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Louisa Flintoft

GENOMICS

Closest relative sequenced

The much anticipated chimpanzee genome sequence has been published. Although a draft, members of The Chimpanzee Sequencing and Analysis Consortium have skillfully analysed it and draw a wealth of important conclusions about chimpanzee and human biology and evolution.

A whole-genome shotgun approach was used to sequence the genome of a single male chimpanzee — Clint. The draft assembly covers ~94% of the genome, but a construction of a BAC-based physical map has begun with the aim of increasing coverage and quality.

Sequence comparisons between the chimpanzee, human and mouse revealed that although regional variation in nucleotide substitution rates is conserved between the three genomes, it is substantially elevated in human and chimpanzee subtelomeric regions. In an accompanying paper, Linardopoulou *et al.* focused specifically on human subtelomeres. The authors report that human-specific sequence duplications and translocations at chromosome ends have given rise to half of all known subtelomeric sequences. The relatively high rate at which the duplications occur could have advantageous or pathological consequences — as the authors point out.

Although single nucleotide substitutions occur at a mean rate of ~1.23% between the human and chimpanzee genomes, each genome also contains 40–45 Mb (~1.5%) of species-specific euchromatic sequences — which are a result of lineage-specific insertions and deletions. In an accompanying paper, Cheng *et al.* report that 33% of human duplications are not present in the chimpanzee and that 60% of those result from *de novo* duplications. Using experimental and computational approaches they estimate that duplications have occurred at a rate of 4–5 Mb per million years since the human–chimpanzee divergence. Cheng *et al.* point out that, per base, large segmental duplications have had a greater effect on the genomic landscape than single base-pair differences.

Human–chimpanzee orthologues turn out to be well-conserved — typically, they differ by only 2 amino acids. When normalized, the rates of non-synonymous substitutions are higher in the chimpanzee and human than in the mouse. As these rates are close to the rate of common human polymorphisms, positive selection might account for only a small portion of evolution in the hominid lineage, contrary to previous suggestions. The observation that substitution rates at silent sites within coding regions are lower than in introns further adds to the growing body of evidence that silent sites are not neutral but are under weak purifying selection.

Focusing on individual gene categories, the authors found that genes involved in immunity and host defence, reproduction and olfaction probably evolve rapidly in all mammals, as similar patterns were seen in the human, chimpanzee, mouse and rat genomes. But genes involved in ion transport, synaptic transmission, spermatogenesis and the perception of sound seem to evolve more rapidly in the hominid lineage. Curiously, the genes that evolve fastest in the human lineage include transcription factors, especially those that have key roles in development.

Having the chimpanzee genome sequence is a tremendous asset — as already demonstrated by Linardopoulou *et al.*, Cheng *et al.* and Hughes *et al.* in these early days of analysis. For once the focus in the comparisons will have to change: whereas we used to look for similarities, given the close relatedness of the human and chimpanzee it is time to zoom in on the differences.

Magdalena Skipper

References and links

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