

Effects of Coenzyme A on Longevity of *Caenorhabditis elegans*

Jordyn Musi

INTRODUCTION

Calorie restriction has been proven to delay aging and increase lifespan in a wide range of organisms, affecting many physiological systems and signaling pathways, but the exact mechanism is not yet well understood. Preliminary data suggests coenzyme A may be a key metabolite in this mechanism. Further research is needed to uncover and test this claim.

OBJECTIVE

The objective of this research study is to determine if coenzyme A is a critical metabolite involved in the increased longevity produced through calorie restriction.

HYPOTHESIS

In reference to Dr. Kondratov's preliminary data regarding elevated coenzyme A levels found in the liver of mice undergoing a calorie restricted diet, it is hypothesized that elevating CoA levels in *C. elegans* in the absence of dietary restriction will lead to an extension of average life span.

Time (Days from Egg)	Number Dead		Percent Alive		Time (Days from Egg)	Number Dead		Percent Alive	
	Wild Type (N = 58)	daf-2 (N = 41)	Wild Type (N = 58)	daf-2 (N = 41)		Wild Type (N = 58)	daf-2 (N = 41)		
0	0	0	100	100	31	0	0	88	88
9	2	0	97	100	32	5	0	76	76
13	5	0	88	100	33	4	0	66	66
14	2	1	84	98	34	4	0	56	56
15	4	0	78	98	35	1	0	54	54
16	1	0	76	98	36	0	0	54	54
17	12	2	55	93	37	1	0	51	51
18	2	0	52	93	39	6	0	37	37
19	4	1	45	90	40	0	0	37	37
20	3	0	40	90	43	2	0	32	32
21	2	0	36	90	45	2	0	27	27
22	2	0	33	90	47	2	0	22	22
23	2	0	29	90	49	2	0	17	17
24	5	0	21	90	51	0	0	17	17
25	2	0	17	90	53	1	0	15	15
26	2	0	14	90	55	2	0	10	10
27	1	0	12	90	58	1	0	7	7
28	2	0	9	90	61	1	0	5	5
29	2	0	5	90	62	2	0	0	0
30	3	1	0	88					

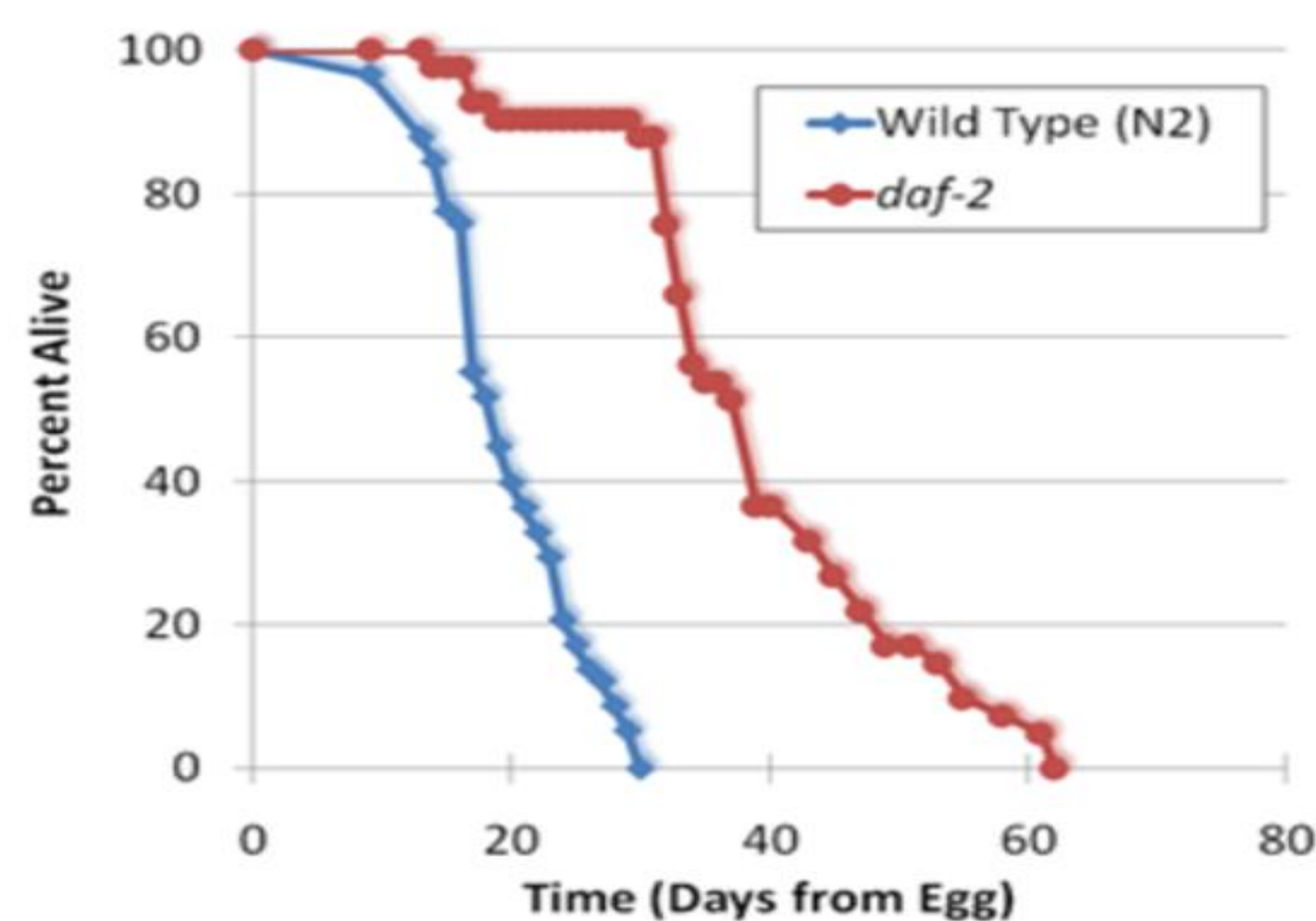


Figure 1. Data collected from a study¹ of *C. elegans* lifespan with a *daf-2* mutated gene. Table and graph show days and the corresponding number & percent of living versus deceased worms.

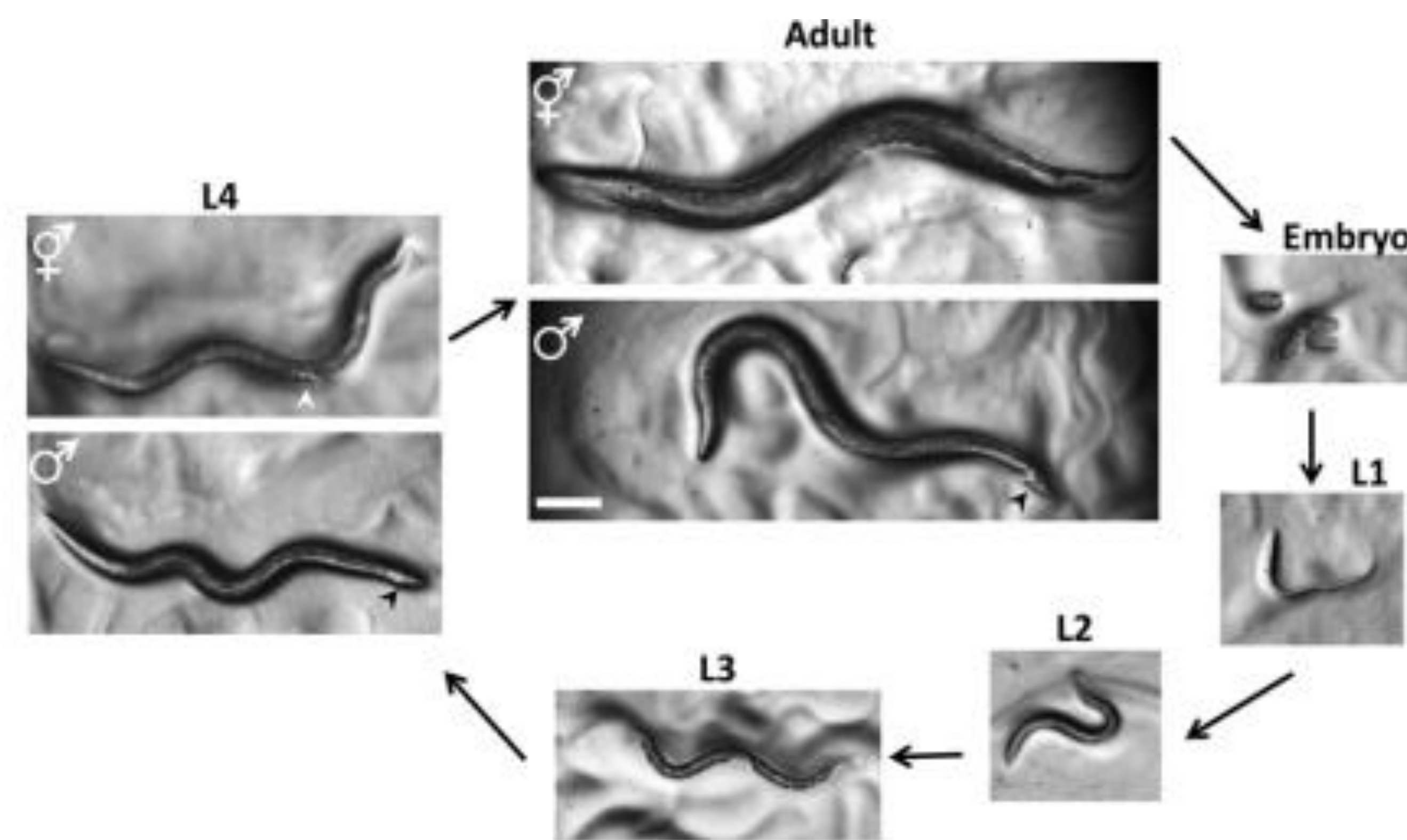


Figure 2. Stages of *C. elegans* life cycle. Larval stages (L1-L4) last approximately 48-52 hours after hatching from embryo. Adult stage is approximately 3 weeks².

CAENORHABDITIS ELEGANS

C. elegans have been used in countless longevity experiments due to their easily measured and short lifespan of approximately 25 days. These nematodes are less than 1 mm in length but are easily observed and handled under a microscope. They are transparent and with proper equipment, their internal organs can be observed without dissection².

Figure 1 represent sample data collected during a study of gene manipulation and *C. elegans* longevity¹. This data is similar to the data that will be collected in this study, though the effects—or lack thereof—that coenzyme A will have life span is currently unknown. This shows that this nematode's lifespan can be easily manipulated through genetic modifications, making them the ideal model organisms for longevity studies.

COENZYME A

Coenzyme A is a high energy metabolite utilized in the tricarboxylic acid (TCA) cycle as well as in beta oxidation of fatty acids. In its acetyl form (acetyl CoA), this molecule is an essential carrier/transporter in metabolic and anabolic pathways throughout the body.

In a fasted state, cells have an increased level of acetyl CoA within the mitochondria as compared to the cytosol, indicating an increase in the TCA cycle, oxidative phosphorylation, and fatty acid oxidation³ necessary for survival. This study will explore if the effects that calorie restriction/fasting has on energy metabolism and longevity in regards to increased utilization of acetyl CoA in the mitochondria can be replicated without dietary manipulation.

Choose **Ohio** First

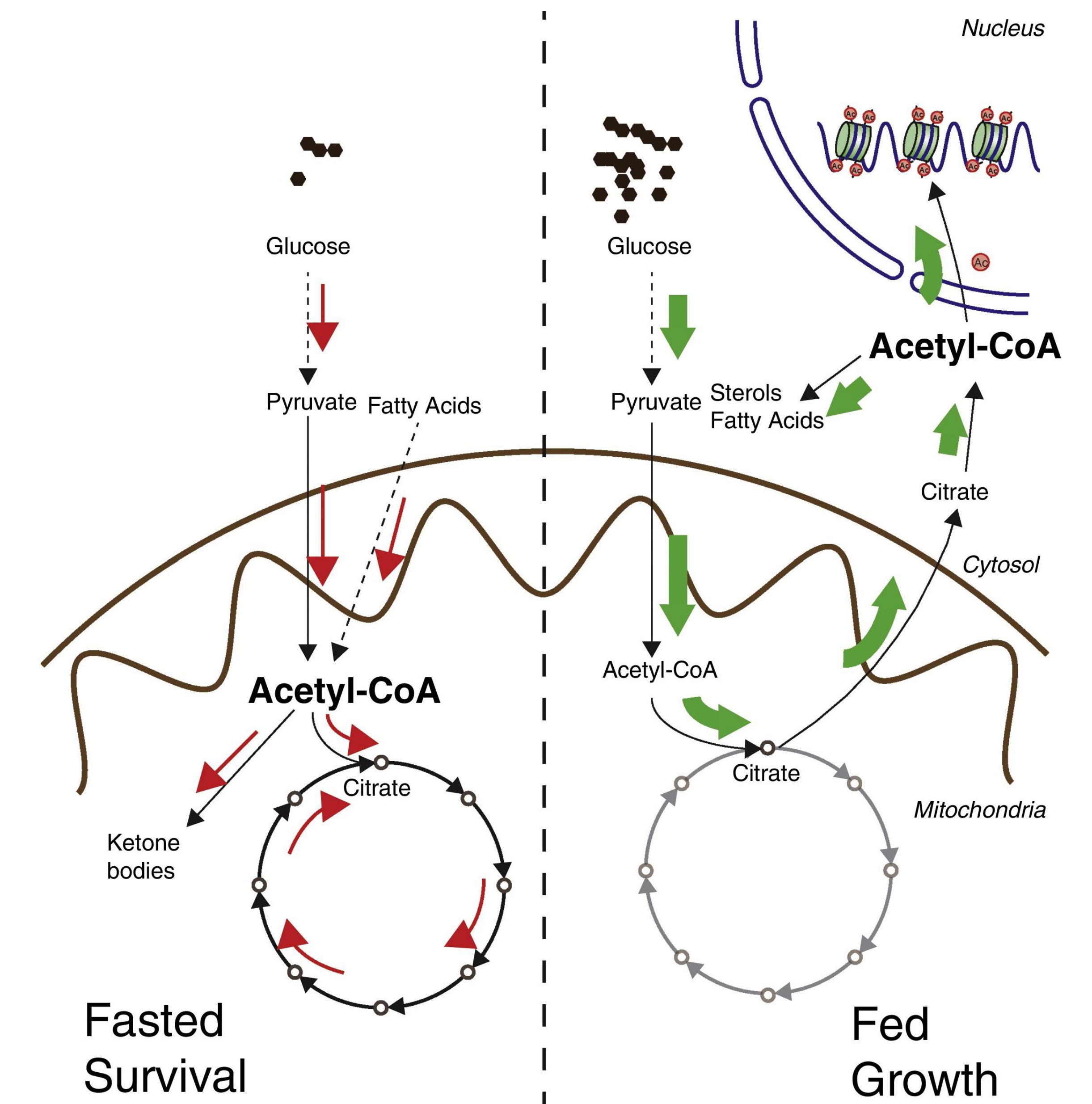


Figure 3. Fasted versus fed states of a cell utilizing acetyl CoA³. The fasted state shows an increased utilization of acetyl CoA in the mitochondria as compared to the cytosol.

PROPOSED METHODS

- Agarose gel is inoculated with coenzyme A
- E. coli* are cultured on agarose in petri dishes
- C. elegans* are grown from eggs on the experimental petri dish as well as on control petri dishes without coenzyme A inoculated agarose gel at 20°C
- Number of living and dead nematodes are counted and documented until all worms are deceased on the given plate
- Data is collected and compared regarding average lifespan on the experimental versus the control plates

References

- Sutphin GL, Kaeberlein M. Measuring *Caenorhabditis elegans* life span on solid media. *J Vis Exp*. 2009;(27):1152. Published 2009 May 12.
- Corsi AK. A Transparent window into biology: A primer on *Caenorhabditis elegans*. *WormBook*. 2015:1-31.
- Shi L, Tu BP. Acetyl-CoA and the regulation of metabolism: mechanisms and consequences. *Current Opinion in Cell Biology*. 2015; 33:125-131.

Acknowledgments

This work is funded by CSU USRA Program. Preliminary data is provided by Dr. Roman Kondratov. The author gratefully acknowledges Dr. Kondratov, Dr. Severson & the COF-Life Science program for their support.