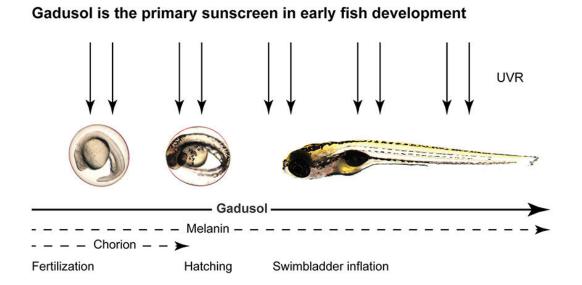
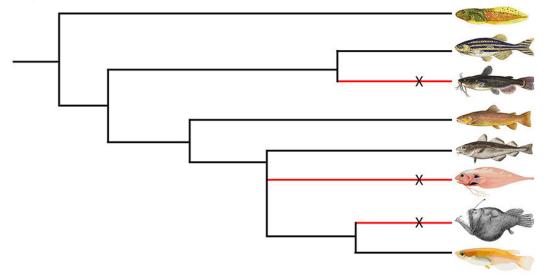


## Gadusol: Powerful 'sunscreen' that protects early stages of fish development

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# Gadusol biosynthesis has been lost repeatedly in species no longer exposed to the sun





Graphical abstract. Credit: *Current Biology* (2023). DOI: 10.1016/j.cub.2023.06.012

As outside activities become more popular with the changing seasons, people are looking to protect themselves from sunburns and melanomas, primarily using commercial sunscreens.

However, humans aren't the only species that have to worry about damage from exposure to the sun's ultraviolet rays. Many creatures use sunscreen, just not the white lotions that humans are familiar with. Their sunblock is encoded in their DNA.

For years, Utah biologist James Gagnon's lab has studied gadusol, a chemical compound in fish, resulting in a new paper demonstrating how females excrete the compound on their eggs. The gadusol molecule was discovered in fish more than 40 years ago, and was originally thought to come from dietary sources. It has since been proven that gadusol is produced from metabolic pathways within the fish. The findings are published in the journal *Current Biology*.

With help from colleagues in the School of Biological Sciences and Department of Human Genetics, doctoral student Marlen Rice is the lead author. Gagnon, an assistant professor of biology, is listed as the senior author.

Rice grew up on a farm an hour south of Salt Lake City and earned a degree in <u>molecular biology</u> at Utah State University. "The fun thing to me about biology is just the fact that [living] things are dynamic and they interact [with] their environment," Rice said. "I like thinking about animals in relation to ecology."



He aspires to bridge the gap between the ecological and molecular fields. Rice's lifelong passion for animals and his industry background inspired him to use laboratory tools to investigate <u>ecological factors</u>, starting with sunlight, which sustains all life, but also presents a danger.

#### Ultraviolet exposure

Nearly all life on Earth depends on the sun, whether it's tapping its energy to produce food, or consuming other organisms. But exposure to ultraviolet radiation (UVR) comes at a cost. Wavelengths in UVB rays are especially dangerous, causing damage at a <u>molecular level</u> and leading to mutations in DNA. Excessive levels of UVR exposure can even kill cells, a process known as apoptosis, resulting in what we know as a sunburn. Even in the water, organisms are not safe because biologically harmful levels of UVB can penetrate more than 10 meters deep.

Protection lies in sunscreens which absorb UV photons before they penetrate vulnerable cells and dissipate this absorbed energy as less harmful heat, according to Rice and Gagnon's paper. They act as physical shields over precious genetic material in cells, preventing damage and mutations.

Organisms across many habitats have developed adaptations, including nocturnal lifestyles and DNA repair mechanisms, to avoid and fix the harm associated with UV exposure. But some have evolved an ability to create their own chemical sunscreens.

"Since sunlit habitats can have significantly nutritive advantages over dark environments and because no repair pathway is completely efficient, many organisms employ sunscreens to avoid UVR damage from occurring in the first place," the paper said.



### Mutant zebrafish

Initially, Rice considered melanin as the primary sunscreen in <u>aquatic</u> <u>life</u>. Melanin is produced in melanophores that migrate to cover parts of the brain and body as fish embryos mature.

To test this hypothesis, Rice altered the genotype in zebrafish to knock out the gene for melanin production. He found that zebrafish embryos died from UVR exposure at the same rate, regardless of whether or not their genotype was altered. There must be something else protecting the embryos.

Through CRISPR-Cas9 gene editing, Gagnon's lab created gadusoldeficient mutant zebrafish to test whether gadusol provide UV protection. Zebrafish were chosen for these experiments because they inhabit sunlit waters, produce gadusol and are amenable to genetic manipulation.

He determined that gadusol is provided for zebrafish embryos by the mother, is the most effective sunscreen over other methods of protection and is lost evolutionarily in <u>fish species</u> when their embryos are not exposed to sunlight.

#### 'Transparency as camouflage'

To demonstrate gadusol's importance to the survival of larval fish, Rice delivered precise doses of UVB to both the mutant and unaltered <u>zebrafish embryos</u> and measured the effect on swim bladder inflation. When exposed to the same dose, the gadusol-deficient mutant fish were all unable to inflate their swim bladders, indicating that the UV exposure had caused significant developmental defects.



A Boston-based beauty company is now looking to synthesize gadusol to create sunscreens that would be safer for both humans and <u>marine</u> <u>environments</u>. For fish, gadusol offers advantages over other sunscreens due to its invisibility. "Transparency as camouflage," the study said, "is a common trait in aquatic animals, especially in the open ocean where there is nothing to hide behind."

Melanin's main drawback is it absorbs most wavelengths in the visible light spectrum as well as the UVB spectrum, so it is detectable by predators. Sunlight, meanwhile, is just one of many challenges that aquatic ecosystems pose to their inhabitants.

"The environment that they evolved in, which is filled with sunlight and viruses and predators and temperature switches and all this crazy stuff that doesn't happen in our fish facility," Gagnon said, "and so if you can bring a little bit of that into our laboratory, now we can apply what's cool to more questions."

These <u>environmental factors</u> will guide the lab's research with zebrafish moving forward. Rice is also curious about the evolutionary history of gadusol itself.

"I'd really like to fill out on the tree of life how widespread gadusol is," Rice said. "At some point, land vertebrates stopped using gadusol. I think evolutionarily it'd be really interesting to think about that. At what point did they move away?"

The answers to these mysteries lie within—within DNA to be specific.

"I really do love the idea of DNA. I think it's a really beautiful thing," Rice said, "the fact that it's an unbroken chain of DNA replication and now lives inside of you."



**More information:** Marlen C. Rice et al, Gadusol is a maternally provided sunscreen that protects fish embryos from DNA damage, *Current Biology* (2023). DOI: 10.1016/j.cub.2023.06.012

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