IN BRIEF

POPULATION GENETICS

African Y chromosome and mtDNA divergence provides insight into the history of click languages.

Knight, A *et al. Curr. Biol.* **13**, 464–473 (2003)

The authors carried out a phylogenetic analysis of Y chromosome and mitochondrial DNA sequences from a number of African ethnic groups, including those that use click consonants. All click-speaking peoples, such as the San, are limited to southern Africa, except for the Hadzabe people of eastern Africa. Sequence analysis shows that the San and the Hadzabe are distantly related, which indicates that the origin of click consonants might date back to early in the history of modern humans.

EVOLUTION

Molecular genetics and evolution of melanism in the cat family.

Eizirik, E. *et al. Curr. Biol.* **13**, 448–453 (2003)

Mutations in agouti signalling protein (ASIP) and melanocortin-1 receptor (MC1R) are associated with melanism in mice. Eizirik *et al.* cloned and sequenced these genes from cat species and found that melanic jaguars and jaguarundis carry two different deletions in *MC1R*, whereas black-coloured domestic cats have a deletion in *ASIP*. Because these mutations were not found in five other species of black cats, there must have been at least four independent genetic origins of melanism in the cat family.

EPIGENETICS

Effects of tethering HP1 to euchromatic regions of the *Drosophila* genome.

Li, Y. *et al. Development* **130**, 1817–1824 (2003)

Heterochromatin protein 1 (HP1) is a non-histone chromosomal protein. Li *et al.* found that, when tethered to euchromatic sites, HP1 silenced nearby reporters. HP1 has been shown to interact with the methylated lysine 9 of histone 3 at centric regions, but in this system, the methylation requirement might be bypassed because silencing is not dependent on the dosage of the histone methyltransferase SU(VAR)3-9.

RNA WORLD

The microRNAs of *Caenorhabditis elegans*.

Lim, L. P. *et al. Genes Dev.* **17** (10.1101/gad.1074403)

Lim *et al.* used a computer program, called MiRscan, to identify 35 new candidate miRNA genes in *Caenorhabditis elegans*. Candidates were verified by sequencing small RNA clones and Northern blots. Extensive cloning of small RNAs identified a further 20 new miRNAs, taking the total of validated *C. elegans* miRNAs to 88 — at least one-third of which have homologues in humans and other vertebrates. The expression patterns of 62 *C. elegans* miRNAs were studied; one-third were differentially expressed during larval development.

FUNCTIONAL GENOMICS

I need a new dictionary

Trying to understand, from a genome sequence alone, how genes interact to produce a whole organism is like trying to speak a strange new language using a dictionary in which most of the definitions have been deleted — all the words are there, but there is no indication of how they link together, or even what they sound like. Now, Eric Schadt, Stephanie Monks and colleagues show themselves to be accomplished genomic linguists by using comprehensive genetic screens of gene expression in mouse, maize and human to identify 'hotspots' of loci that influence gene expression.

Although it is known that some genes influence the expression of others, there have been few attempts to take a genome-wide approach to mapping the loci that are involved in controlling gene expression. The impressive efforts of Schadt, Monks and colleagues indicate that this approach is not only feasible, but is probably preferable in species for which we have libraries of gene expression probes and genome-wide markers.

The authors' approach is similar to that used to map standard quantitative trait loci (QTLs): a segregating population — in this case produced by crossing inbred lines of mice — is scored for the trait (gene expression) and for a suite of genetic markers (microsatellites that differ between the parental strains). By statistically identifying the changes in gene expression that correlate with marker differences, the authors map loci that influence the expression of a specific gene.

The study looks at an impressive 7,861 genes that were expressed differently in the two parental strains. The segregating population consists of 111 F_2 mice, which also had to be typed for more than 100 microsatellite loci. However, the pay off for all this effort comes when the authors analyse the genome-wide patterns of QTLs that control gene expression (eQTLs). As well as showing (unsurprisingly) that many eQTLs map at, or near to, genes the expression of which they influence — corresponding to gene-specific *cis*-acting elements — they show that other eQTLs cluster together in hotspots on different chromosomes, indicating *trans*-acting elements that influence multiple loci.

With analyses of eQTLS in maize and humans, the authors show the approach can easily be extended to other species. Further analyses show that using gene expression and genetic analyses in conjunction with phenotypic data (in this case, a measure of obesity) can allow more accurate identification of clinical trait QTLs and candidate genes.

Regardless of the immediate practical pay offs, the most exciting aspect of this approach is that the eQTL hotspots might point to important regulatory elements. So, studying and identifying more of them should help to build up a picture of the network of gene interactions.

Effectively, Schadt, Monks and colleagues have shown that we have the tools to start deriving the rules of genetic grammar and phonetics, giving us hope that we will eventually learn how to say "live long and prosper" in the language of the genome.

Nick Campbell

References and links

ORIGINAL RESEARCH PAPER Schadt, E. E. *et al.* Genetics of gene expression surveyed in maize, mouse and man. *Nature* **422**, 297–302 (2003)

FURTHER READING Jansen, R. C. Studying complex biological systems using multifactorial perturbation. *Nature Rev. Genet.* **4**, 145–151 (2003)

WEB SITE

Rosetta Inpharmatics: http://www.rii.com