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C. elegans senses oxidants via head neurons and reacts through *daf-7/TGFβ*

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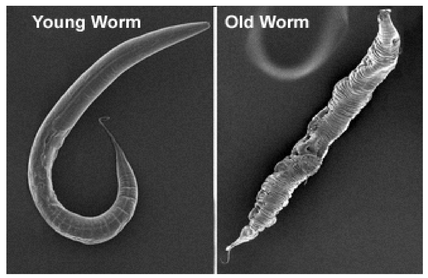
Abstract

C. elegans is a model to study genetic interactions and molecular biology. In this study, we investigated how these microscopic worms regulate their responses to environmental oxidants. We determined that the protein DAF-7 is produced in sensory neurons in response to oxidants, and that DAF-7 inhibits the DAF-3 transcription factor, which in turn modifies the production of tyramine and glutamine-mediated fat accumulation.

Background

The Apfeld lab and many others use the microscopic worm *C. elegans* as a model because it is a simple and well-studied multicellular animal that experiences aging.

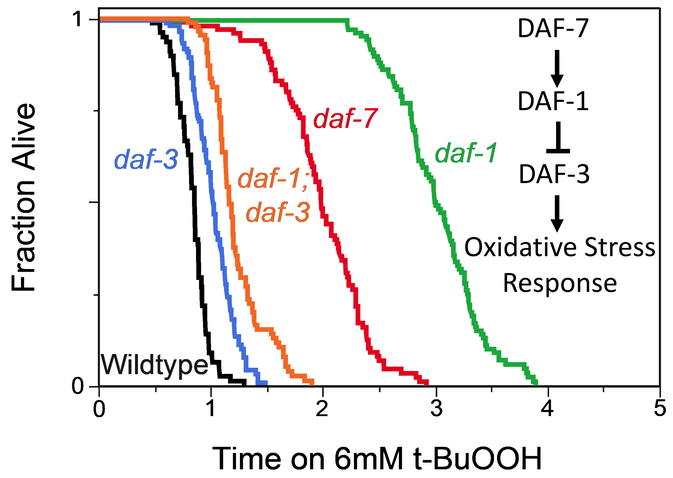
In the environment, worms are exposed to harmful conditions such as high temperature and oxidants. This project aimed to investigate how a whole multicellular organism, not just an individual cell, coordinates a response to oxidative stress. Understanding how worms mitigate oxidative damage could reveal strategies used by humans to cope with oxidative stress and ways that oxidative damage can lead to disease.



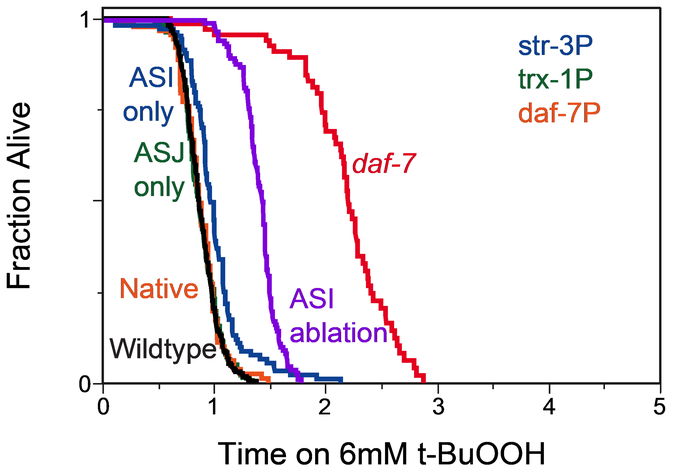
C. elegans worms are small but easy to visualize under a microscope, and they noticeably grow old and die.

Picture taken by the Ghazi Lab at Children's Hospital of Pittsburgh.

Results

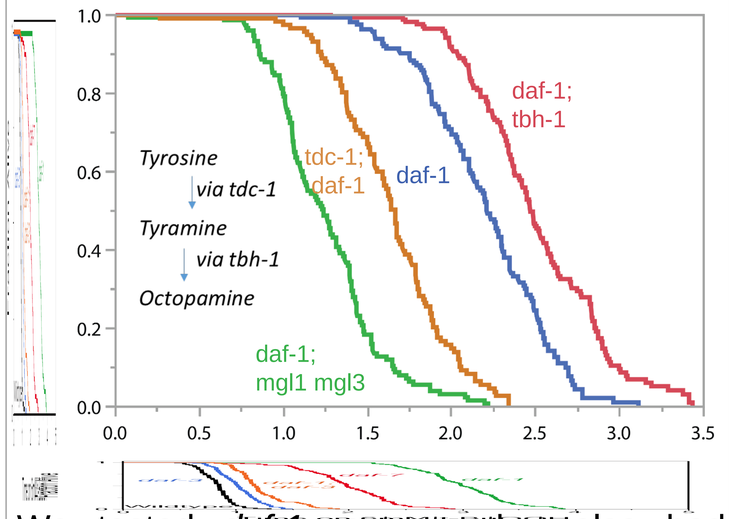


We performed a multi-gene screen of survival on a common oxidant by utilizing a cluster of flatbed scanners called the Lifespan Machine[1]. *daf-7(-)* mutants live twice as long as wildtype under these conditions.



In a long-surviving *daf-7(-)* mutant, specifically expressing *daf-7* either of two particular neurons called ASI and ASJ was sufficient to return to wildtype survival. Ablation of ASI was sufficient reduce survival.

More Results



We tested *daf-1* mutants that also had mutations in tyramine/octopamine synthesis or glutamate receptor genes. *tdc-1* and *mgl1 mgl3* both suppress the long-survival phenotype of *daf-1*.

Conclusions & Future Directions

The *daf-7/TGFβ* pathway plays a role in regulating a worm's response to oxidative stress via tyramine synthesis and glutamate receptors. The Apfeld lab will further characterize interactions within this pathway, including the role of FOXO/DAF-16.

Acknowledgements

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References

1. Stroustrup N, Ulmschneider BE, Nash ZM, Lopez-Moyado IF, Apfeld J, Fontana W. The *Caenorhabditis elegans* Lifespan Machine. Nature Methods. 2013;10(7):665-70.
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