Figure 7: A UVB irradiation mortality assay was conducted to determine an appropriate UVB dosage. 60mJ results in a ~10% survival rate, so this dose will be used for the study.

REFERENCES

- Lama, J. et al. Genetic variation in P-element dysgenic sterility is associated with double-strand break repair and alternative splicing of TE transcripts. *Plos Genet* 18, e1010080 (2022).
- Macdonald, S. J., Cloud-Richardson, K. M., Sims-West, D. J. & Long, A. D. Powerful, efficient QTL mapping in *Drosophila melanogaster* using bulked phenotyping and pooled sequencing. *Genetics* 220, iyab238 (2022).

ACKNOWLEDGEMENTS

We would like to acknowledge NIH-NIGMS R35GM138112, awarded to ESK; and to thank Stuart McDonald for providing us with the DSPR genomic sequencing data and over 700 RIL stocks for the establishment of the mass-bred population. Further thanks are given to the entire Kelleher Lab for helping us utilize these lines in the construction of the mass-bred population. Additional members of Team Egg-Pick: Savana Hadjipanteli, Lorissa Saiz, Sherry Hajjarbabi, Hasan Nooruddin, Natalie Copeland, An Bui, and Juan Rojas. Additional thanks are awarded to Llew for her unending guidance and mentorship.