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Genome duplications may separate humans from other great apes

Copying and rearranging of DNA led to structural differences

By Tina Hesman Saey

Although it may not be as dramatic as the Big Bang birthing the universe, an explosion of DNA duplication in the common ancestor of humans, chimpanzees and gorillas may be responsible for many of the differences among those species, a new study suggests. The blowup happened 8 million to 12 million years ago, and its effects are still apparent today.

Human and great ape genes are famously similar, with few differences in the genetic letters that make up the instruction manual for building each of the primates. But gorillas, orangutans, chimpanzees and humans are obviously different. A new analysis of the entire genomes of humans and their ape cousins, published in the Feb. 12 *Nature*, suggests the differences may have roots in DNA duplications.

Researchers led by Evan Eichler, a Howard Hughes Medical Institute investigator at the University of Washington in Seattle, compared the genomes of macaques, orangutans, gorillas, chimpanzees, bonobos and humans. The scientists found that chunks of the genomes had been copied and rearranged, sometimes multiple times, within each lineage.

After orangutans branched off the primate family tree, duplication rates accelerated dramatically in the common ancestor of gorillas, chimpanzees and humans. The burst continued in the common ancestor of humans and chimps, but then slowed again. While duplication rates were heating up, other types of mutation – such as single-letter changes in the genetic sequence – slowed down.

All the duplication activity resulted in structural differences in the genome architectures among the species on a scale not previously appreciated. Earlier studies had looked only at single genes or small parts of the genome, so large-scale changes were not apparent.

"This paper suggests that the real variation leading to the human lineage is structural," says Mark Gerstein, a bioinformatician at Yale University. "I think it's plausible that copy number or structural variation can affect things even more than mutation – single base changes – can."

Changing a single base, or DNA letter, probably has limited effects because such mutations could alter only one gene. But large duplications of 20,000 bases or more, such as those mapped in the new study, may contain more than one gene or parts of genes and regulatory regions.

Doubling, tripling or quadrupling the number of copies of a stretch of DNA in the genome can potentially increase activity of genes contained in the chunks by a corresponding amount. A duplication might contain some parts of a gene, but not all of it, which could change the gene's function. And the extra copies might contain control panels for genes, Gerstein says. Inserting those control panels, in full or in part, somewhere else in the genome could change the activity of genes adjacent to the insertion point.

Duplications don't appear to happen randomly, the researchers found. Most duplications occurred next to more ancient duplications, creating hot spots in the genome susceptible to copying and rearranging. These slippery parts of the genome provide flexibility for adaptation to new environments, but have a downside as well.

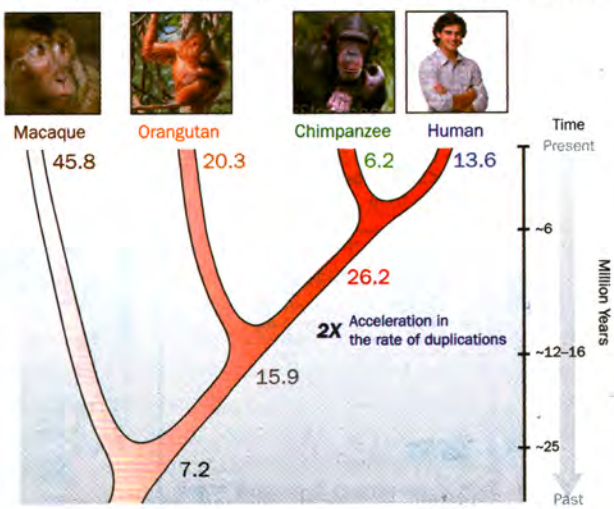
Genomic instability has been linked to disease in humans. Cancer cells are notorious for genetic duplications, rearrangements and deletions. Unstable DNA also predisposes people to disorders such as autism, mental retardation and schizophrenia. Because duplications linked to autism and schizophrenia are so recent, it is likely that these neurodevelopmental disorders are also quite young.

About 20 percent of the duplications identified in the study are found only in humans. Most of the replicated chunks contain genes with unknown functions, so the next step of the project is to figure out how the duplications happen and how the genes inside them contribute to making humans human.

But humans aren't the only ones with extra DNA specific to their species, says Jeff Kidd, a genomics researcher in Eichler's lab. "If you and I were two chimpanzees talking, we'd be talking about how 20 percent of duplications are unique to chimps," Kidd says. "It's all a matter of perspective."

Accelerated rearranging

A burst of genetic duplications between 8 million and 12 million years ago helped make humans different from their great ape relatives. The numbers on the tree below indicate millions of duplicated bases specific to each species and each common ancestor.



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