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NEWS AND COMMENTARY

Comparative genomics

The economies of evolution

MA Ferguson-Smith

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Now that whole genome sequence drafts are becoming available for species other than human and mouse, comparative studies are yielding new information about our evolution. An example of the sort of insights such analyses can offer has now come from Murphy *et al* (2005) in a recent issue of *Science*, who compare the genomes of eight species from five mammalian orders and show that sites of evolutionary rearrangements are frequently re-used.

These new observations should be set in the context of the knowledge that the genomes of all species are highly conserved. This conservation includes homology of transcribed sequences, genetic linkage groups and often large segments of chromosome. Differences in chromosome number and structure result largely from illegitimate meiotic recombination between DNA repeats within and between nonhomologous chromosomal regions. The number of rearrangements that have become fixed in the evolutionary history of mammals seems comparatively small, so that many distantly related species are found to share whole chromosomes or chromosome arms. When compared to humans, most mammals have 20–40 blocks of homology with the human genome; dogs and gibbons have about twice as many and the mouse has at least 217 (Mouse Genome Sequencing Consortium, 2002). Such homologous segments are arranged in different order on the chromosomes of different species and it was known that the sites of rearrangement tended to occur in regions containing duplicated sequences or members of gene families.

The authors of this new study recognise 1159 homologous blocks between humans and six non-primate species and confirm the presence of duplications at the breakpoint sites. They note that the breakpoint regions are gene rich and are associated with ancestral telomeres and centromeres. A total of 20% of the breakpoint regions were re-used in other species, which indicates that these regions are hot spots for evolutionary rearrangements. The authors note that some of the same sites are also hot spots for chromosome rearrangements in cancer cells.

It is well known that patterns of chromosome homology provide clues about phylogenetic relationships. Closely related species tend to share similar patterns and some patterns are ancestral to distantly related species. The G-banding patterns provided the earliest cytological data for constructing evolutionary trees, but chromosome painting studies that use chromosome-specific DNA probes – a method with much higher resolution – have superseded this approach. Cross-species chromosome painting has revealed the likely ancestral karyotype of a number of mammalian orders and has suggested the most likely ancestral karyotype of all mammals (Yang *et al*, 2003). As a rule, painting maps do not reveal the orientation of each homologous segment unless they are coupled with FISH mapping of single-copy sequences at either end of the segment. The new article uses sequence information from each breakpoint region, which gives even higher resolution than chromosome painting for the construction of phylogenetic trees. It is impressive that the two approaches reach similar general conclusions.

Murphy *et al* use their data to calculate the likely rate of chromosome breakage through mammalian evolutionary history and show that there has been an increase in breakage rates in the last 75 million years (ie since the K-T boundary). However, such rates show great variation, from the comparatively low rate in the cat lineage to the high rates in the dog and mouse lineages. Chromosome painting has shown that the lesser apes have an unexpectedly high rate compared to other primates and a comparison of four gibbon species shows that none share a single autosome with identical painting patterns (Nie *et al*, 2001). We do not yet know what factors are responsible for this variation.

It is now clear that evolutionary breakpoint regions are associated with segmental chromosome duplications, contain many genes and seem to be where telomeres and centromeres tend to cluster. Among the 84 centromeres characterised in the Science paper, 38 were assigned to homologous segments and 74% of these occur at breakpoint boundaries. Most of the breakpoint boundaries defined by the human genome are associated with the formation of acrocentric chromosomes in other species. This observation helps to explain why chromosome fission and fusion that occur close to centromeres are common evolutionary mechanisms. All classified telomeres were found to occur at breakpoint boundaries or at the ends of non-human chromosomes. Centromeres, but not telomeres, were associated with re-use breakpoints. This implies that re-use breakpoints occur preferentially at sites of ancestral centromeres, or that these ancestral regions are unstable and have a tendency to form new centromeres.

Most interchromosomal rearrangements are the result of accidental crossing-over between homologous segments on nonhomologous chromosomes, and these events are often promoted by chromosomal inversion within one of the segments. It is not clear why some of these rearrangements and not others have become fixed in evolution and why some are prone to further evolutionary rearrangement. The answers to these questions may be found in the comparative study of additional species using the analysis of sequence data of the type initiated by the authors of this interesting study.

MA Ferguson-Smith is at Department of Veterinary Medicine, Madingley Road, Cambridge CB3 0ES, UK.

e-mail: maf12@mole.bio.cam.ac.uk

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