GENES & CELLS

Protein paints chipmunks' stripes

Scientists find molecular architect of mammalian fur patterns

BY TINA HESMAN SAEY

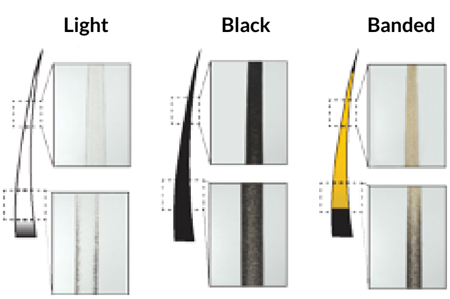
Chipmunks and other rodents' light stripes are painted with a recycled brush, a new study suggests.

A protein previously known to guide facial development was repurposed at least twice during evolution to create light-colored stripes on rodents, scientists report November 2 in *Nature*. The protein, called ALX3, could be an important regulator of stripes in other mammals, including cats and raccoons, says Michael Levine, a developmental biologist at Princeton University.

African striped mice evolved a new trick for the protein ALX3, which helps direct development of facial cartilage. ALX3 also paints light stripes down the rodents' backs, a new study suggests.

Some research has shown how butterflies and other insects create their often elaborate wing patterns (*SN: 7/17/10, p. 28*). But scientists still don't understand the biological machinery used by mammals to generate the dots, spots, splotches and stripes that decorate their coats. Identifying that molecular equipment may illuminate the processes that help animals camouflage themselves and adapt to their environments.

In the new study, evolutionary developmental biologist Ricardo Mallarino of Harvard University and colleagues examined the multicolored stripes of African striped mice (*Rhabdomys pumilio*). Two light-colored stripes, each flanked by black stripes, run down the mice's backs. A strip of fur the same brownish color as most of the rest of the body separates the dark-light-dark striping. The patterns are created by three types of hair. Hairs with banded yellow shafts growing from a black base populate the strip in the middle, while completely black hairs from base to tip are found in the black stripes. Hairs with a black base but no pigment in the shaft make up the light stripes.



Hair of the mouse African striped mice have three different types of hair: light (left), black (center) and banded (right). All the types have a black base.

Those unpigmented hairs were puzzling, says Hopi Hoekstra, the Harvard evolutionary biologist who led the new study. Usually, white hair arises because animals have a mutation that prevents cells from making pigments, she says. But since the African striped mice carry no such mutations, the mice must create the stripes in a different way.

In vertebrates, pigment-producing cells called melanocytes migrate around the body as the embryo develops. One way stripes could form is by melanocytes moving to create the pattern. Previous research in zebrafish indicated that stripes on the fish's sides form that way (*SN: 2/22/14, p. 9*). Light stripes might result if the melanocytes don't migrate into a strip of the mice's skin, the researchers reasoned. Hair would grow there, but wouldn't have any pigment.

That's the first thing Mallarino checked. He examined white stripes in the skin of striped mouse embryos a couple of days before birth. Melanocytes had no trouble infiltrating the light striped area. But once there, the cells did not mature properly and so made no pigment.

In the light stripes, the researchers found, the gene that produces ALX3 is much more active than in the brown or black stripes. That was a surprise because no one knew that ALX3 is involved in pigmentation, Hoekstra says. It was known for helping to regulate the formation of bones and cartilage in the face.

It wasn't clear whether the high levels of ALX3 caused the light stripes or not. So Hoekstra's team did experiments in lab mouse cells to find out how the protein might affect pigmentation. Raising levels of ALX3 in cells interfered with activity of a gene called *Mitf*, a master regulator of pigment production and melanocyte maturation.

It turns out that even in lab mice, more of the protein is made on the belly, which tends to be light colored. Previous pigmentation research failed to turn up ALX3 because researchers were working with white mice, Hoekstra says.

Eastern chipmunks (*Tamias striatus*), whose last shared ancestor with African striped mice lived about 70 million years ago, also made more ALX3 in the light stripes on their flanks, the researchers found. Those results suggest that different rodents independently recycled ALX3's ability to make light-colored belly fur and also used it to paint light stripes on the back. Stripes may help rodents that are active during the day blend into the background and avoid the sharp eyes of predators, Hoekstra says.

Evolution tends to be thrifty, often reusing old genes for new purposes, says Nipam Patel, an evolutionary developmental biologist at the University of California, Berkeley. The new study is "a really nice illustration that evolution isn't biased," he says. "It takes what it gets and works with that."

The researchers still don't know how ALX3 production gets turned up in the light stripes. Another protein may turn on its production, or rodents may have found other ways to dial up ALX3 production in certain places. Researchers need to discover what turns on ALX3 to pinpoint the exact evolutionary change responsible for the striped pattern, Patel says. ■

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