Medical Xpress

Small DNA changes separate chimp and human brains

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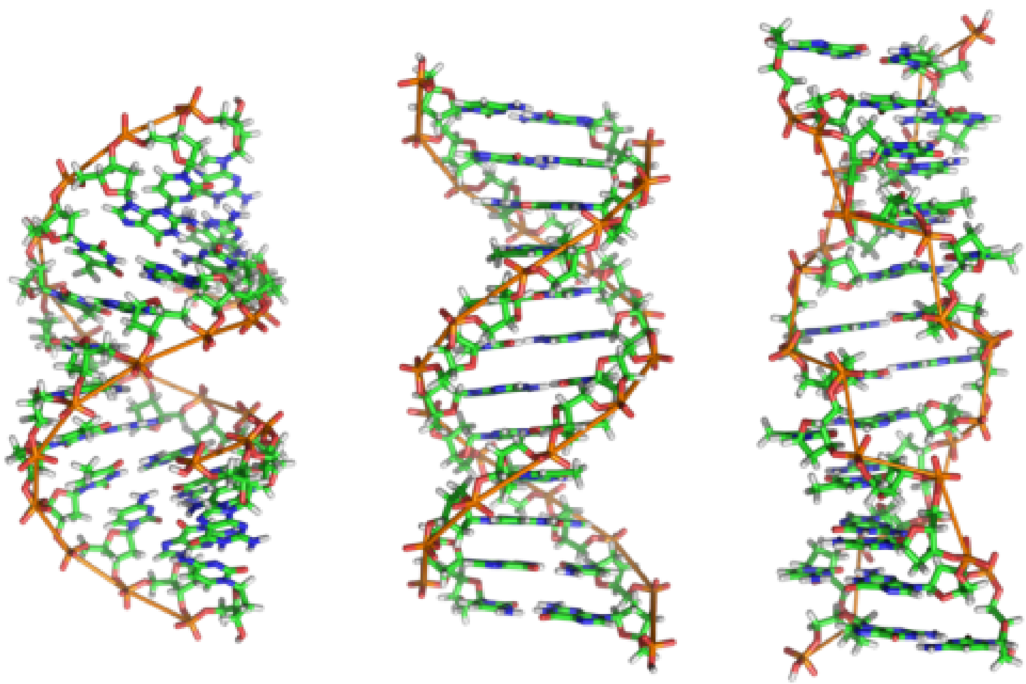

From left to right, the structures of A-, B- and Z-DNA. Credit: Wikipedia

Modern humans share about 95 percent of their genetic code with chimpanzees. Yet human brains, and what we do with them, are vastly different.

In the decade since the human genome was mapped, researchers have identified hundreds of small regions that differ between humans and fellow primates. Many show evidence of accelerated changes that might offer evolutionary clues to such fundamental differences as skeletal structure, motor skills and cognition since our human ancestors parted ways with chimpanzees some 6 million years ago.

A new study suggests that just 10 differences on one particular strand of human DNA lying near a brain-development gene could have been instrumental in the explosive growth in the human neocortex.

The DNA region, containing just 1,200 base pairs, is not a gene. But it lies near one that is known to affect early development of the human neocortex, according to the study, published online this week in *Current Biology*.

Researchers showed that the region, known as HARE5, acts as an enhancer of the gene FZD8. Embryos of mice altered with human HARE5 developed significantly larger brains and more neurons compared with embryos carrying the chimp version, according to the study.

"It could contribute to making us unique, and making our brains unique," said Duke University developmental neuroscientist Debra Silver, co-author of Thursday's study. "We're seeing the human enhancer turn on gene activity right at the onset of when a population of cells called neural stem cells are rapidly proliferating. They shift within a day or two to making neurons."

The type of neurons and the timing of their development are significant - these excitatory neurons arise later in utero, which is consistent with human fetal brain development patterns driven by the gene in question.

So have they found the genetic missing link between chimp brains and human brains?

"We think it's likely that there's many additional accelerated regions that are contributing to human brain development, and they may be impacting other aspects that make our brains unique," Silver said.

"It still would be a pretty big gap to go all the way to: 'Oh, and that's why we have a spoken language, or different types of fine muscle movements or different cognitive abilities,'" said Katherine Pollard, an evolutionary genomics researcher at the University of California, San Francisco's Gladstone Institutes, who was not involved in the study. "But this is certainly a big step in that direction."

Pollard conducted early research that identified many regions of the human genome that appear to be evolving fast.

"Almost all of these sequences were outside of genes and in most cases had no annotated function," Pollard said. "Nobody had ever considered that genome sequence before or studied them in any way."

Pollard's lab and others have been trying to fill in those gaps.

"This paper is part of that growing body of work," Pollard said. "What's particularly exciting about it is that it goes a little bit further than just saying this particular sequence functions as a regulatory enhancer, and tries to get at the question of what would be the molecular- or ultimately organismal-level trait associated with the changes in the human DNA."

The full-grown mice with the larger brains are still around, and Silver's lab will be trying to devise ways to test whether they show behavioral differences attributable to the brain changes.