To Be, or Not to Be, Chimpanzee

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MOLECULAR-LEVEL COMPARISONS

If there were a cosmic cheat sheet with the answer to just one question, wouldn't we want it to tell us what makes us human? Having entered the postgenomic era with the sequencing of the human genome, we continue to probe our DNA for what sets us apart. But because chimpanzees are 98 to 99 percent identical to humans in genomic coding regions, our answer would also need to explain how we're not chimps.

A recent study published in the 15 November issue of *Genes and Development* is the first to ask whether the post-transcriptional process of alternative splicing can account for some of the major differences between humans and chimps. More than half of human genes yield pre-mRNA transcripts that are alternatively spliced, giving rise to alternate mRNA transcripts and in many cases different resultant proteins from each individual gene sequence. In this way alternative splicing, a process common to all eukaryotes, increases the proteomic complexity of a genome and provides the basis for many tissue-specific—and perhaps species-specific—distinctions.

The University of Toronto scientists and their colleagues, led by John Calarco, Yi Xing, and Mario Cáceres, assessed chimp and human splicing differences in two ways. In one analysis, they compared genomic sequences of orthologous human and chimp exons, along with short segments of their flanking introns, looking for regions near exon–intron splice sites with elevated nucleotide substitution rates between the two species. These regions, which are known to be enriched in splicing regulatory elements, were then analyzed for alternative splicing in heart and brain tissues from several humans and chimps. Of the 31 regions examined that showed such elevated rates, 5 displayed splicing-level differences between humans and chimps in at least one tissue.

They also examined microarray profiles with an alternative splicing microarray that can profile around 5000 alternative splicing events, using cDNA made from poly(A)$^+$ mRNA of the heart and brain tissue samples from each species. As would be expected for closely related species, the profiles were largely similar, but a surprisingly large fraction, 6 to 8 percent, of the exons studied showed splicing-level differences. This subset of genes with alternative splicing differences does not significantly overlap, however, with the subset of genes with steady-state transcript-level differences between humans and chimpanzees. Alternative splicing is evidently a distinct type of gene regulation.

Genes that exhibit alternative splicing differences play roles in diverse cell functions, including those involved in immune and stress responses, signal transduction, and regulation of transcription and splicing, among others. The effects of splicing-level differences are not yet clear, but this form of gene regulation is among the possible means by which we are distinguished from our primate relatives.

SHORT-TERM MEMORY

Although many of the cognitive skills thought to be uniquely human are continually being discovered in other species (to varying degrees), it isn't easy to impress us. Our closest relatives, chimpanzees, can use tools, learn sign language, make inferences, and remember where food is cached, and yet their abilities have not exceeded ours—until now.

Young chimps outperformed college students in a test of short-term memory. Sana Inoue and Tetsuro Matsuzawa, whose study appears in the 4 December 2007 issue of *Current Biology*, made videos of their test subjects at a touchscreen monitor that are well worth watching (*www.current-biology.com/cgi/content/full/17/23/r1004/DC1/*).

The task begins when the test subject touches a circle near the bottom of the screen. Numerals 1 through 9 appear scattered across the screen in a unique pattern each time, and subjects successfully complete the test when they touch each numeral in the correct order. The six chimpanzees, three mother–offspring pairs, all of which had been trained to use Arabic numerals to count objects, performed the task accurately both for all nine numerals and for abbreviated sequences, such as 2-3-5-8-9.

The test in which the young chimpanzees outperformed the adults, both human and chimp, was a masking task. Soon after the numerals appeared on the screen, they were replaced with white squares. Test subjects had to complete the sequence on the basis of what they could remember. When all the chimpanzees had mastered this task, the scientists tested the limits of their memory by masking the numerals after different durations: 650, 430, and 210 milliseconds. The adult subjects all performed worse the shorter the duration became, but the young chimp (shown in a video clip) accurately completed the limited-hold memory task, appearing almost nonchalant. Perhaps the chimps should give Sudoku a try.

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