SCIENCE

Scientists Can Now Repaint Butterfly Wings

Thanks to CRISPR, scientists are studying animal evolution in ways that were previously thought to be impossible.

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The wings on the left belong to a normal Gulf fritillary butterfly, and the ones of the right belong to one whose optix gene has been deleted. (ROBERT REED)

When the butterfly emerged from its pupa, Robert Reed was stunned. It was a Gulf fritillary—a bright-orange species with a few tigerlike stripes. But this butterfly had no trace of orange anywhere. It was entirely black and silver. “It was the most heavy-metal butterfly I’ve ever seen,” Reed says. “It was amazing to see that thing crawl out of the pupa.”

Reed’s team at Cornell University had created the metal butterfly by deleting just one of its genes, using the revolutionary gene-editing technique known as CRISPR. And by performing the same feat across several butterfly species, the team showed that this one gene, known as *optix*, controls all kinds of butterfly patterns. Red becomes black. Matte becomes shiny. Another gene, known as *WntA*, produces even wilder variations when it’s deleted. Eyespots disappear. Boundaries shift. Stripes blur.

These experiments prove what earlier studies had suggested—that *optix* and *WntA* are “paintbrush genes,” says Anyi Mazo-Vargas, one of Reed’s students. “Wherever you put them, you’ll have a pattern.”

Biologists have long been smitten by butterflies, and not just for their pretty colors. These insects are perfect subjects for addressing two of the most fundamental questions in the study of evolution. First, where do new things come from? Butterflies all evolved from a moth ancestor, so how did a presumably dull-winged insect give rise to a kaleidoscopic dynasty of some 18,000 species, each with a distinctive pattern of colors and shapes plastered on its wings? Also, what are the genes behind these patterns? How did a limited set of DNA come to produce patterns of such astonishing diversity and often-baffling complexity?

Many scientists, Reed included, have addressed that second question. By carrying out painstaking cross-breeding experiments, and by working out where in the wings various genes are active, they identified a handful of pattern-defining genes, with colorful names like *optix*, *doublesex*, and *cortex*. "It was convincing but we didn't know exactly what these genes were doing," says Reed. Without the ability to delete the genes, and see if their absence changed the butterfly wings, "we didn't have the final proof. There's been this frustrating wall that I've banged my head against."

CRISPR changed everything. This technique, used by bacteria for billions of years and harnessed by scientists in the last five, allows researchers to cut and edit DNA far more easily and precisely than ever before. As I've argued before, the oft-cited concerns that CRISPR will usher in a dystopic era of designer babies are overblown. But scientists are already exploiting it, to do experiments that would have been impossible a decade ago. They've used CRISPR to probe the weaknesses of cancer cells, study how bodies are built, and to learn how our feet evolved from fishy fins. And Reed has used it to finally do the gene-deleting experiments that had long eluded him.

By deleting the *optix* gene in a wide variety of butterflies, team member Linlin Zhang showed that red parts of the wing consistently turn black. The Gulf fritillary transforms from a vivid orange insect into a dark inky one. The small postman loses the vivid red streaks on its hind wings. And the painted lady loses its complex psychedelic patterns and becomes almost monochrome. "They just turn grayscale," says Reed. "It makes these butterflies look like moths, which is pathetically embarrassing for them."

Painted lady wings: normal (left) and with optix deleted (right) (Robert Reed)

These results reveal another side to CRISPR's power: It's so versatile that scientists can quickly manipulate the *same* genes in *many* species, including those that aren't standard parts of laboratory life. For years, scientists have relied on a few handfuls of "model systems"—species that they can easily breed, study, and manipulate in laboratories. But CRISPR "fully unlocks butterflies as a model system," says Wei Zhang from the University of Chicago, who published the first study that used the technique on butterflies.

These butterfly experiments reveal evolution's penchant for both conformity and innovation. For example, *optix* does the same thing in species that have been separated by at least 80 million years of evolution. "It acts like a color/grayscale switch across the whole wing—quite incredible," says Chris Jiggins from the University of Cambridge. But different species deploy it in different ways to produce their own distinctive patterns. If *optix* is a paintbrush, then other genes act as the painter's hands, determining where the brush will go, and yet other genes act as the paints, determining which colors the brush eventually lays down. All of this can be easily rewired, producing a wide kaleidoscope of patterns from the same basic toolkit.

"This is the stuff of evolution—it's very unpredictable what each species might do with the same gene," says Antónia Monteiro from Yale-NUS college in Singapore, who also studies butterfly patterns.

Consider the common buckeye. It's a mostly brown butterfly, with a few vivid eyespots and orange splashes. When Reed deleted *optix*, sure enough, the orange bits blackened. But unexpectedly, the buckeye's wings also gained a blazing iridescence—a shiny, metallic blue. "With one gene, we could turn this little brown butterfly into a morpho," says Reed, referring to a group of butterflies known for their stunning iridescent blues.

Common buckeye wings: normal (left) and with optix deleted (right) (Robert Reed)

That was a huge surprise. There are no blue pigments in the wings of the altered buckeyes. Instead, their iridescence is the work of microscopic layers in the wings, which collect, reflect, and amplify blue light, so that it's especially vivid from certain angles. That's an entirely different way of producing colors than the red and black pigments that *optix* typically governs.

It seems that buckeyes have all the right ingredients for making glossy wings, but *optix* typically restrains this potential in favor of a matte finish. Perhaps the same is true for other butterflies like morphos and pipevine swallowtails, which have independently evolved blue iridescence. "We haven't tested this hypothesis yet but it's plausible that simply altering this one gene is sufficient to produce this pattern again and again," says Reed.

The team, including Mazo-Vargas and Arnaud Martin from George Washington University, also deleted a different gene called *WntA* in various butterflies—and found an even wider range of effects. In the painted lady and common buckeye, it looked like someone had taken an eraser to the middle of the wing, removing the splotches and spots that normally live there. In two species—the small postman and the Sara longwing—black parts of the wing recede while red and yellow regions expand to fill the void. In the Gulf fritillary, some silver spots disappear, and in the monarch, white scales emerge amid the usual tiger colors.

WntA "is more of a tinkerer," says Jiggins. Rather than deploying particular colors, like *optix* seems to do, it merely sets boundaries that other genes fill in with colors and shapes. And just like *optix*, different species have repurposed it to govern their own particular patterns.

The details are still unclear though. How do these gene networks get rewired? When did they take on their roles as master regulators of wing patterns? Why have only a few genes done so? Did butterflies recruit these genes to paint their wings once during their evolution, or many times independently? A decade ago, these would have been fanciful questions. But in the CRISPR era, it suddenly seems possible to answer them.

"CRISPR is a miracle," Reed says. "The first time we tried it, it worked, and when I saw that butterfly come out ... the biggest challenge of my career had just turned into an undergraduate project."

Link to the original article: https://www.theatlantic.com/science/archive/2017/09/the-genes-that-paint-butterflies/540159/