UNIVERSITÉ DE GENÈVE

PRESS RELEASE

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One gene defines the many patterns of snake skin

A UNIGE team has identified a single gene behind the corn snake's skin pattern diversity.

In many animals, skin colouration and its patterns play a crucial role in camouflage, communication, or thermoregulation. In the corn snake, some morphs display red, yellow, or pink blotches, and their dorsal spots can merge or turn into stripes. But which genetic and cellular mechanisms determine these colourful patterns? A team from the University of Geneva (UNIGE) discovered that a single gene, CLCN2, is involved in these variations. The study, published in *Genome Biology*, offers new insights into the evolution and genetics of animal colouration.

The skin colouration and patterns of the corn snake, *Pantherophis guttatus*, are produced by the arrangement and localization of chromatophores—cells found in the skin of many animals that contain pigments or light-reflecting crystals. These reptiles typically have their back covered with red blotches outlined in black on an orange background, and a ventral black-and-white checker. Yet, different morphs can exhibit a wide variety of other colours and patterns.

Among the commonly observed variations is the Motley morph, where dorsal spots are fused or interrupted, creating a more linear pattern, and the Stripe morph, which features continuous longitudinal stripes along the back. Both variants share a distinct characteristic: a plain belly with no checkered pattern.

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In corn snakes, certain lineages have red, yellow or pink colours, and their dorsal spots can merge or form stripes.

High resolution pictures

A Single Gene Behind Distinct Patterns

The team led by Athanasia Tzika and Michel Milinkovitch, respectively Senior Lecturer and Professor in the Department of Genetics and Evolution at UNIGE's Faculty of Science, aimed to characterize these mutations. Through crossings between Motley and Stripe snakes, and genome sequencing of the offspring, the researchers found that both phenotypes were linked to mutations in a single gene: CLCN2. This gene encodes a protein located at the cell membrane, forming a channel that transports chloride ions across the membrane. The differential distribution of ions creates an electrical potential between the inside and outside of the cell, enabling the transmission of cellular signals.

In Motley snakes, the variation is not due to a mutation in the gene itself but rather a strong reduction in its expression level. In Stripe snakes, however, a small piece of DNA – a transposon – is inserted into the CLCN2 gene, rendering the protein non-functional. "These results were quite surprising, because in humans and mice, the CLCN2 channel is essential for neuronal activity, and mutations in this gene are associated with serious conditions such as leukoencephalopathy, a disease affecting the brain's white matter," explain Sophie Montandon and Pierre Beaudier, researchers in the Milinkovitch/Tzika lab and co-first authors of the study. "We therefore developed genetic experiments in corn snakes to inactivate the CLCN2 gene. The resulting mutants displayed the Stripe phenotype, confirming the gene's involvement."

An Unexpected Player in Pattern Formation

To better understand the role of CLCN2, the scientists investigated in which organs and cell types the gene is expressed in corn snakes. Transcriptomic analyses revealed that CLCN2 is expressed in the adult brain – similar to mice and humans – but also in chromatophores during embryonic development. The researchers then focused on how colour patterns form in embryos. They observed that in mutants, chromatophores fail to aggregate properly to form the characteristic blotches. Instead, they organize into stripes, as seen in Stripe individuals. "Our results show that a mutation in the CLCN2 gene in corn snakes does not cause neurological or behavioral disorders. However, the protein plays an essential, and previously unknown, role in the development of skin colouration patterns," concludes Asier Ullate-Agote, co-first author of the study.

The next phase of the research will focus on understanding the role of the CLCN2 chloride ion channel in chromatophore membranes, particularly how it influences the interactions between pigmented cells. The goal is to decipher the cellular mechanisms that give rise to the spectacular diversity of colouration patterns observed not only in corn snakes but also in other reptiles.

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