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RESEARCH NEWS

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Human Y Chromosome Preserves Itself Better Than the Chimp Y

By using human and chimpanzee Y chromosomes as a genetic fossil record to examine our past, scientists have seen a surprising difference in the way the male-making chromosomes from the two species cope with the inexorable pressures of evolution.

After comparing the Y chromosome sequences of the human and chimpanzee, Howard Hughes Medical Institute researcher David C. Page, postdoctoral fellow Jennifer F. Hughes and their colleagues have seen evidence that the human chromosome has found a way to stabilize itself and survive in the roughly 6 million years since humans and chimpanzees have been following different evolutionary paths. In other words, the human Y chromosome is not rotting away, as some scientists have argued.

In contrast, the chimpanzee Y chromosome is not faring quite as well. Studying the same family of single-copy genes shows that the chimp's Y has been accumulating mutations that are gradually making some of its genes useless.

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- David C. Page

About 6 million years ago humans and chimps shared a common ancestor, Page explained. Since then the chimp genome and the human genome have evolved along separate paths. Why natural selection has created such differences in their Y chromosomes is not clear.

Page, who is interim director of the Whitehead Institute for Biomedical Research, collaborated with genome researchers at Washington University School of Medicine in St. Louis. A detailed report on their findings appears in the September 1, 2005, issue of the journal *Nature*. Page's co-authors at the Whitehead Institute included Hughes, Helen Skaletsky, Tatyana Pyntikova and Steve Rozen. Washington University team members were Patrick J. Minx, Tina Graves and Richard K. Wilson, who are at the Genome Sequencing Center.

“The big idea has been that the Y chromosome's genes are going away—that it's not long for this world,” Page explained. But these new data—based on comparing the chemical sequence, the “spelling” of single genes found on the two primate species' Y chromosomes—indicates that the chimp Y is falling behind, while the human Y is maintaining the status quo.

“So the bottom line is that the human Y looks to be doing a better job of preserving its single genes than anyone expected. And it looks like natural selection can work very well in Y chromosomes, even though they cannot swap genes with a counterpart chromosome,” Page said. For the other so-called autosomal chromosomes, the swapping of genes between matching pairs from parents is considered important to maintain the health of the genome. This process gets rid of mutant genes and provides new gene combinations to improve the overall genetic “vigor” of the species.

The Y chromosome genes the researchers studied occur in single copies, and make substances used throughout the body to perform basic functions in cells.

In 2003, Page and his colleagues reported that another set of genes on the Y, those that are active only in the testes and make the sperm, come in pairs and somehow repair or replace themselves.

“At that time, we were coming to the defense of the Y chromosome,” Page said. “But it turns out that the human Y chromosome is far more able to defend itself because it carries spares—back-up copies—of these testis-expressing genes.” As part of the mating game, chimpanzees make much more sperm than humans do, so their testes need to be operating at high capacity.

As a result of the newest research, Page added, “we can also draw some inferences about that common ancestor” shared by humans and chimps some 6 million years ago. By examining and comparing the Y chromosomes from both species, “we're getting a gene catalog of the common ancestor's Y chromosome” even though that ancestor lived long ago and cannot be studied directly. Evidence suggests, too, that the X and Y sex chromosomes became separate and distinct from the autosomes, the other type of chromosomes, about 300 million years ago.

Unlike the autosomes, the X and Y do not pair up and exchange genes during reproduction. As a result, the Y chromosome remains essentially stable - a clone from deep in the past - carried down through eons of time. Yet when damaging mutations do occur, the Y chromosome is stuck with them, having no means to reshuffle its genes to jettison the junk.

Page and his colleagues wrote that their new studies suggest the human Y chromosome is able to cleanse itself of genetic errors by a process they call “purifying selection.” In fact, mathematical models have been proposed which suggest how this occurs - pointing to a slowing of the rate of gene decay for the human Y chromosome late in evolution.

“These findings also suggest that `purifying selection' on the Y chromosome has been more effective during recent human evolution than previously supposed,” the researchers conclude.