Neurological and Behavioral Effects of L-Serine Concentration Alteration in Caenorhabditis elegans Diet

ALLISON SHAY, YUXI CHEN, and Katsushi Arisaka

UCLA, *Elegant Mind Club* @ Department of Physics and Astronomy

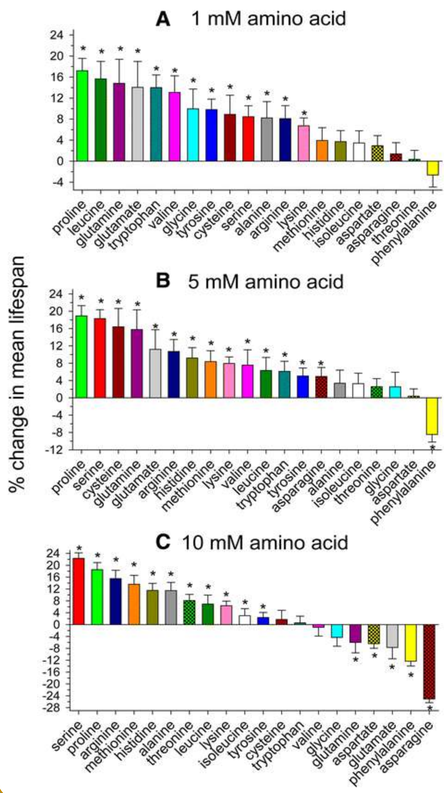
http://www.elegantmind.org

UCLA Science Poster Day on May 23, 2017

ABSTRACT

- Acetylcholine deficiency creates disparaging effects on muscle stimulation and sensory neurons, but it is unknown whether creating additional acetylcholine through L-serine precursors salvage neural function.
- Without this distinction, the connection between synapse development to behavior loss is undefined.To elucidate this mechanism, we look at the networks of forward and backward motion in *Caenorhabditis elegans*, which interact with each other to regulate escape reflexes.
- Because acetylcholine is crucial for worm synaptogenesis, we predicted that excessive concentrations exceeding 12 micromolars in L-serine will lead to the dauer stage and hypoxic conditions instead of aerobic metabolism.
- This study investigates the neurological effects of changing L-serine concentrations to understand the relationship between the nervous center and the metabolic pathway of C. elegans.

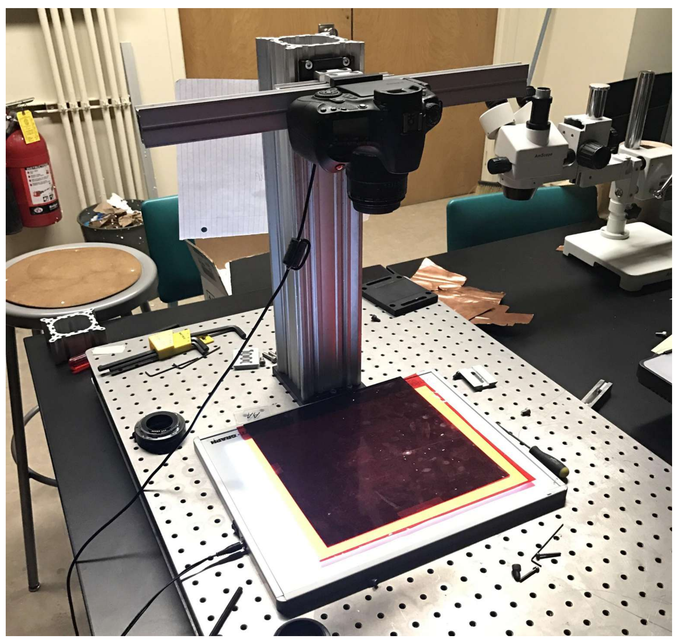
EXPECTED LOCOMOTION BEHAVIOR



According to a study on the effect of all essential amino acids for *C. elegans,* the majority of amino acids will provide an extension in average lifespan. The evidence provided by this study suggests that an increase in the rate of DNA repair causes hormesis in molecular level for the worms. 15 um appears to be the percent change in mean life span that will cause a negative change in average lifespan, in which case certain synaptic connections may have been damaged from excess urea release into the worm circulation system. Because amino acids cannot be stored, if the worm body cannot metabolize the amino acids quickly enough, free-floating urea will cause deamination in DNA, leading to negative percentages in lifespan and neural development.

C. Edwards et al. 2015

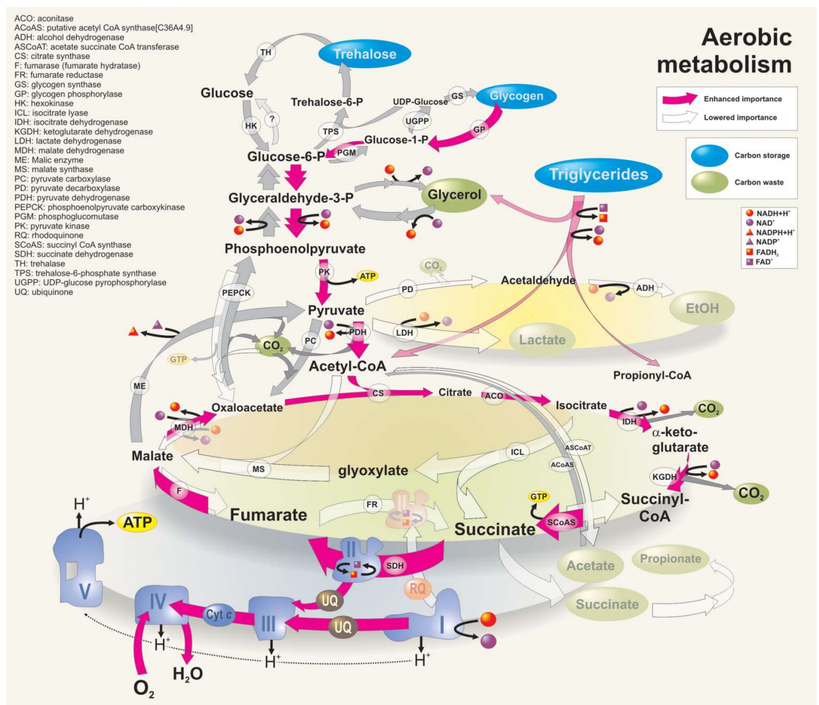
WORM TRACKING EXPERIMENTAL SETUP



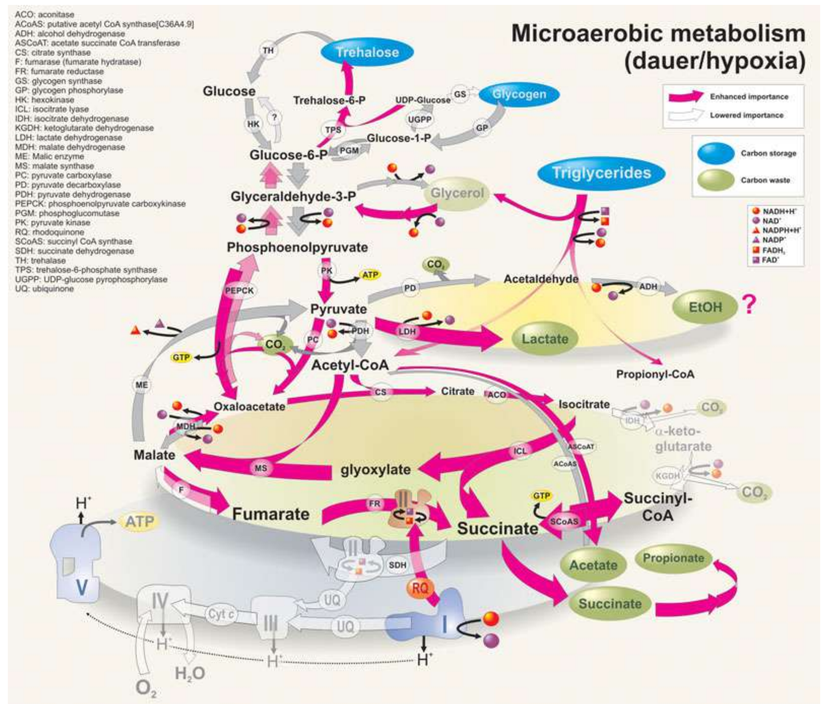
Above: Microscope setup with Canon 60-D camera and filtered light. Control QW1217 worms with regular dietary levels are traced in agar plates, then behavior is tracked and compared to that of L-serine treated worms using Worm Tracker.

OUR MODEL: TWO TYPES OF METABOLISM

C. Elegans Aerobic Metabolism



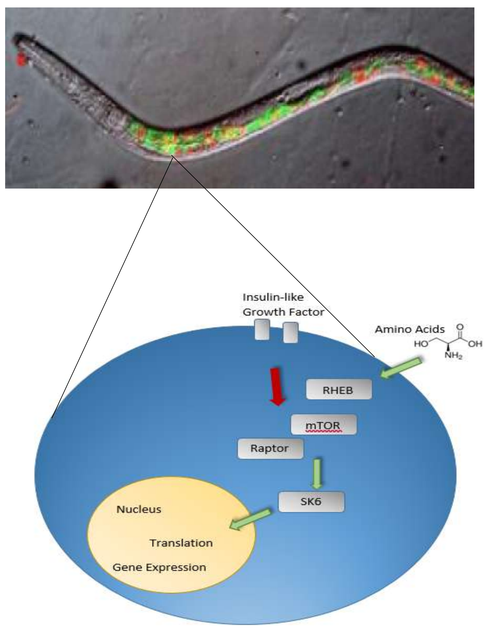
C. Elegans Dauer



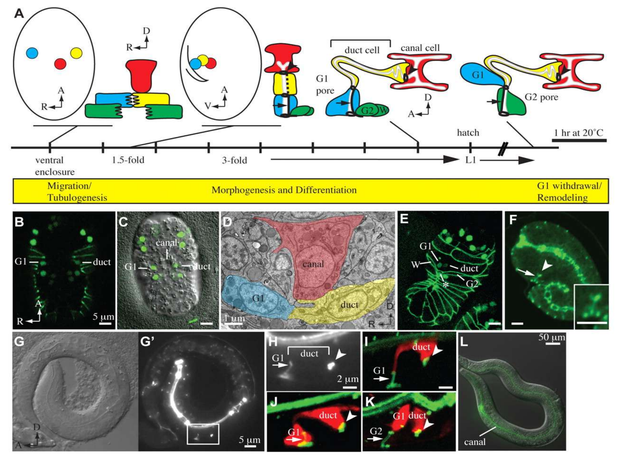
Left: Standard aerobic metabolism in *C. elegans.* Similar metabolic pathway to that of humans, beginning with glycolysis and utilizing similar co-factors. Note the difference in energy exchange requirements.
Right: Hypothetical model where dauer is a proportionally long term hypoxic state for *C. elegans*, in which the electron transport chain is not participant. This skips the production of alpha-ketogluatarate, which is often induced between growth stages, or as a means of survival in nutrient deficient states.

McElwee et al. (2006), Holt and Riddle (2003), and Burnell et al., (2005)

PATHWAY PREDICTION OF METABOLITES



Left:
- Excess serine levels will lead to rapid hydrolysis of acetylcholine, triggering the release of acetylcholinesterase.
- This subjugates the worm to a condition analogous to neurogenerative disease, disrupting the insulin-like signaling pathway (ILS).
- Following the protein signaling cascade within the cell, the genetic pathway is affected within the cell nucleus, increasing risks for life-span mutations and locomotion in inhibition.
- Changes in gene expression support the correlation between dauer length and adult durability.



I. Abdus-Sabooret al. 2011

Above: Excess L-serine molecules in concentrations of 15um or more will result in excessive urea productions leading to circulation of urea via intestine to the brain.

CONCLUSION

- As a result of excess serine intake, increasing levels of ammonia inhibit potassium transport into the brain's glial cells, causing an accumulation of potassium within the cell.
- The basicity of ammonia molecules will offset the pH in the worm, shutting off the chemo-electric gradient similar to the action potentials humans fire.
- Excess ammonia in the central nervous system may therefore lead to paralysis in the worm, or alteration in behavior and motion.
- Developmental defects in neural transmitters, behavior, and epigenesis (if worms are able to survive and mate) will yield a greater understanding of the relationship between the nervous center and the metabolic pathway of C. elegans, providing a new model for analysis on the connectivity in neurotransmission, supporting a connection between loss-of-function and endplate deficiency in the AChR.
- Further testing with various compounds to reverse hyperstimulation of nicotinic and muscarinic receptors can be used to observe effectiveness in counteracting hormesis in medical applications.

REFERENCES

[1] Edwards, Clare, John Canfield, Neil Copes, Andres Brito, Muhammad Rehan, David Lipps, Jessica Brunquell, Sandy D. Westerheide, and Patrick C. Bradshaw. "Mechanisms of Amino Acid-mediated Lifespan Extension in Caenorhabditis Elegans." BMC Genetics. BioMed Central, 03 Feb. 2015. Web. 08 May 2017.

[2] Abdus-Saboor, I., V. P. Mancuso, J. I. Murray, K. Palozola, C. Norris, D. H. Hall, K. Howell, K. Huang, and M. V. Sundaram. "Notch and Ras Promote Sequential Steps of Excretory Tube Development in C. Elegans." Development (Cambridge, England). U.S. National Library of Medicine, Aug. 2011. Web. 08 May 2017.

[3] Bart P. "Figure 2, Metabolic Flux in Aerobic Conditions. - WormBook - NCBI Bookshelf." WormBook: The Online Review of C. Elegans Biology [Internet]. U.S. National Library of Medicine, 01 Jan. 1970. Web. 08 May 2017.

ACKNOWLEDGEMENTS

Special thanks to:

- National Science Foundation IDPR program
- California Nanosystems Institute at UCLA
- UCLA Department Physics and Astronomy
- Javier Carmona
- Etta D'Orazio
- Steve Mendoza
- Phat Mai
- Joseph Thatcher