Selective expression of genes through epigenetics can regulate the social status of african cichlid fish

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Stanford researchers have demonstrated how flexible gene expression can enable male cichlid fish to achieve higher social status. Credit: L.A. Cicero

For a small African fish species, a colorful dominant male does better in

life, winning access to food and females. New research by Stanford biologists suggests that this lucky outcome is regulated at a genetic level, by turning genes on and off.

People generally think that our genetic code, and thus the expression patterns of our genes, is fixed throughout life. Indeed, this is true in some cases such as eye color, a characteristic that is determined by gene expression early in development. However, scientists have recently found that gene regulation can also happen in an ongoing fashion through epigenetic processes, with the potential to change behavior throughout a lifetime.

Through epigenetics, gene expression can be turned on and off like a light switch via several mechanisms. Through one of these mechanisms called DNA methylation, methyl molecules are added to genes, preventing them from being expressed.

In a study published in *PLoS ONE*, researchers from Stanford report that social status in cichlid fish may be regulated by DNA methylation.

"Status differences exist in all social organisms," said Russell Fernald, a biology professor at Stanford University and senior author of the study. "Our work reveals how social dominance status is possibly regulated through methylation, which is important because individuals higher in rank generally enjoy better health and quality of life."

A show of social dominance

In 2004, a study by researchers at McGill University showed that the nurturing behavior of mother rats affected their offspring. Pups that were nurtured more grew up to be less stressed as adults, while pups that received less nurturing grew up with more anxious tendencies. This difference was caused by methylation of a gene for a stress receptor,

explained Fernald, the Benjamin Scott Crocker Professor of Human Biology. Subsequent research has revealed other examples through which epigenetics can alter our gene expression patterns by experiences during our lifetimes.

Fernald studies Astatotilapia burtoni, one of the hundreds of cichlid fish species inhabiting Lake Tanganyika in eastern Africa, because of the unique ways they have evolved over time. For male A. burtoni, dominance is everything. They battle frequently for territory, with the victor winning access to the two most important resources – food and females.

Sporting bright rainbow-colored scales, high-ranking males aggressively defend their foraging grounds and lure females into their territory to dine on decaying matter on the lakebed. In contrast, the low-ranking males, which are dull grey in color, comprise 80 percent of the population but cannot reproduce and must swim with the females to get access to food.

But even the dominant males must fool the females into mating. This is tricky, as A. burtoni are mouth-brooders. After laying eggs in the sand, the female scoops them up in her mouth to brood them until hatching, which poses a logistical challenge for fertilization. The ingenious evolutionary solution to this dilemma is a version of oral sex.

The dominant male flashes his anal fin, which is adorned with spots that look like enormous eggs, and which are laced with sperm. When the female sees those spots, she goes after the male's anal fin as if trying to collect some eggs she dropped, collecting sperm in the process and fertilizing the eggs in her mouth.

"In this species, only the macho males get to mate and non-dominant males cannot reproduce, so the stakes are enormously high," Fernald

said.

Changing social status

But some social mobility is possible. Because the flashy dominant males are more vulnerable to predation, whenever a boss fish disappears, a major battle ensues as non-dominant males fight to take over the vacant territory. The winner then ascends to dominant status resulting in an astonishing series of physiological changes, including rewiring of parts of the brain as previously reported by Fernald's group.

Given the importance of status, Fernald wondered whether these dramatic changes were driven by gene expression.

"If we altered gene expression through changes in methylation, could we influence change in social dominance?" he asked.

With a graduate student, Kapa Lenkov, Fernald tested this directly in cichlids raised in his Stanford lab. Several pairs of non-dominant males matched in size were each placed in an aquarium that could support only one territory. In each pair, one male was injected with a methylating agent while the other received a methylation suppressor, and the two fish fought for dominance.

"We could see the behavioral change in a matter of minutes, as one animal began to dominate the other," Fernald said. "Videos of these confrontations showed that the fish injected with the methylating agent were much more likely to be the winners, while those receiving the methylation suppressor typically lost the fight for dominance.

"It was remarkable that we could determine which fish became dominant by changing the range of genes expressed in this context," he said.

Fernald's work suggests that epigenetic processes may cause, rather than simply reflect, changes in dominance status in hierarchically organized species, said Tom Boyce, a professor at the University of California, San Francisco School of Medicine, who was not involved in the study.

"This has implications for humans and nonhuman primates, since hierarchical behavior and social dominance relations appear early in life and remain important throughout the lifespan," Boyce said.

"DNA methylation is potentially a way through which social dominance is regulated in many social organisms, including people," Fernald said. "The next step will be to identify which genes are responding to methylation in causing this change in dominance."

More information: Kapa Lenkov et al. Epigenetic DNA Methylation Linked to Social Dominance, *PLOS ONE* (2015). DOI: 10.1371/journal.pone.0144750

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