Was Lamarck Just a Little Bit Right?

Pity poor Jean-Baptiste Lamarck. Today, he is remembered mostly for the discredited theory that evolution occurs when parent organisms pass on to their offspring characteristics they have acquired during their lifetimes. But this French naturalist, who lived from 1744 to 1829, was one of the great scientists of his age. He was the first to study invertebrate animals systematically, and he was an early champion of the idea that evolution rather than divine intervention was responsible for changes in plants and animals over time. But by the early 20th century, Lamarck's concept of evolution had been superceded by Darwin's theory of natural selection and the genetic laws of Gregor Mendel. And since then his name has become inextricably linked to that of his most notorious disciple—the Stalin-era agronomist Trofim Lysenko—who forced Soviet geneticists to accept Lamarckian ideas or be banned from doing research (see main text).

Recently, however, Lamarck's name has been creeping back into the scientific literature. The reason: an explosion in the field of epigenetics, the study of changes in genetic expression that are not linked to alterations in DNA sequences. Some of these epigenetic changes can be passed on to offspring in ways that appear to violate Mendelian genetics. And although these new findings do not support Lamarck's overall concept, they do raise the possibility that "epimutations," as they are called, could play a role in evolution. "I don't know of any evidence that Lamarck was even a little bit right, but this is possible," says molecular geneticist Eric Selker of the University of Oregon, Eugene. "It is increasingly clear that epigenetic mechanisms play important, sometimes critical, roles in biology."

Epigenetic changes, which include the "silencing" of genes by such biochemical tricks as attaching methyl groups to segments of DNA so they will not be read by the cell's protein-making machinery, are involved in a host of processes, including gene regulation, development, and even cancer (*Science*, 15 October 1999, p. 481). Although these alterations in gene expression can clearly be passed from mother to daughter cells—for example, when a muscle cell divides into two or cancerous cells proliferate to form a tumor—they are normally "erased" when the germ cells, which give rise to the next generation, are formed.

Yet evidence is accumulating that sometimes the epimutations are not erased. This phenomenon has been spotted in plants, fruit flies, and yeast. And the first convincing case in mammals was reported in the November 1999 issue of *Nature Genetics* by biochemist Emma Whitelaw at the University of Sydney in Australia and co-workers in Scotland and the United States. Whitelaw's team worked with an inbred strain of mice in which all are genetically identical and so should look exactly the same. But the coat colors of these mice varied wildly, ranging from yellow to mottled with every combination in between. Moreover, the coat color of newborn mice was highly influenced by the color of the mother, but not of the father: A yellow mother had more yellow pups than mottled, and a mottled mother had more mottled pups than yellow, violating Mendelian principles that traits are randomly distributed during reproduction.

The team found that coat color apparently depends on the degree to which a stretch of regulatory DNA just upstream from a gene controlling coat color, called *agouti*, is methylated. This in turn depends on how much of this methylation state, if any, has been transferred from the mother through the germ line to its offspring. Azim Surani, a developmental geneticist at the University of Cambridge in the United Kingdom, comments that the germ cells are normally "a very efficient cleaning machine, which wipes out many of these epigenetic modifications. … The [Whitelaw] paper shows there are exceptions to this rule." As for whether epimutations could play an important role in evolution—that is, whether they, like alterations in DNA sequence, could be favored by Darwinian natural selection—Surani says this partly depends on whether they are fairly common, compared to classic genetic mutations, or rare.

Moreover, Surani and other researchers say, the likelihood that epimutations acquired by adult organisms will be passed on to their offspring is limited by the fact that in most animals the germ cells are segregated very early in life. In mammals, the germ cells are formed and migrate to the embryonic ovaries and testes long before the fetus is born, presumably shielding them from epigenetic modifications in the adult. But the situation might be different in plants, which produce their germ cells much later in their life cycle. In the 9 September 1999 issue of *Nature*, molecular geneticist Enrico Coen and colleagues at the John Innes Centre in Norwich, U.K., reported that a mutant version of the toadflax plant (*Linaria vulgaris*)—which results in flowers with radial rather than bilateral symmetry—is due to an epimutation. In the mutant plant, a gene called *Lcyc* is extensively methylated and thus not expressed—and this methylated state is heritable by subsequent generations of toadflax plants. Coen and his colleagues conclude that such epimutations might have both short- and long-term effects on plant evolution, both in their own right and because methylated genes are more susceptible to classic mutations that alter DNA sequences.

Jean-Baptiste Lamarck. Non-Mendelian inheritance of "epimutations" has resurrected his name but not his overall theory.

Coen points out that Darwin, like Lamarck, believed that the inheritance of acquired characteristics played a role in evolution. The main difference between them was that Lamarck thought evolution was driven by an organism's inner need to adapt to its environment, such as in the famous example of the giraffes who stretched to reach the upper branches of trees and then passed on the phenotypic trait for longer necks to their progeny. Darwin, on the other hand, posited that natural selection of genetic alterations, rather than some "inner striving," drives adaptive changes. Coen cautions that although the new studies of epimutations challenge the dogma "that the only heritable mutations of significance are caused by DNA sequence changes," they offer no support at all for the idea that morphological changes acquired during the lifetime of an adult organism can be inherited in the Lamarckian sense.

But some researchers say that the new research does suggest a potential mechanism for how epigenetic changes could play an adaptive role. "Although it would be stretching it to regard epigenetic traits as adaptations comparable to Lamarck's view of how the giraffe acquired its long neck," comments Selker, "we do know that environmental factors, such as temperature, can influence epigenetic marks such as methylation." And one thing seems sure: The explosion in epigenetic research has helped restore Lamarck to his rightful place in scientific history, even if he did get the big picture wrong. Says Coen: "Lamarck was a true pioneer of evolutionary theory."

—MICHAEL BALTER