GENETIC VARIATION

Recombination's local role revealed

A recent study has taken a new approach to unravelling the complex relationship between recombination and human genetic diversity. Contrary to previous findings, recombination seems to influence variation only at a localized scale in the human genome.

Spencer and colleagues took a three-pronged approach to addressing the link between recombination and variation. First, they generated a fine-scale recombination map using genotyping information from human populations. This allowed them to study recombination rates at a much higher resolution than was previously possible. Second, they analysed human chromosome 20 in detail for other factors, such as GC-content, that might influence diversity. Finally, they used an approach known as wavelet analysis to investigate correlations between diversity, recombination and other factors over various scales. Importantly, this method provides a measure of how much a change in one factor influences a change in another factor over the same scale, reducing the likelihood that apparent correlations are actually due to the influence of a third factor.

This approach showed that recombination affects nucleotide diversity only at a localized level, at a scale of 2–4 kb. This corresponds to the size of recombination hotspots, which are areas that have particularly high rates of crossing over. The larger-scale correlation between recombination and diversity in previous studies probably results from an indirect relationship that involves other factors, such as GC-content.

The authors surmised that such a localized effect of recombination is probably due to a mechanism that does not involve selection. For example, recombination might cause an increased mutation rate. Alternatively, the frequency of existing mutations might be altered due to phenomena such as biased gene conversion (BGC), which can result when single-base mismatch repair is mediated by the pairing of homologous chromosomes (as occurs in recombination). In support of the second theory, biases towards GC substitutions have been reported in regions of high recombination. Indeed, when the authors looked at mutation frequencies in regions of very high and very low recombination, the pattern that they saw was highly indicative of a role for BGC in shaping nucleotide diversity in these localized regions.

As well as increasing our understanding of the factors that shape human genetic diversity, these findings have important practical applications. For example, we now know that correlations between recombination patterns and diversity at the local level need to be factored in when looking for signs of adaptation in genome sequences. Furthermore, additional findings of this study support the growing evidence that recombination hotspots are rapidly evolving, and are different even between chimpanzees and humans, adding to the difficulty of assessing evidence for adaptive change between humans and our primate relatives.

Louisa Flintoft

ORIGINAL RESEARCH PAPER Spencer, C. C. A. et al. The influence of recombination on human genetic diversity. *PLoS Genet.* **2**, e148 (2006)

WEB SITE

Gil McVean's web site: <http://www.stats.ox.ac.uk/~mcvean>

IN BRIEF

SEX CHROMOSOMES

Expression profile of a degenerating neo-Y chromosome in *Drosophila*.

Bachtrog, D. *Curr. Biol.* **16**, 1694–1699 (2006)

The evolutionary mechanism that drives the loss of gene expression on degenerating Y chromosomes is unclear. By examining the expression levels of 58 genes on the newly formed but degenerating Y chromosome of *Drosophila miranda*, Doris Bachtrog shows that most of these genes (80%) are expressed at lower levels than genes on the X chromosome. This decreased expression occurs randomly, indicating that it is caused by the indiscriminate (non-selective) accumulation of mutations on this non-recombining chromosome, and that it is independent of chromosomal context.

EVOLUTION

Large punctuational contribution of speciation to evolutionary divergence at the molecular level.

Page, M., Venditti, C. & Meade, A. *Science* **314**, 119–121 (2006)

Most evidence in the debate over punctuated equilibrium — whether evolutionary change happens at a constant rate or in bursts — comes from the fossil record. At the sequence level, the authors found evidence for punctuation in twice as many fungal and plant lineages as animal ones, but the contribution of punctuation to molecular diversity — 22% — did not vary. However, the proposed periods of morphological stasis between bursts had no counterparts at the molecular level. Therefore, the inference of dates from phylogenies might be biased in lineages that have undergone punctuated bursts.

TECHNOLOGY

A recombineering pipeline for functional genomics applied to *Caenorhabditis elegans*.

Sarov, M. et al. *Nature Methods* **3**, 839–844 (2006)

This paper describes an efficient, high-throughput approach to generating transgenes from genomic clones. Taking advantage of a high-fidelity version of the recombineering method (which involves homologous recombination in *Escherichia coli*), the authors eliminated the need for sequential cloning and checking stages, which allowed efficient transgene engineering in liquid culture. The authors validated the method by constructing transgenes from *Caenorhabditis briggsae* genomic clones, which were expressed correctly on transformation into *C. elegans* and rescued RNA-mediated knockdown of the endogenous genes.

GENOME EVOLUTION

Epistasis correlates to genomic complexity.

Sanjuan, R. & Elena, S. F. *Proc. Natl Acad. Sci. USA* **103**, 14402–14405 (2006)

Epistasis is central to several evolutionary theories, but the extent and nature of epistatic interactions at a genome-wide level are unclear. This study shows a correlation between genome complexity and the nature of epistasis. In organisms with simple genomes, such as RNA viruses, combinations of mutations have smaller effects than are expected on the basis of their individual effects (antagonistic epistasis); the reverse (synergistic epistasis) is seen in metazoans with more complex genomes. This correlation might be related to decreased pleiotropy and increased mutational robustness in complex genomes.