Scientists discover the gene that codes for the gold coloration of Midas cichlids

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A pair of Midas cichlids (here: Amphilophus xiloaensis) from the Nicaraguan crater lake Xiloá, protecting their offspring. Credit: Ad Konings, Cichlid Press

All he touched turned to gold, according to the legend of King Midas from Greek mythology.

All Midas cichlids from Central America start out life as black-and-white striped fish and then some of them gradually lose their black colouration and turn bright gold. Behind the "golden touch" in this case is not the Greek god Dionysus, but a heretofore unknown gene. A team of scientists led by Konstanz biologist Professor Axel Meyer has now published the discovery and characterization of the gene in the journal *Nature Communications*, along with a description of variants that might cause the color polymorphism in these fish.

One species, different versions

Sometimes, individuals of the same species differ greatly in their shape or colouration. Scientifically, this phenomenon is referred to as "polymorphism." The 13 fish species that belong to the Central American Midas cichlids (Amphilophus cf. citrinellus) and live in crater lakes in Nicaragua are a vivid example: While these fish always have a dark colouration at first, the "genetically golden" ones turn orange—usually when they become sexually mature—resulting in two color variants among the adults.

The color change from dark to golden, which occurs in about 10 percent of the animals, is, strictly speaking, a decolourization: Over the course of a few weeks, cells containing the dark pigment melanin in the skin of the fishes increasingly die and thus cause the bright orange/yellow color of the golden adult animals. This pigment is the same that determines the color of hair and eyes in humans. So it is the loss of dark, melanin-containing cells that brings out the vibrant colors of the fishes.

In search of the genetic cause

As the colouration of the Midas cichlids has fascinated scientists since its discovery over 100 years ago, it has been known that the gold colouration is passed on from one generation to the next. The inheritance of the trait follows classical Mendelian rules, and the gold colouration is the dominant trait.

"Similar to us humans, the chromosome set of the fishes is present in duplicate in every cell. Since the golden colouration is dominant over the dark color type, a single genetic copy of the 'gold variant' per cell is sufficient for the fish to develop the golden colouration in the course of their lives," explains Axel Meyer, professor at the Department of Biology at the University of Konstanz.

In past studies, the Meyer lab was able to narrow down the location of the genetic cause for the color polymorphism of the Midas cichlids to chromosome 11. However, the genetic mechanism responsible for the color change of the fish remained unknown until now. To get to the bottom of the mystery, the researchers analyzed genetic material from dark and golden Midas cichlids from crater lakes using association mapping. The observable trait of colouration is mapped onto a genetic map of the fishes' genome over generations through genetic crossing, whereby the variation between cohorts of siblings and their grandparents localizes the genetic cause of the trait on the genetic map.

"The first thing we noticed in this analysis were inconsistencies in the results. Something did not quite fit; literally, a piece of the puzzle was missing," says Axel Meyer.

The 'goldentouch' gene

The Konstanz scientists suspected that the existing reference genome of the Midas cichlid used for the analysis might be incomplete, in the sense that it did not contain the gene responsible for the colouration at all.

Consequently, they decided to produce an improved reference genome using the new long-read sequencing method. This part of the study was mainly carried out by Dr. Frederico Henning, now professor at the Federal University of Rio de Janeiro (Brazil), and Dr. Claudius Kratochwil, now working as a group leader at the University of Helsinki (Finland). Both are former postdocs of Axel Meyer's research group.

To do this, the complete genome of a lab-raised Midas cichlid that was heterozygous for colouration was sequenced. Heterozygous means that the individual fish has the genetic information for the golden colouration on one copy of its chromosome 11, and that for the dark color variant on its other chromosome 11. Then the researchers repeated their original analysis.

"We first discovered a previously undescribed gene on chromosome 11 in our new reference genome, which was present in two different variants in our fish: Variant d for 'dark' and variant G for 'golden,'" Axel Meyer reports.

Repeating the mapping studies then revealed that this gene is very likely to be associated with the colouration of the Midas cichlids: Fishes with a double copy of the d variant showed a dark colouration in adulthood, whereas those with one or two copies of the dominant G variant showed an orange/yellow colouration. In reference to the legend of King Midas, the researchers named the newly discovered gene "goldentouch."

Further investigations

The results thus provided the first strong indication that the goldentouch gene is likely to play a significant role in the development of different color variants in Midas cichlids. To learn more about the newly described gene, the researchers continued with a series of molecular follow-up experiments. Initially, they found that the gold variant of the gene is significantly longer than the dark variant. The reason for this is a piece of selfish DNA that has migrated into the gene—a "jumping gene," or transposon. This extra piece of genetic code causes the gold variant of the gene to fold differently at the molecular level than the dark variant. This, in turn, has consequences for the gene expression—the synthesis of proteins as the end product of the information contained in the gene.

The researchers also found that in all color variants of the Midas cichlid, the gene is switched on mainly in the scales, but almost not at all in other locations, such as the internal organs. This underpins a specific function of the gene products in the outer skin layers of the fishes. "We also found that the goldentouch gene is expressed to a lesser extent in the scales of the golden Midas cichlids than in the dark ones. So there are differences in the number of gene products between the color variants, which might explain the different color types," Axel Meyer explains.

Thus, even if the final proof that the variants of the goldentouch gene described in the current study are the direct cause for the development of the color variants in the Midas cichlid is still pending, there are already several indications that this is the case.

"With our study, we have come a big step closer to deciphering the mystery of the Midas cichlids. In future studies, we will have to confirm the causal link to the goldentouch gene and figure out how the gene controls the color change of the fishes at the molecular level in detail," Axel Meyer adds.

More information: An intronic transposon insertion associates with a trans-species color polymorphism in Midas cichlid fishes. *Nature Communications*; DOI: doi.org/10.1038/s41467-021-27685-8

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