IN BRIEF

EVO–DEVO

Ancestral role of *caudal* genes in axis elongation and segmentation.

Copf, T. *et al. Proc. Natl Acad. Sci. USA* **101**, 17711–17715 (2004)

Caudal genes are known for their role in posterior patterning. By using RNAi, Copf *et al.* showed that loss of *caudal* in two arthropods (the *Tribolium* beetle and the *Artemia* crustacean) causes axis truncation and disrupts segment formation. Unlike in *Drosophila*, segments are laid down sequentially in these arthropods, just as they are during vertebrate somitogenesis. Given this similarity and the involvement of vertebrate *caudal* homologues (*Cdx* genes) in axis elongation and somitogenesis, these might represent ancestral, evolutionarily conserved *caudal* function.

TECHNOLOGY

Using protein–DNA chimeras to detect and count small numbers of molecules.

Burbulis, I. *et al. Nature Methods* **2**, 31–37 (2005)

The authors describe a powerful new tool for detecting a range of biological targets. The key to the technique, the sensitivity of which surpasses that of the routinely used ELISA, is a DNA–protein hybrid molecule (the 'tadpole'): the 'head' is made up of protein that has a targeted affinity for a specific molecule; the 'tail' is a unique DNA tag that allows PCR-based quantification. The two halves are joined in a naturally occurring splicing reaction.

EPIGENETICS

Histone demethylation mediated by the nuclear amine oxidase homolog LSD1.

Shi, Y. *et al. Cell* **119**, 941–953 (2004)

Histone methylation levels are crucial in the regulation of gene expression. In contrast to acetylation (both acetylases and deacetylases are known), methylation was thought to be a permanent modification. The authors provide evidence that LSD1, a nuclear-localized homologue of amine oxidases, functions as a histone demethylase of histone H3 lysine 4. Since this modification is linked with active transcription, LSD1, which is conserved from fission yeast to humans, is probably a transcriptional co-repressor.

HUMAN GENETICS

The influence of *CCL3L1* gene-containing segmental duplications on HIV-1/AIDS susceptibility.

Gonzales, Z. *et al. Science* 6 January 2005 (doi:10.1126/science.1101160)

Segmental duplications are enriched for genes that are involved in immunity, although the consequences of this fact remain unknown. The authors found that copy number of *CCL3L1*, a gene that encodes a ligand for the HIV co-receptor CCR5, varies significantly among individuals and populations. Fewer *CCL3L1* copies mean greater susceptibilty to HIV infection, whereas high levels of CCL3L1 are thought to block the association between CCR5 and HIV that is required for virus internalization. These findings support the crucial involvement of CCR5 and its ligands in determining HIV pathogenesis.

Image courtesy of J. Fondon, Southwestern Medical Center, USA.

EVO–DEVO

Dog — an agile genome

Although 50 years of molecular genetics might have come a considerable way towards answering age-old questions in evolutionary biology — not least the realization that DNA mutations provide the substrate for evolution — the fathers of evolutionary biology have still left us something to argue about. How, for example, to reconcile the rate of DNA mutation and its effects with the observed step-like pattern of morphological change? Supporters of the predominant and largely substantiated hypothesis would claim that the answer lies in the changes in gene *cis*-regulatory elements. John Fondon and Harold Garner have now addressed the same question but propose a different answer. Their conclusions, based on comparative genomics and morphological studies of more than 90 dog breeds, point instead to the importance of promiscuous variation in the length of tandem repeats within coding regions.

Dogs provide an appropriate subject for studies into morphological evolution as they have been bred intensively for specific traits (see also the review by Sutter and Ostrander). Many dog genes, like those of other vertebrates, are also characterized by the presence of tandem repeats in both coding and non-coding regions — repeats that, by expanding or contracting, can alter the genome at a rate that is 100,000 times higher than point mutations. Could these two features be used to correlate recent morphological variation with variation in tandem-repeat length?

The authors initially discovered that the 'purity' of the repeats in 29 of 36 developmental genes was substantially higher in dogs compared with humans — the repeats in the dog homologues had fewer interruptions and were more homogeneous; a sign that the active cutting and pasting by which the repeats grow and contract has removed the imperfections that would otherwise accumulate. This is evidence that the repeats in this species have been evolving recently. Sequencing the repeats of the same genes in 92 dog breeds confirmed the suspicion that repeat lengths vary among morphologically different breeds. Although most of the variation in repeat length was modest, the repeat length for 5 genes — including *Alx-4* and *Runx-2* — differed by up to 51 bp. Alleles of these two genes were used in different ways to correlate repeat and morphological variation. The deletion of 17 amino acids in an extreme *Alx-4* allele was found to contribute specifically to the polydactyly phenotypes seen in Great Pyrenees (known in Europe as the Pyrenean Mountain Dog); the study of a range of *Runx-2* repeat alleles with subtly different repeat lengths, by contrast, was used to correlate allelic length with the severity of the skeletal malformations that are caused by *Runx-2* mutations in dog, mouse and human.

The rapid morphological changes that have been selected for in dogs over a short period of time betrays a means of generating genetic diversity that cannot be accounted for simply by the rate of point mutation. As the authors show, the amount of SNP diversity among breeds is modest compared with differences in repeat length, which are abundant, robust and of recent origin, and could therefore plausibly facilitate rapid evolutionary change.

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References and links

ORIGINAL RESEARCH PAPER Fondon, J. W. III & Garner, H. R. Molecular origins of rapid and continuous morphological evolution. *Proc. Natl Acad. Sci. USA* 13 December 2004 (doi: 10.1073/pnas.0408118101)

FURTHER READING Sutter, N. B. & Ostrander, E. A. Dog star rising: the canine genetic system. *Nature Rev. Genet.* **5**, 900–910 (2004)

WEB SITES

Harold Garner's laboratory:
http://www8.utsouthwestern.edu/findfac/personal/0,2358,12465,00.html

Online Mendelian Inheritance in Animals (OMIA):
http://www.angis.org.au/Databases/BIRX/omia/