MOLECULAR ANTHROPOLOGY

When It Comes to Evolution, Humans Are in the Slow Class

Molecular evolutionist Morris Goodman turned 70 earlier this year, and the Wayne State University scientist couldn't have asked for a better birthday present. At a symposium held in Goodman's honor in Detroit,* a speaker presented new genetic evidence bolstering a controversial idea Goodman introduced 34 years ago: that evolution, as measured by mutation rates, is slower in humans than in other primates and mammals.

Goodman recalls he was "attacked pretty strongly" by researchers ,who were reconstructing evolutionary trees that assumed equal rates of evolution among many animals. But at the Detroit conference, University of Texas, Houston, population geneticist Wen-Hsiung Li presented extensive new data from the DNA sequences of humans, apes, monkeys, and rodents showing that humans indeed undergo fewer changes in their DNA each year.

His work has helped convince many scientists that there is a slowdown in molecular evolution in humans—and, to a slightly lesser degree, in other apes. "I don't think there's much doubt about it," says molecular biologist Roy Britten of the California Institute of Technology. "This is the most compelling evidence so far," agrees University of California, Irvine, molecular evolutionist Walter Fitch. Although a few skeptics note that the results don't cover the whole genome, parts of which might mutate at a faster rate, Goodman is feeling vindicated: "If they're going to knock me for the idea, I might as well get some of the credit for it too."

Scientists at the meeting were not overly concerned with the effects the slowdown might have on the future of humans. Li noted that whereas other animals need genetic diversity to cope with disease and environmental change, human beings use tools, medicine, and innovation to survive crises. But the same researchers said the slowdown raised important questions about the use of a universal "molecular clock" to sort out relationships among species by using mutation rates to calculate the time since those species shared a common ancestor. If species mutate at different rates, Li says, the clocks could be grossly inaccurate.

The first hint that humans and other primates evolve more slowly than other mammals came in 1961. Goodman, who was comparing protein chemistry from various species, noticed that the blood protein albumin appeared nearly identical in humans, chimpanzees, and gorillas. That was a surprise, because albumins from other animals with close evolutionary relationships, such as antelopes and cows, appeared more disparate. The similarity within the apes suggested to Goodman that, after the great apes split from a common ancestor, their albumin had mutated at a much slower rate than the albumins of other mammals.

Other scientists, however, were quick to criticize the notion of a slowdown. Anthropologist Vincent Sarich of the University of California, Berkeley, and his collaborator, the late Allan Wilson, argued that humans and other apes had split much more recently—5 million to 7 million years ago—than Goodman and most anthropologists thought they did at the time. As a result, the Berkeley pair argued, there shouldn't be much difference in blood proteins anyway. Goodman recalls that "Vince and I argued about this for years." Today, most researchers believe Sarich was right about the divergence date, but Goodman appears to have carried the day on the issue of the clock's accuracy.

The clincher, many say, is the data Li presented in Detroit. And the reason his data are so convincing is that they were culled from not just one gene, but from many. Li described a series of studies examining noncoding stretches of DNA—eight different introns, as well as pseudogenes and flanking sequences—from humans, baboons, and squirrel monkeys. Noncoding DNA isn't expressed as protein products, so it is thought to be immune to the pressure of natural selection, which can retain an advantageous gene, thereby slowing its mutation rate and making a baseline rate harder to discern.

To determine whether one group of animals was mutating faster than a second group, Li used a procedure known as a relative rate test. For the test, you actually need three groups of animals: the two you are concerned with, and a third group, known as an outgroup, which serves as a common starting point for the comparison. Li, for instance, wanted to compare humans and Old World monkeys such as baboons and used as his outgroup New World monkeys. It is believed that the ancestors of humans and Old World monkeys split off from New World monkeys at the same time (in fact as one ancestral group of animals), and then, millions of years later, humans and the Old World monkeys went their separate ways.

New World monkeys, then, are the starting point. The number of mutations separating them from humans can be compared to the number of mutations separating them from Old World monkeys. The difference reveals whether the DNA of humans or Old World monkeys is mutating faster. After Li did this comparison for all the introns and a pseudogene, he found that, on average, Old World monkeys had undergone about 1.5 times more mutations within their sequences than did humans.

In an earlier study, Li also compared humans with mice and rats. He used chickens as the outgroup, because they are thought to have separated from the common ancestor of primates and rodents about 300 million years ago. He found that the rodents had accumulated about twice as many mutations as had the human lineage. "This provides evidence for a slower rate in humans than in Old World monkeys since the separation of the two lineages, and for a much slower rate in higher primates than in rodents," says Li. Just to check, Li also calculated mutation rates for each species over a specific period of time, using dates of species splits from the fossil record—which is always somewhat uncertain. These also showed that humans were the slowest (see chart above).

The human-ape slowdown makes sense, Li says, in terms of life-span and generation

	Rats	New World monkeys	Old World monkeys	Humans
Base pairs studied	4038	8478	8478	8478
Changes per nucleotide site per billion years	4.8	2.1	1.8	1.2

Going slow. During the time since each of these groups split off from a common ancestor (dated according to the fossil record), their DNA sequences diverged. The degree of that divergence during that time yields a mutation rate; humans appear to have the slowest rates.

SOURCE: WEN-HSIUNG LI PHOTOS BY (LEFT TO RIGHT) MICHAEL DICK, GÉRARD LACZ, M. DICK, KEN COLE / ANIMALS ANIMALS

*"Molecular Anthropology: Toward a New Evolutionary Paradigm," 12 to 14 March, Wayne State University School of Medicine, Detroit.

time. He presented data showing that most mutations arise in humans and other species when their DNA is being copied to produce sperm in males, and to a lesser degree, egg cells in females (Li *et al.*, *Nature* **362**, 745–747, 1993). Because rodents and monkeys go through more generations per unit time than humans do, they accumulate mutations at a faster rate. Britten, whose genetic studies also point to a primate slowdown (*Science* **231**, 1393–1398, 1986), has suggested that longer lived animals may have a greater ability to repair their DNA than do short-lived species, and this would also serve to reduce mutation rates. Says Li: "On the whole, this means molecular evolution may have slowed down for longer generation organisms."

One consequence of this work, say Li and Goodman, is that scientists are going to have to be a lot more careful when they use evolutionary rates to date the separation of different species of animals from each other. An interspecies "molecular clock" hypothesis was put forth in 1965 by the late Linus Pauling of Stanford University and his collaborator, Emile Zuckerkandl. They proposed that for any protein, rates of change were roughly the same over time in all lineages of mammals. The implication was that differences among proteins or DNA sequences could be used to date the separation of mammalian lineages. One such study, using a mutation rate derived from primates, joined rats and mice through a common ancestor that lived 40 million years ago. Most researchers today, however, put that split at 15 million years ago. "If you look at all of the mammalia and use the same mutation rate, you could come up with wildly wrong dates," says Goodman.

That doesn't mean every scientist is now ready to reset the molecular clock using data for individual species. Sarich, for one, argues that the new studies represent sequence data from only a small portion of primate genomes and says he is unconvinced that there are rate differences between primates. "I hardly find it surprising that there can be slowdowns in individual molecules," says Sarich. He cites a 1985 DNA hybridization study by Raoul Benveniste of the National Cancer Institute that showed no slowdown between humans and baboons.

Li thinks his sequence data are stronger. And he gets the same results from very different parts of the genome: "In every kind of noncoding sequence of DNA we look at we see a slowdown," including introns, pseudogenes, and flanking regions. Goodman agrees, citing his own DNA sequence studies and DNA hybridization data. "This gives me confidence that the results from noncoding DNA tell the whole story," says Goodman. And for him, it's a story with a very satisfying ending.

–**Ann Gibbons**

ARCHAEOLOGY

The Earliest Art Becomes Older—and More Common

Rare and recent. When archaeologists discuss the earliest cave paintings and other symbols made by modern humans, those two terms are usually applied. In the consensus view, the spectacular red or black mammoths, horses, and geometric figures occasionally found on cave walls, which are among the first signs of fully modern human behavior—the ability to manipulate symbols—are at most 40,000 years old.

But these twin notions were severely undermined 2 weeks ago at a conference called "Upper Paleolithic Image and Symbol" at the California Academy of Sciences in San Francisco. Much of the undermining data came from the land down under: Australia. Researchers presented new results that may push the first signs of human artistic behavior—and Australia's first colonization—back an extra 20,000 years. Other scientists demonstrated that art may have been all around, both in Australia and Europe, and apparently was a part of everyday life for our ancestors rather than just a mysterious underground event.

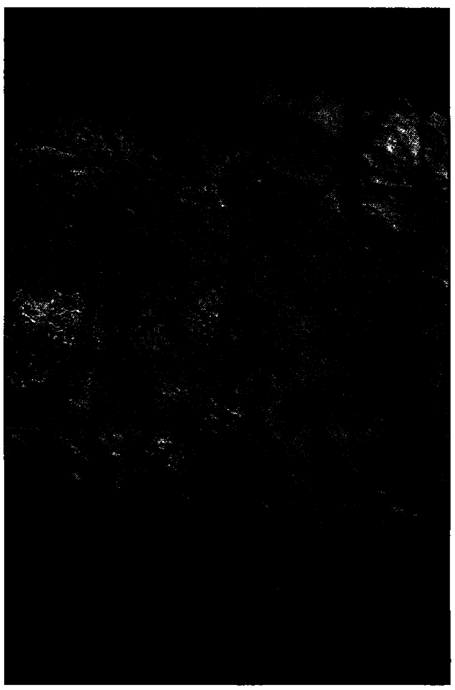
Toss another paint brush on the barbie. Australians have long been viewed by archaeologists as Johnny-come-latelies to the human settlement scene. Based on genetics and the fossil record, many scientists believe modern humans evolved in Africa 100,000 to 140,000 years ago, arrived in Europe around 50,000 years ago, and found their way to Australia 10,000 years later. And it wasn't until 30,000 years ago, according to this consensus view, that early Australians began decorating rock shelters and cliff faces with elaborate paintings of animals and geometric shapes.

But Rhys Jones, an archaeologist from the Australian National University in Canberra, told the San Francisco gathering that he has concluded that human beings arrived in Australia at least 60,000 years ago. And, he suggested, they were already painting when they landed.

Jones drew on recently published data from two northern Australian sites, rock shelters known as Nauwalabila I and Malakunanja II. Both sites were excavated in the 1970s and early 1980s, but because their lowest occupation levels—3 meters down—lacked charcoal for radiocarbon dating, their age remained unknown. But in the last 15 years, geochronologists have developed and refined two dating techniques that don't require carbon samples and are not subject to the 40,000-year limit that applies to radiocarbon dating.

The methods, thermoluminescence (TL) and optical dating, rely on a type of quartz timing unused by even the finest Swiss watchmakers. In essence, the methods date sediments containing grains of quartz by counting electrons trapped by quantum mechanical or physical defects in the mineral. The electrons are bumped into these traps at a regular rate, providing the basis for a clock. They can be released by energy absorbed from sunlight, which sets the quartz timing to zero; if the grains are then buried safely in sediments, the clock starts ticking. Millennia later, by heating the quartz in a lab or flashing it with light, geochronologists can release the electrons. Before returning to their natural places within the material, the freed particles release energy in the form of photons, producing a brief glow whose intensity is in direct proportion to the number of released electrons. Measuring this light thus reveals the ticks of the clock, and the techniques can date deposits exposed to sunlight from 1000 to several hundred thousand years ago.

TL frees the electrons by heating them, and Jones's team first used the method in 1990, on deposits at Malakunanja II. He obtained an age of 55,000 to 60,000 years for the lowest level. That level contained flaked



DATA-ROCHE WATCHMAN

Early arrivals. Australians who painted figures like these may have been on the continent 20,000 years earlier than previously thought.