On the wings of flies

UW researchers determined how specific spot patterns appear on fruit fly wings, paving the way to conclusions about evolution.

By Mark Johnson
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Milwaukee — In the lab that summer morning, Thomas Werner's heart pounded. The UW-Madison post-doctoral researcher sat down and took deep breaths before continuing the experiment.

Werner, who grew up in East Germany hoping to study butterflies, devoted more than three years to a species of the North American fruit fly, Drosophila guttata.

Focusing on this species of fruit fly, he and the other researchers in the lab of molecular biologist Sean Carroll made a prolonged assault on one of the key questions in evolutionary biology: how nature endows creatures with their colorful patterns, from a leopard's dark spots to a butterfly's bold swirls. In different species, the patterns serve to attract mates or provide camouflage or other advantages in the struggle to survive.

But what causes the colors to fall so precisely into place?

Werner's hands shook as he removed the fruit fly pupa's wing and placed it under the microscope in the darkroom. Three years of work now came down to a single image.

He needed to see green fluorescent light in the places where black spots would one day appear on the wing of the adult fruit fly. That would mean he had discovered the secret of the fly's spots.

"I almost fell on the floor because I saw all of these spots. Every place there was a spot on the wing, I saw a fluorescent light," he said.

Werner and his colleagues had found a protein that tells certain fruit fly cells to make the spots.

"Koshi," he cried, rushing to find his colleague on the project, Shigeyuki Ko- shikawa. "Come immediately! It's urgent. We have the spots. All of them."

Understanding color patterns

Their work, reported online Wednesday in the journal Nature, established that the protein Wingless — which is found in embryonic tissue — spreads through the fruit fly's wings, prompting cells in very specific areas to make color. In the case of Drosophila guttata, Wingless triggers the production of 16 spots that appear in precise positions on the wing.

"Understanding how color patterns are generated during development is a prerequisite to addressing fundamental questions about their evolution, such as how complex patterns are assembled over evolutionary time," Werner, Carroll and colleagues wrote in Nature.

Carroll added, "This has built up our confidence that we can look at great diversity and make sense of it. Somewhere in history, probably 40 to 50 million years ago, there was a connection between Wingless and the making of pigment, and nature has exploited that in myriad ways.

"We'd like to pinpoint the exact molecular events that made that happen."

While such research adds to our understanding of evolution and development, it may have implications for human health. Mutations in the Wingless gene are associated with certain cancers. Also, many of the genes that play important roles in human birth and developmental defects were first identified in fruit flies.

Evolution not random

Cliff Tabin, a professor and chairman of Harvard University's department of genetics, called the UW work "a really nice study" and said it shows that the changes brought about by evolution "are not completely random."

Tabin, who was not involved in the UW research, said what is particularly interesting in the paper is the observation that pre-patterns exist: Cells lie in precise positions on the wing so that when a specific gene is switched on inside them, they make spots.

He compared this phenomenon to a child drawing a mustache on a magazine photograph of a face; the child does not need to draw the whole face, only the mustache on the image already imprinted.

"We still don't know the individual events that led to that, but this paper is an important step in being able to dissect that," said Nipam Patel, a professor in the department of molecular cell biology at the University of California-Berkeley.

In all, Werner estimated it took a couple of million fruit flies to do the work for the Nature paper. It took three years to develop the techniques to create special modified fruit flies that turn on green fluorescent protein where they have yellow pigment.

The scientists also made other modified fruit flies that were able to turn on the spot-making gene in new places. In doing so they were able to control the pattern-making process, inducing fruit flies to make stripes, new configurations of spots and other designs not found in nature.

Werner said he hopes to build on the work in fruit flies by studying the common buckeye butterfly found in most of the U.S. and known for its pattern of dark eyespots and white bars.

"This would finally lead me to the dream of my life," he said, "to describe the pigmentation patterns in butterflies and how they have changed in evolution."