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HHMI Research on Evolution in Action Highlighted in *Science's* "Breakthrough of the Year"

The journal *Science* has announced that the scientific "Breakthrough of the Year" is evolution in action. Recent experiments by four HHMI investigators were among those mentioned by *Science* as having provided evidence of evolution in action during the past year.

"It's been a great year for understanding how evolution works, through both experiment and theory. No single discovery makes the case by itself; after all, the challenge of understanding evolution makes multiple demands," stated *Science* editor-in-chief Donald Kennedy in an accompanying editorial.

The research on evolution and nine other research advances make up *Science's* list of the top 10 scientific developments in 2005, chosen for their profound implications for society and the advancement of science. The Top Ten list appears in the December 23, 2005, issue of the journal *Science*.

In citing recent studies on evolution, *Science* highlighted recently published research from HHMI investigators Sean Carroll at the University of Wisconsin, Madison, David Kingsley at Stanford University, Bruce Lahn at the University of Chicago and Christopher Walsh at Harvard Medical School.

Sean Carroll

By analyzing the genetic origin of a modest spot on a fruit fly wing, Howard Hughes Medical Institute researchers 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.

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.

David Kingsley

In a stunning example of evolution at work, HHMI scientists discovered that changes in a single gene can produce major changes in the skeletal armor of fish living in the wild.

The surprising results, which were published in the March 25, 2005, issue of journal *Science*, bring new data to long-standing debates about how evolution occurs in natural habitats.

HHMI investigator David Kingsley and graduate student Pamela F. Colosimo, in collaboration with zoologist Dolph Schluter at the University of British Columbia, and Rick Myers and colleagues at Stanford, focused on a well-studied little fish called the stickleback. The fish — with three bony spines poking up from their backs — live both in the seas and in coastal fresh water habitats all around the northern hemisphere.

Kingsley, Schluter and their co-workers picked one trait — the fish's armor plating — on which to focus intense research, using the armor as a marker to see how evolution occurred. Sticklebacks that still live in the oceans are virtually covered, from head to tail, with bony plates that offer protection. In contrast, some freshwater sticklebacks have evolved to have almost no body armor.

Using genetic crosses between armored and unarmored fish from wild populations, the research team found that one gene is what makes the difference. “Now, for the first time, we've been able to identify the actual gene that is controlling this trait,” the armor-plating on the stickleback, Kingsley said.

Bruce Lahn

Howard Hughes Medical Institute researchers who have analyzed sequence variations in two genes that regulate brain size in human populations have found evidence that the human brain is still evolving.

They speculate that if the human species continues to survive, the human brain may continue to evolve, driven by the pressures of natural selection. Their data suggest that major variants in these genes arose at roughly the same times as the origin of culture in human populations as well as the advent of agriculture and written language.

The research team, which was led by Bruce T. Lahn, a Howard Hughes Medical Institute investigator at the University of Chicago, published its findings in two articles in the September 9, 2005, issue of the journal *Science*.

Their analyses focused on detecting sequence changes in two genes - *Microcephalin* and “abnormal spindle-like microcephaly associated” (*ASPM*) - across different human populations. In humans, mutations in either of these genes can render the gene nonfunctional and cause microcephaly - a clinical syndrome in which the brain develops to a much smaller size than normal.

Christopher A. Walsh

Humans evolved in the most recent few moments of evolution's grand pageant. The evolutionary lineage leading to humans split off from the lineage leading to chimpanzees some 6 to 8 million years ago. But anatomically modern humans—people who looked as we do today—appeared only about 150,000 years ago (less than one three-thousandth of the time between us and the Cambrian period).

The lineage leading to humans obviously underwent profound changes since the time of our common ancestor with chimps. HHMI investigator Christopher A. Walsh at Harvard Medical School has been studying those changes in the brain.

Walsh points out that three genetic mechanisms could have caused the human brain to diverge from the chimpanzee brain. New genes may have been added to the human genome that are not present in the chimpanzee genome. Some of the genes that the two organisms share could encode subtly different proteins. Or the regulation of genes could vary—shared genes might be more or less active in the two organisms during different periods of development and in different tissues.

"We have some evidence for the action of all three of those mechanisms, and we're sorting out which of them is likely to be most important," said Walsh. Publication of the chimp genome revealed that a number of genes in humans have been duplicated and then altered since the days of our common ancestor, and some of those genes may influence the development of human brains. Similarly, many of our genes are slightly different from the corresponding genes of the chimp, although that animal's genome reveals a striking similarity in coding sequences across the two species.

But Walsh thinks that regulatory changes eventually will prove to be the most important distinguishing factor. Small changes in the expression of a gene can have dramatic effects on an organism. Researchers also have shown that levels of gene expression have changed more over time in the human lineage than in the chimpanzee lineage. Unfortunately, said Walsh, "Our tools for studying changes in noncoding DNA are very poor."