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HUMAN Y CHROMOSOME STAYS INTACT WHILE CHIMP Y LOSES GENES

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CAMBRIDGE, Mass. (August 31, 2005) - The human and the chimpanzee Y chromosomes went their separate ways approximately 6 million years ago. But ever since this evolutionary parting, these two chromosomes have experienced different fates, new research indicates.

While the human Y has maintained its count of roughly 27 genes and gene families over the last 6 million years, some of these same genes on the chimp Y have mutated and gradually become inactive. The authors speculate that one likely reason for such disparity is due to chimpanzee mating habits.

"Contrary to the dire predictions that have become popular over the last decade, the sky is *not* falling on the Y," says Whitehead Member and Howard Hughes Medical Institute investigator David Page, senior author on the study that will appear in the September 1 issue of the journal Nature. "This research clearly demonstrates that natural selection has effectively preserved regions of the Y chromosome that have no mechanisms with which to repair damaged genes."

For many years, it's been assumed that the Y chromosome is headed for extinction because, unlike other chromosomes, it has no genetic "mate" with which to swap genes. In 2003, Page published a landmark paper in Nature challenging that claim by demonstrating how a certain region of the Y chromosome possessed a unique mechanism for repairing mutated genes.

Through sequencing the Y, the Page lab and collaborators at Washington University School of Medicine in St. Louis discovered that many of its genes were located in palindromes-long stretches of DNA letters that read the same forwards and backwards. By folding into a hairpin, the authors suggested, a gene might then swap the appropriate genetic material with itself. This demonstrated a process for the Y chromosome to maintain its integrity despite lacking a mate.

However, there is another region of the Y, called the "X-degenerate" region, where the genes are not situated in palindromes.

"The genes in the palindrome region are primarily sperm-producing genes, and most other genes unique to the Y aren't located there," says Jennifer Hughes, a postdoctoral scientist in Page's lab and first author on the paper. These other genes have no obvious means for self-repair. Because of this, many proponents of the "Y's demise" theory remained undaunted.

Once again collaborating with Richard Wilson from the Washington University School of Medicine in St. Louis Missouri, Page and his research team sequenced this X-degenerate region of the chimpanzee Y chromosome and compared it to the human Y.

"We were looking for any evidence that the human Y has lost genes since parting ways with the chimp," says Hughes. "Had we found active genes on the chimp Y that had become inactive on the human, that would be the smoking gun. But we didn't find any such evidence. In fact, we found the opposite."

On the chimp Y, five genes have suffered mutations that rendered them inactive. On the human Y, those same genes continue to function perfectly. "So then," says Hughes, "even though the Y has lost many genes since its origin about 300 million years ago, it's been holding steady in humans for the last 6 million years."

In other words, if the one region of the Y can depend on itself for survival, the other region has found a friend in evolution.

"We now see that natural selection *is* working to conserve this unpartnered region of the Y," says Page, who is also a professor of biology at MIT. "If mutations do occur in any of these genes, they don't seem to pass on in the lineage. This is a clear example of how evolution is not just about moving ahead, it's also about not falling behind."

Fortunately for the primate world, male chimps, just like male humans, are probably not bound for early extinction. Those genes in the X-degenerate region are what scientists call "housekeeping" genes, meaning that they are active in most cells in the body and don't carry out any male-specific functions.

Page and his team speculate that the loss of genes on the chimpanzee Y may be due to the chimp's mating habits. Both male and female chimps engage with multiple partners when they mate. This gives a strong selective pressure on those genes that produce sperm. Conversely, it puts less pressure on evolution to preserve those genes on the Y whose functions have nothing to do with reproduction. Because humans historically have been largely monogamous, our Y chromosomes have been spared such selective-pressure imbalance.

"Of course," acknowledges Page, "this is a hypothesis that we have no way to scientifically prove or disprove. However, we believe it's currently the best explanation."

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