

Evolution & Behaviour

Algae Living in Salamanders, Friend or foe?

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This Break was edited by Anatoly Kozlov, *Scientific Editor* - TheScienceBreaker

Roughly speaking, our bodies use energy from the sun, but we can't use sunlight directly. Instead, plants and algae collect sunlight and store it as chemical energy through the process of [photosynthesis](#). We can access that fuel directly when we eat plants, or indirectly when we eat other animals that eat plants.

However, in some invertebrate animals (those without a backbone) the relationships to algae are more intimate. Tiny single-celled algal "symbionts" can actually live inside the cells of living corals and small animals like hydra that live in water. The algae live in a safe environment inside animal cells and are provided with building block materials to function. They use sunlight to convert the building block materials into larger molecules to store energy and build cellular structures. At the same time some of that stored solar energy is directly transferred to the host animal, allowing it to live in otherwise nutrient poor environments. Thus the algae and their hosts depend on one another to live and thrive. These mutually beneficial relationships are called **photosymbioses**.

Photosymbiosis was thought to be absent between algae and vertebrate animals (those with a backbone). One reason for that absence is differences in the immune system between vertebrates and invertebrates. Vertebrate immune systems very specifically recognize invaders and remember them, precluding the long and frequent interactions thought necessary to form a cell-in-cell symbiosis. But there is an exception for that.

The egg fluid of the yellow spotted salamanders is colonized by a microscopic green alga. The relationship was first described by naturalist

Henry Orr in 1888. Then, in 2011 it was discovered that the algal cells actually enter the salamander's tissues and sometimes live within the salamander's cells. In a way the algal cell inside salamander cell relationship resembles the interaction of algae and corals, but on the other hand the only known cases of cell-in-cell relations in vertebrates are parasitic infections, like malaria. So how complementary is this salamander-algal interaction?

To understand the salamander-alga relationship, we had to look inside the cells. The variety of [RNA molecules](#) (or "expressed genes") in a cell can tell us if a cell is experiencing stress, enacting an immune system response, or undergoing metabolic changes due to some external or internal perturbations. We decided to measure gene expression differences that occur in the alga and the salamander when algae enter salamander cells. This can be done by sequencing (stable) DNA molecules that are reconstructed from (short-lived) RNA molecules of each sample.

Gene expression differences in the algal cells revealed a remarkable response to their new intra-cellular environment. Green algae live off sunlight; making sugars from light, then like us metabolizing them through aerobic respiration. But in low oxygen environments they can also live like yeasts, metabolizing sugars through fermentation. Our experiments showed that algae swimming around in water and in egg fluids use the more common photosynthesis and respiration combination for life. However, algae living inside salamander cells have switched from respiration to fermentation.

In contrast, differences in the salamander RNAs revealed subtle differences from salamander cells that lacked algae. The most striking was the lack of an all-out assault on the algae, as would be expected if the alga was recognized as a pathogen that caused disease. Instead, the salamander cells had what looked like a tuned down immune reaction in response to these entirely foreign algae. It could be that the salamander deliberately recognizes the alga as "friend". But it also could be that the alga tricks the salamander's immune system through some crafty, but unknown mechanisms.

This revelation about the alga's metabolism puts a new twist on the relationship between alga and salamander. It is unlikely to be perfectly analogous to coral-algal photosymbioses because the alga in the salamander is converting sunlight to useable sugar with much lower efficiency. Also fermentation is seen in other cell-in-a-cell relationships in vertebrates, but so far only in parasites, like malaria. At the same time the salamander's tepid immune response has implications for the flexibility of our own immune systems during early development. The algae are entering salamander cells during early development, while the salamander immune system is still learning to differentiate between self and non-self. It is possible that in these salamanders, the alga is becoming recognized as "self" to the salamander.

It is the parallels with beneficial symbionts, such as those found in corals, or parasites, like malaria, that makes the unique relationship between salamander and alga so exciting. Our research has found similarities with both. Future work will further reveal the rules that govern when and how cells coexist in these intimate cell-in-a-cell relationships.