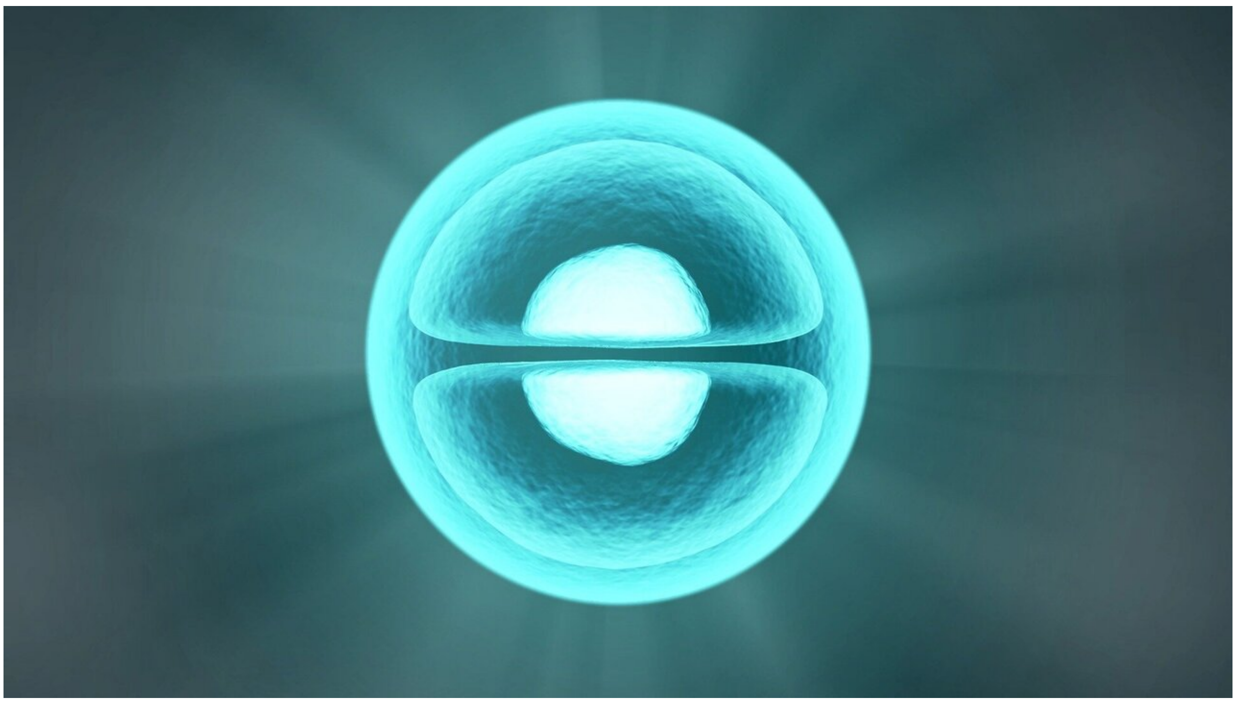
Biologists zero in on cells' environmental sensing mechanism

July 28 2020, by Craig Albertson



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Evolutionary and developmental biologist Craig Albertson and colleagues at the University of Massachusetts Amherst report that they have identified a molecular mechanism that allows an organism to change the way it looks depending on the environment it is exposed to, a process known as phenotypic plasticity.

In addition to lead investigators Albertson and Rolf Karlstrom, the team includes recently graduated doctoral students Dina Navon and Ira Male, current Ph.D. candidate Emily Tetrault and undergraduate Benjamin Aaronson. Their paper appears now in *Proceedings of the National Academy of Sciences.*

Albertson explains that the project stems from a desire to better understand how genes and the environment interact to direct anatomical shape. "We know that our features are determined by genes, but we also know that many physical features are shaped by the environment as well. In identical twins, for example, if one becomes a long-distance runner and the other a body builder, they are going to end up with very different physiques. The skeleton is especially sensitive to such environmental inputs."

Albertson works with a system—cichlid fishes—known throughout the scientific world as champions of phenotypic plasticity that can alter, in a single season, jawbone hardness or shape to match feeding conditions. They are also well known for their rapid evolution and diversity in jaw shapes, which has enabled cichlids to adapt to many different food sources, including algae, plankton, fish, snails and even the scales of other fishes.

Albertson has spent much of the past two decades trying to reveal the genetic differences that underlie differences in jaw shape between species. Now he and colleagues identify the well-studied chemical/molecular system known as the Hedgehog (Hh) signaling pathway as an important player. More recently he explored whether the same pathway might also contribute to differences in jaw shape that arise within species through phenotypic plasticity.

An important clue came as Albertson learned more about how this molecular pathway works. He explains, "There is a well-known mechanosensor on most cells, including those that make the skeleton, called the primary cilium. Cells that lack this organelle are unable to sense or respond to environmental input, including mechanical load. It turns out that several key protein components of the Hedgehog pathway are physically associated with this structure, making it an obvious candidate for an environmentally sensitive signal."

In the current study, the research team first showed that plasticity in the rate of bone deposition in cichlids forced to feed using different foraging modes was associated with different Hh levels. Greater levels of the signal were detected in fish from the environment where more bone was laid down and vice versa. To really nail the question, Albertson teamed up with Karlstrom, who had previously developed sophisticated tools to study Hh signaling in zebrafish.

He explains, "Rolf has a bunch of really slick transgenic systems for manipulating that molecular signal in real time. It is sort of like a volume knob on your stereo—you can turn it up or turn it down, and then see how it influences your trait of interest." In this case, they wanted to see whether Hh levels influenced plasticity in bone deposition rates.

They found that unmanipulated zebrafish deposited different amounts of bone in different foraging environments. When Hh levels were reduced, these differences went away, but when Hh levels were increased, differences in bone deposition rates were dramatically increased.

Albertson, explains, "Bone cells in these fish are innately sensitive to different mechanical environments. But we were able to play with this system using a single molecular switch—you turn up the Hh signal and the cells become more sensitive to the environment, or you turn the molecular sensor down and the cells become almost deaf to the environment."

"That the same molecular machinery underlies both the evolutionary divergence and plasticity of the jaw is notable," Albertson explains. "It is consistent with long-held theory that suggests short-term plasticity might bias the direction of long-term evolution, which explains why evolution can be predictable in lineages that have repeatedly evolved to similar habitats." Albertson adds, "The Hh signal has also been shown to regulate plasticity in beetle horns, so there may be something special that positions it to be an environmental sensor across tissues and animals."

Such intriguing questions will be the topic for future investigations, the authors add.

More information: Dina Navon et al, Hedgehog signaling is necessary and sufficient to mediate craniofacial plasticity in teleosts, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.1921856117

Provided by University of Massachusetts Amherst