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A Fly's-Eye View of Evolution

Howard Hughes Medical Institute researchers have found that mutations in a single structural protein can determine whether an insect develops the highly organized, light-harvesting eye that flies have, or the optically simpler compound eye of a beetle or bee.

In their experiments, the scientists showed that flies without this structural protein develop a more primitive eye. This outcome was reversed in the laboratory when researchers supplied the missing protein to a more primitive eye system, inducing it to “evolve” into the more advanced eye.

These findings “help illustrate the beauty and power of evolution -- how small changes can have such an incredible impact,” said HHMI investigator Charles S. Zuker, who led the study. Zuker and his colleagues at the University of California, San Diego reported their findings October 1, 2006, in an advance online publication in the journal *Nature*. The lead author of the paper was Andrew Zelhof. Robert Hardy and Ann Becker were co-authors.

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Working with the fruitfly *Drosophila*, the researchers explored the formation of transparent rod-like structures in the compound eye called rhabdomeres. Rhabdomeres feed light to the bundles of photoreceptors that comprise each of the 800 unit eyes in the fly's compound eyes. Rhabdomeres are fused into a single light-gathering structure in the more primitive “closed rhabdom” compound eyes of beetles, bees, and some mosquitoes. Flies, on the other hand, have evolved a more advanced “open rhabdom” structure. In the more sophisticated eyes of flies, the rhabdomeres are separated, and as a result, fly

eyes have significantly better angular resolution, and can detect smaller moving objects.

Zuker, Zelhof, and their colleagues planned their experiments to identify the genes and biological pathway required to assemble the light-harvesting system of photoreceptor neurons. To define those genes, they used a chemical to induce mutations in fruitflies and examined the mutant flies under a microscope in search of any with malformed eyes.

“Much to our delight, we discovered two mutant lines that looked as if their eyes had been transformed from an open-rhabdom to a closed system,” said Zuker. “In fact, in looking at the eyes of one of those, you could easily mistake them for the eyes of an insect with a closed-rhabdom system,” he said.

The researchers' genetic analysis of these flies resulted in the identification of three genes, *spacemaker*, *prominin* and *chaoptin*, which together orchestrate the assembly of rhabdomeres into the fly's elegant photoreceptor system.

Zelhof, the lead author of the study, then compared the expression of *spacemaker*, *prominin*, and *chaoptin* genes in the housefly and a mosquito, whose eyes have the open structure —with that of the honeybee and flour beetle - insects with closed-rhabdom eyes. Although *spacemaker* was expressed in the body of all the species of insect that were studied, the scientists found that the gene was not turned on in the eyes of species with closed rhabdom systems. “These findings led us to hypothesize that Spacemaker protein may be a key determinant of the evolutionary transition from closed to open-rhabdom systems,” said Zelhof. “Validating that proposal required one critical acid test; and that was to introduce the protein into a closed system and see whether we could transform it into an open one,” he said.

Fortunately, in addition to its open rhabdom eye, the fruitfly itself also possesses a primitive closed version of an eye. This is found in the light sensors called ocelli, which are located on the top of the head, and used for navigation. When the researchers engineered fruitflies that expressed the Spacemaker protein in their ocelli, they found that the ocelli completely reorganized into an open rhabdom system.

Zuker said the findings offer an important lesson about the beauty of evolution. “It's not unusual to see alterations in regulatory proteins with a profound effect on form and function,” he said. “For example, altering a single transcription factor that controls a hierarchy of downstream products can cause an insect to grow extra legs or lose wings. This new finding, however, is unique because it illustrates how a change in a single structural protein can lead to such a spectacular change in form and function.”