How does a leopard get its spots? Scientists find out

UW researchers unlock mystery of color patterns

By MARK JOHNSON
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In the lab that summer morning, Thomas Werner’s heart pounded. The University of Wisconsin-Madison post-doctoral researcher had to sit down and take deep breaths before continuing the crucial experiment.

Werner, who had grown up in East Germa-

ny hoping to study butterflies, had instead de-

voted more than three years to a species of the

North American fruit fly, Drosophila guttifera.

Focusing on this species of fruit fly, he and

the other researchers in the lab of molecular

biologist Sean B. Carroll, had made a pro-
longed 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, provide camouflage or pro-

vide other advantages in the struggle to sur-

vive.

But what causes the colors to fall so precise-

ly 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 pro-
tein that tells certain fruit fly cells to make the

spots.

“Koshi,” he cried, rushing to find his col-
league on the project, Shigeuki Koshikawa.

“Come immediately! It’s urgent. We have the

spots. All of them.”

Their work, reported online Wednesday in

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Carroll named to top institute post

But UW biologist will still maintain his lab

By MARK JOHNSON
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Sean B. Carroll, a molecular biologist at University of Wisconsin-Madison, has been chosen by the Howard Hughes Medical Institute to be its next vice president for science education.

Carroll, 49, has forged a reputation as one of the nation's leading evolutionary biologists, writing six books, including "Theicle Creatures: Epic Adventures in the Origins of Species," which was a finalist for the 2009 National Book Award in nonfiction. He also writes a monthly column for the science section of The New York Times.

In addition to his new post, Carroll will maintain his lab at UW. Howard Hughes Medical Institute bills itself as the nation's largest private supporter of science education, having invested more than $1.6 billion in programs to engage top scientists in teaching and to boost life science education at research universities, liberal arts colleges and other institutions.

"Sean is a gifted scientist who also displays an extraordinary talent for translating complicated scientific ideas in compelling, understandable ways to members of the public of all ages," Robert Tjian, president Howard Hughes Medical Institute, said in a news release announcing the appointment. "He is in a unique position to connect our scientific and educational programs."

Carroll, who succeeds Peter J. Bruns in September, caught snakes as a boy and admired their patterns of stripes and spots, an interest that continues in his recent work with other species.

"I want to help other people have as much fun as I have," Carroll said about his new post at Howard Hughes Medical Institute. "That requires thinking about how to foster creativity and innovation on a larger scale. We all need in spiration, but how do we nourish curiosity and inspire an interest in science particularly among young people.

"These are crucial challenges, and I hope to promote the very positive role that science can play in our culture."

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Scientists unlock mystery

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 guttifer, Wingless triggers the production of iris spots that appear in precise positions on the wing, including the intersections of veins and cross-veins.

"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.

In an interview, 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.

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.

"I think this phenomenon is seen in 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 top of the image already implanted."

"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. Patel did not work on the Nature paper.

Patel added that other scientists have been studying the development of color patterns and other characteristics of different species. Hopi E. Hoekstra, a Harvard researcher, has looked at hair color patterns in mice, and Patricia Simpson at University of Cambridge has examined the positioning of bristles in flies.

"It's very time-consuming research," he said.

Detective work

Werner began the work around the beginning of 2006, working with a species that is extremely difficult to raise in the lab. Often the fruit flies died quickly and lay few eggs. Scientists needed to supply the flies' food with yeast in order to get them to produce more eggs. But ethanol from the yeast killed the flies. Werner found that he needed to space out the Plexiglass containers with Drosophila guttifer to allow space for the ethanol to steam out.

Along the way, the UW researchers followed a few false leads that led to the pattern-making mechanism. In particular, they found that in a group of aberrant fruit flies in the lab, there was a strict correlation between the formation of spots and the presence and absence of physical wing landmarks. "This really was detective work," Carroll said.

In all, Werner estimated that it took a couple of million fruit flies to do the work required for the Nature paper. It took three years to develop the skills and techniques to create special modified, or transgenic, fruit flies that turn on green fluorescent protein wherever 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 striped, 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 group 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."