RISE:2017
RESEARCH, INNOVATION AND SCHOLARSHIP EXPO
Undergraduate
Category: Physical and Life Sciences
Degree Seeking: Cell and Molecular Biology
Abstract ID# 1543
Northeastern University

How Do Genetic Interactions Regulate Aging In *C. elegans*?

Abigail Vogelaar and Julian Stanley, Advised by Javier Apfeld

Introduction

Goal

Aging is a universal process – yet poorly understood.

We want to understand the genetic basis of aging through use of the nematode *C. elegans*.

There are dozens of identified aging genes, but aging is a complex process, and it is important to understand the pathways and interactions between these genes to get a full picture.

This experiment begins the systematic analysis of characterizing genetic interactions by starting with transcription factors known to be implicated in aging and testing mutants and double mutants under normal and oxidative conditions.

Why C. elegans?

- Entire genome sequenced
- Genes conserved in many mammals
- Simple organism
- Experiences aging

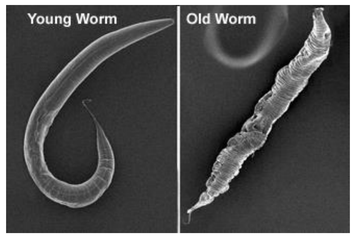


Figure 1: Comparison of young and old worm. Photos taken by the Ghazi Lab at Children's Hospital of Pittsburgh.

Transcription Factors

Transcription factors are proteins that are involved in converting DNA into RNA. They are interesting because they coordinate the function of many other genes. We started with 3 that are implicated in aging:

daf-16	- Part of the most well-known aging related pathway: Insulin Signaling Pathway - Conserved in humans through the FOXO family
daf-12	- Part of the steroid signaling pathway - Has roles in the Insulin Signaling Pathway - Conserved in humans
hlh-30	- Involved in autophagy - Known to interact with many lifespan related pathways - Has a human ortholog: TFEB

Approach

Mutants and Double Mutants

Mutants:
All of the strains used for this experiment were mutants in which the gene of the transcription factor in question was not expressed.

Double Mutants:
In order to explore the interactions of these genes, double mutants can be created that will have both genes of interest not expressed. As a starting point, *daf-16* was combined with both of the other genes, *daf-12* and *hlh-30*. This provided us with five strains to test:

daf-16
daf-12
hlh-30
daf-16; daf-12
hlh-30; daf-16

Conditions

We tested these strains under 2 conditions:

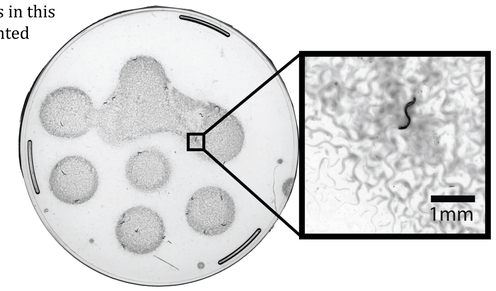
Lifespan:
Worms were put on agar plates on *E. coli* OP50, their food source, at 20°C. They were counted every day and marked as dead or alive.

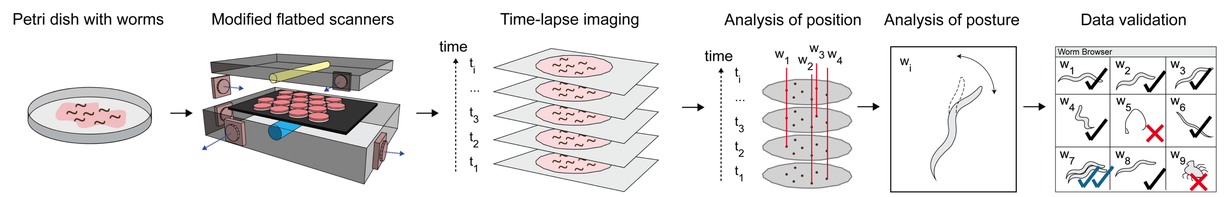
Oxidative Stress:
Worms were put on agar plates with 4mM tert-butyl hydroperoxide, an oxidant. As worms usually die within a few days in this condition, they must be counted much more frequently. This becomes impractical to do in a large scale by hand, so we used a lifespan machine.

Lifespan Machine

This machine automates the process by placing plates of worms on a flatbed scanner, which takes pictures of the plates at set time intervals. When there has been no movement of the worm between pictures, it is scored as dead.

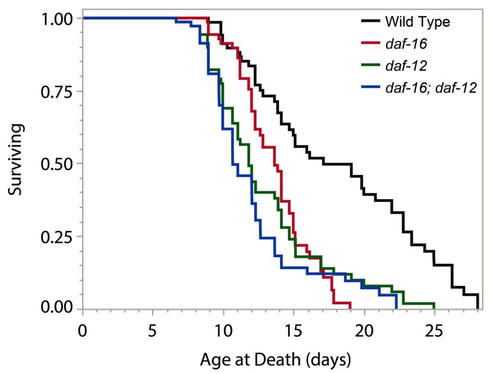
Figure 2: Imaging from a lifespan machine scanner.
Figure 3: Lifespan machine setup.

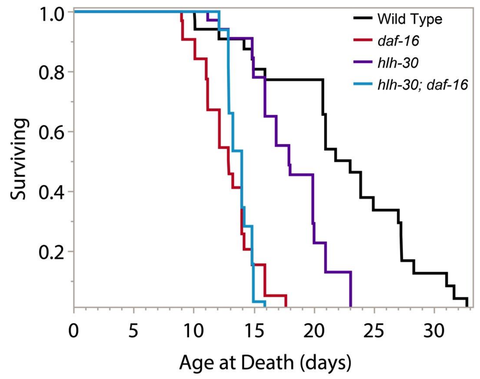




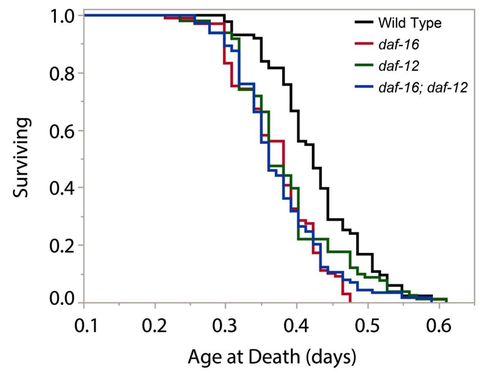
Results

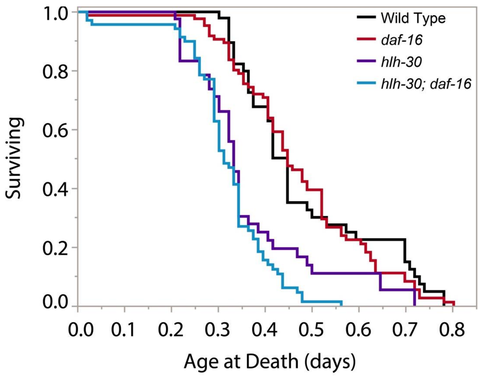
Lifespan





Oxidative Stress





Conclusions

Conclusions

This data suggests that *daf-12* and *daf-16* regulate aging in a very similar way.

It suggests similar interaction between *hlh-30* and *daf-16* in both lifespan determination and resistance to oxidants.

Impact

The unique feature of this research is the investigation of broad interactions between aging related genes.

It helps work towards the problem of beginning to understand the genetic control of aging. This becomes important in age related diseases, especially those with genetic linkages.

Going Forward

There is more work to be done, with hundreds of genes that can be studied. We have recently begun an in-depth analysis of another pathway implicated in aging, Transforming Growth Factor Beta, that looks promising in terms of analyzing interactions. This experiment demonstrates one small part of a much larger undertaking that still has much work to be done.

Acknowledgements

We would like to thank the entire Apfeld Lab, especially Javier Apfeld, for their support on this project.

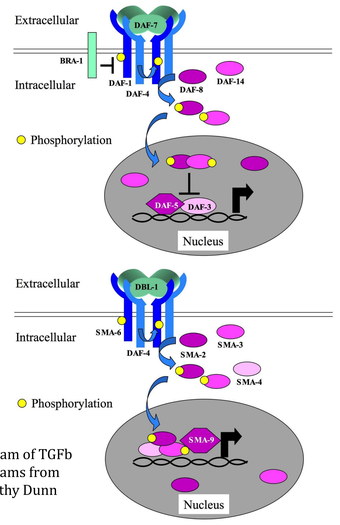


Figure 4: Diagram of TGFb Pathway. Diagrams from Wormbook, Cathy Dunn 2005.