Comparing Genomes Shows Split Between Chimps and People

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By NICHOLAS WADE

By comparing the human genome with that of chimpanzees, people's closest living relative, scientists have identified a partial list of the genes that make people human.

They include genes for hearing and speech, genes that wire the developing brain, genes for detecting odors and genes that shape bone structure.

The comparison, reported yesterday in Science, was undertaken by Dr. Michele Cargill and colleagues at Celera Diagnostics in Alameda, Calif., who decoded most of the genes in the chimp's genome, and Dr. Andrew G. Clark and colleagues at Cornell, who made the analysis.

A more complete version of the chimp genome is being prepared by government-financed DNA sequencing centers at the Massachusetts Institute of Technology and the Washington University School of Medicine. The two centers made a draft of their sequence available yesterday on public DNA databases.

Humans and chimps shared a joint ancestor as recently as five million years ago. Biologists have long supposed that if they could identify the genes that changed in the evolutionary lineage leading from the joint ancestor to people, they would understand the genetic basis of how people differ from chimps and, hence, the essence of what makes humans human.

Because the sequence of DNA units in the two genomes is 98.8 percent identical, it seemed that just a handful of genes might define the essence of humanity.

The project received a lift two years ago when a large London family with barely intelligible speech was found to have mutations in a gene called FOXP2. Chimpanzees also have a FOXP2 gene, but it is significantly different. The human version shows signs of accelerated evolutionary change in the last 100,000 years, suggesting that the gene acquired a new function that helped confer the gift of speech.

But the process of transforming the joint human-chimp ancestor, who was probably a very chimpanzee like creature, into a human seems much more complicated in light of the new analysis. In a preliminary screen, Dr. Clark and his colleagues have found that a large number of genes show signs of accelerated evolution in the human lineage. Those are genes that, by a statistical test applied to changes in their DNA, appear to be under strong recent pressure of natural selection and so are likely to be those that make humans differ from chimpanzees.

A prominent set of accelerated human genes are those involved in hearing, particularly the gene that makes a protein called alpha-tectorin, a component of the tectorial membrane of the inner ear. Dr. Clark suggests that the genes governing speech and hearing are most likely to have evolved in parallel and that evolutionary tweaks in the alpha-tectorin gene may make humans hear somewhat differently from chimps.

Another group of selected genes is involved in brain development. Of particular interest is SEMA3B, which helps guide growing nerve axons to the proper regions in the brain. Differences in the human version might help explain the different wiring in the two brains, Dr. Clark said.

Genes involved in recycling amino acids, the building blocks of proteins, have changed in the human line, the Science article reports. Those could reflect changes in diet when humanlike descendants of the mostly fruit-eating ancestor switched to meat. There are also changes in the human genes for odor detection. Some of those genes have become inactive, reflecting a lesser reliance on the sense of smell, while others have developed new sensitivities, suggesting adaptations to a new environment.

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Geneticists can often estimate the time a gene started to evolve by looking at how variations in the gene have evolved from a single ancestral form. Dr. Clark said similar dates could be derived for the genes that he has found, if their variations in the human population were known. That may shed light on the timing of many milestones in human evolution. But the dates derived by geneticists often have very large ranges, which can make them less useful.

The authors of the Science article note that many of the human genes they found to have undergone accelerated evolution turn up in the list of Mendelian diseases, those caused by defects in a single gene. The reason for that curious association could be that the genes serve new functions, ones that emerged so recently that evolution has not had time to install backups, Dr. Clark said.

The human version of the FOXP2 gene has been estimated by that method to be 100,000 years old.

The authors of the report conducted the first genomewide comparison of human and chimp genes, but for technical reasons were able to test for accelerated evolution in fewer than 8,000 of the 30,000 or so genes in the two genomes. Dr. Clark said the statistical power of the test for evolutionary acceleration was limited and would fail to detect any that might have occurred in shorter genes.

"It's exciting how much you are able to illumine the difference between humans and chimps," he said.

But the differences at the genetic level need to be checked in terms of biology. Only in rare cases like that of FOXP2 is the link between the accelerated genes and actual biology more than a guess at present.