

FEBRUARY 04, 2005

Spotting Evolution on the Wing

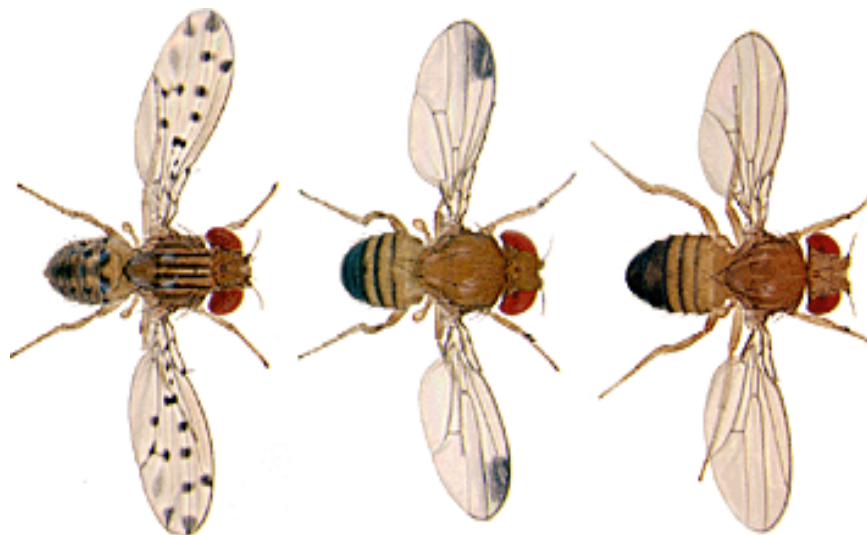


Image Title: Different species of fruit flies exhibit remarkably different patterns of wing decoration. At the far right is the familiar *Drosophila melanogaster*, the workhorse model organism of genetics, which differs markedly from other fruit fly species. - Courtesy of Nicolas Gompel and Benjamin Prud'homme.

By analyzing the genetic origin of a modest spot on a fruit fly wing, Howard Hughes Medical Institute researchers have discovered a molecular mechanism that explains, in part, how new patterns can evolve. The secret appears to be specific segments of DNA that orchestrate where proteins are used in the construction of an insect's body.

In the February 3, 2005, issue of the journal *Nature*, HHMI investigator Sean B. Carroll and his colleagues at the University of Wisconsin-Madison, published evidence showing that regions of DNA known as *cis*-regulatory elements have major evolutionary importance. *Cis*-regulatory elements are DNA segments that nestle around and even within gene segments that code for specific proteins. Rather than coding for a protein, however, these segments regulate the function of a nearby gene □ and can allow for variations in that function depending on the tissue or developmental stage of an organism.

"Some biologists, including myself, have for many years suspected that *cis*-regulatory elements would be key to the evolution of form," said Carroll. "The essence of our argument has been that proteins can have multiple jobs in the body--at different times and in different tissues. Mutations in a gene's protein-coding region could exact an enormous penalty by affecting the function of that protein throughout the organism. But mutations in a regulatory region could affect only the production of the resulting protein in one setting--allowing fine-scale variation with no collateral damage.

"The amount of direct evidence for the role of *cis*-regulatory elements in evolution has been very small and very narrow in scope," he said. "But in this study, we believe we present evidence that is of a smoking-gun variety."

"We like to use a Christmas tree analogy. These systems already have all the structural details in place, like the structure of a Christmas tree. And all evolution has to do is to alter these regulatory elements mutationally to bring out a pattern □ like hanging ornaments on the tree."

- Sean B. Carroll

The researchers chose to study the evolution of the wing spot on the fruit fly because it is a simple trait with a well-understood evolutionary history. While ancient fruit fly species lack the spots, Carroll said, some species that evolved later have developed them under the pressure of sexual selection. The wing spots offer a survival advantage to males, who depend on the decorations to "impress" females to choose them in the mating process.

In fruit flies, wing pigmentation depends on a gene known as *yellow*, which is found in fly species both with and without the spot. Since differences in the *cis*-regulatory elements controlling the *yellow* gene might account for variations in the spot, the researchers began by transferring potential *cis*-regulatory elements from the spotted species *biarmipes* into the spot-free species *melanogaster*. They attached the regulatory region to a gene for a fluorescent protein, and found that that gene was expressed in the spot-free species just as the *yellow* gene was in the spotted species, demonstrating the importance of the *cis*-regulatory region.

While the researchers later found evidence that changes in other genes were also involved in evolution of the wing spot, it was clear that evolution of the *cis*-regulatory regions of *yellow* was a critical step in the process. They therefore next sought to explore the origin and function of the *cis*-regulatory region itself. By comparing *biarmipes*, *melanogaster*, and other species, the scientists established that mutation of a preexisting regulatory region lead to

the evolution of the spot pattern.

Importantly, they discovered that in the species with the wing spot, multiple mutations of the *cis*-regulatory region had created binding sites for existing regulatory proteins in the cell. By allowing these regulatory proteins to interact with the *yellow* gene, these new binding sites resulted in formation of a spot pattern. For example, the newly evolved binding sites included ones for a regulatory protein called Engrailed, which was already known to be used by all fruit flies to govern formation of wing structure. Binding of Engrailed to the regulatory region of the *yellow* gene is a necessary step in development of the wing spot.

"Co-opting" is central to the success of such an evolutionary mechanism, said Carroll. "A key concept here is that this novelty arose from new combinations of old parts," he said. "Through constant mutation, new binding sites for these existing regulatory proteins randomly evolve. And when the pressure of natural selection makes them create advantageous structures -- such as a useful wing spot -- they are preserved."

The evolutionary process of co-opting existing regulatory systems explains why the same structures -- such as spots on fly wings -- can evolve independently in distantly related species, said Carroll. "The architecture of the wing is old and stable," he said. "The vein pattern, the sensory organs, the attachment to the body -- all are ancient. So, for tens of millions of years, the same proteins have been available to modify patterns on the wings because they are there to do other jobs. When we see the same patterns evolving in distantly related species, we can theorize that it's just the same regulatory alteration of these existing systems happening again and again when selection favors it.

"We like to use a Christmas tree analogy," said Carroll. "These systems already have all the structural details in place, like the structure of a Christmas tree. And all evolution has to do is to alter these regulatory elements mutationally to bring out a pattern -- like hanging ornaments on the tree."