To Breathe, or Not to Breathe: Salmon Parasite Is the First Animal That Does Not Aerobically Respire

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Filet a juicy, pink salmon, and you might see white bulbs smaller than a grain of rice. These bulbs are known as tapioca, or milk flesh, a disease caused by the parasite *Henneguya salminicola*. For the consumer, these pests are a nuisance; yet for the scientific community, they are now a cause of great intrigue.

For a long time, it was believed that all animals depend on oxygen to survive. Collaborators from Oregon State University, the University of Kansas, and Tel Aviv University identified that this parasite no longer synthesizes energy using oxygen. Their paper in the Proceedings of the National Academy of Sciences describes the microscopic parasite, *H. salminicola*, and what makes it so different from us that allows it to live without air.

What is *Henneguya salminicola*?

Henneguya salminicola is a parasite that grows in annelid worms and the skeletal muscles of salmon off the Pacific coasts of Oregon, Canada, Alaska, and Japan. More broadly, it belongs to a group of organisms known as cnidarians, which include jellyfish, sea anemone, and coral. According to the peer-reviewed book *Transmission Biology of Myxozoa*, *H. salminicola* does not harm its hosts but poses a threat to fisheries due to the reduced marketability of the fish. The unsightly appearance of the salmon due to tapioca disease makes them harder to sell.

Why do we need oxygen to stay alive?

Our bodies use oxygen to produce adenosine triphosphate (ATP), a chemical compound that fuels all of our physiological processes. This process termed aerobic, or oxygen-dependent, cellular respiration occurs in compartments within our cells termed mitochondria.

Although we can produce some ATP under anaerobic (without oxygen) conditions, such as when we are performing rigorous exercise, it is not sustainable to generate energy. We only generate 2 ATP per round of anaerobic respiration, in contrast to the ~32 ATP that we can produce in a round of aerobic respiration. Additionally, anaerobic respiration makes an acidic byproduct, which proves to be toxic to our cells. While some organisms solely use anaerobic respiration, before *H. salminicola*, none that were previously identified were multicellular.

What makes *Henneguya salminicola* different from other multicellular organisms?

While most of the genes in complex organisms are found in the nucleus, mitochondria also contain genetic information, mtDNA, which helps them produce some of the key factors involved in aerobic cellular respiration. In the study where the anaerobic property of *H. salminicola* was found, the researchers originally sought to compare the mitochondrial genome between *H. salminicola* and its close relative.

When the researchers examined all of the genetic information in *H. salminicola*, they found that there was no mtDNA, meaning that they are deficient in some of the factors for aerobic ATP synthesis. Further, the parasite lacks the nuclear-encoded proteins that are needed to make additional mtDNA copies. This explains why *H. salminicola* lacks mtDNA altogether, rather than the alternative of having mtDNA with so many mutations that renders it unusable by the parasite.

Next, the researchers asked if the loss of mtDNA meant that the parasite no longer relied on aerobic respiration. To do so, they examined the parasite's nuclear genome, which encodes additional aerobic respiration factors. They found that *H. salminicola* has a large reduction in the proteins involved in the oxidative phosphorylation, the specific step that uses oxygen to make ATP. The close relative of *H. salminicola*, *Myxobolus squamalis*, has about 18-25 genes in common with the fruit fly, an organism with aerobic respiration genes similar enough to our own that many researchers use it as a model for human metabolic process. In stark contrast, *H. salminicola* only has seven of these genes. More specifically, genes encoding complex I, III, and IV — the main cellular machinery for oxidative phosphorylation — can be found in *M. squamalis* but are missing in *H. salminicola*. Overall, these results are enough evidence to strongly suggest that *H. salminicola* does not perform aerobic respiration.

Why and how the parasite rid itself of mtDNA is still a cause for speculation. The researchers posited that the *H. salminicola* adapted to its reduced-oxygen environment inside of its hosts, both inside annelid worms and the skeletal muscles of salmon. This is in contrast with the environment of *Myxobolus squamalis* — its relative that resides in the skin of fish like rainbow trout — which would have access to oxygen. The authors also cited research suggesting that losing extra genetic information is energetically favorable for small organisms. Together, these findings suggest that the ancestors of *H. salminicola* that were both tolerant of the reduced oxygen environment and were amenable to acquire massive genetic mutations, were able to outcompete others in their population and thrive without air.

The future of *H. salminicola* research

The knowledge that *H. salminicola* respires anaerobically provides new insight on how to treat salmon with tapioca disease; researchers from Sweden previously found that single-cell anaerobic organisms are sensitive to certain drugs. Perhaps in the future, *H. salminicola* may be completely eradicated by treating the salmon with these antibiotics.

This research challenges the general notion that over evolutionary history, organisms become more complex. For *H. salminicola* to lose aerobic respiration, a hallmark function of animals, it raises the questions: have other closely related animals also lost this function, and what evolutionary lineages of animals can accomplish this under the right evolutionary pressure? It is still unclear how *H. salminicola* produces energy; investigating the anaerobic respiration mechanism utilized by *H. salminicola* may aid researchers in screening for other animals that do not perform aerobic respiration. If researchers identify any novel genes involved in the parasites' metabolic processes, they could search for analogous genes in other organisms.

It would also be of interest to continue to study subsequent populations of *H. salminicola* to see if the remaining nuclear genes involved in aerobic respiration become further mutated over time. As we continue to change the environmental landscape, including the chemical composition of the ocean, it is worthwhile to understand how other organisms will adapt to these changes.

REFERENCES

Löfmark, S. and Edlund, C., Nord, C. E., (2010). 'Metronidazole is still the drug of choice for treatment of anaerobic infections', *Clin. Infect. Dis.*, 50, S16–S23. available: https://www.jstor.org/journal/clininfedise.

Lynch, M. and Marinov, G. K., (2015). The bioenergetic costs of a gene. *Proc. Natl. Acad. Sci.*, 112, 15690–15695. available: https://www.pnas.org/content/112/51/15690.long.

Yahalomi D., Atkinson, S. D., Neuhof, M., Chang, E. S., Philippe, H., Cartwright, P., Bartholomew, J. L., and Huchon, D. (2020). 'A cnidarian parasite of salmon (Myxozoa: *Henneguya*) lacks a mitochondrial genome', *PNAS*, 201909907; available: https://www.pnas.org/content/117/10/5358.

Yokoyama, H., Grabner, D., Shirakashi, S. (2012). 'Transmission Biology of the Myxozoa, Health and Environment in Aquaculture' in *Transmission Biology of Myxozoa*. Carvalho, E. D., David G. S., Silva, IntechOpen; available: https://www.intechopen.com/books/health-and-environment-in-aquaculture/transmission-biology-of-the-myxozoa.