IN BRIEF

GENE EXPRESSION

Association and spreading of the *Drosophila* dosage compensation complex from a discrete *roX1* chromatin entry site

Kageyama, Y. *et al. EMBO J.* **290**, 2236–2245 (2001)

Last month's Highlights discussed mechanisms that underlie the spreading of repressive chromatin. This paper reports the spreading of active chromatin, which is required for dosage compensation in flies to increase X-linked transcription in males. Dosage compensation is controlled by the male-lethal specific (MLS) complex, comprising five proteins and two non-coding (*roX*) RNAs. MLS binds to chromatin entry sites, one of which is the *roX1* gene. This study identifies a small DNase hypersensitive *roX1* fragment that, when located on autosomes, produces an ectopic chromatin entry site, which binds the MSL complex, allowing it to spread into neighbouring regions. This occurs even when *roX1* transcription is prevented, raising questions as to the role of the *roX1* transcript.

BACTERIAL GENETICS

Regulation of differentiation to the infective stage of the protozoan parasite *Leishmania major* by tetrahydrobiopterin.

Cunningham, M. L. *et al. Science* **292**, 285–287 (2001)

Leishmania is an important human parasite, the life cycle of which involves an infective stage (in the sand-fly vector) and an uninfective stage (in vertebrate macrophages). Cunningham *et al.* investigate the mechanisms that underlie the progression from the uninfective to the infective stage, and discover that knocking out a gene involved in pteridine metabolism, *PTR1*, results in increased virulence. In normal development, *PTR1* downregulation is necessary for the infective stage. This study reveals that virulence correlates inversely with PTR1 levels and that they can be used by *Leishmania* as a natural virulence-control mechanism to avoid killing its host.

IMMUNOGENETICS

Artemis, a novel DNA double-strand break repair/V(D)J protein, is mutated in severe combined immune deficiency.

Moshous, D. *et al. Cell* **105**, 177–186 (2001)

Human severe combined immunodeficiency with increased radiosensitivity (RS-SCID) is characterized by a defect, in V(D)J recombination, which causes RAG-induced double-stranded breaks to remain unrepaired, thus resulting in arrested B- and T-cell maturation. This study reports the positional cloning of Artemis, the RS-SCID disease gene, and the finding of eight independent mutations in RS-SCID patients, three of which involve deletions that span several exons. Artemis encodes a novel V(D)J recombination/DNA repair factor that belongs to the metallo-β-lactamase superfamily, but its precise role in DNA repair remains to be found.

POPULATION GENETICS

Linkage disequilibrium — a global view

As recent studies have shown (see Highlights, November 2000), an important issue for those mapping human disease genes is how and why linkage disequilibrium (LD) levels vary across the genome. Often such studies have looked at only a few loci. Now a genome-wide study of LD has found that long-range LD is a feature of European genomes but not of some African ones. These results illustrate how a population's history can determine its usefulness for disease-mapping studies and indicate that northern European populations experienced a severe bottleneck — perhaps during the emergence of modern humans out of Africa.

In this study, Reich and colleagues documented the extent of LD around 19 high-frequency coding single nucleotide polymorphisms (cSNPs) selected from a multi-ethnic DNA panel. They chose high-frequency SNPs for several reasons but, most importantly, because they represent the 'worst-case' scenario — the extent of LD is usually less around common SNPs than around rare, younger SNPs, as haplotypes with common SNPs have often been broken down over time by recombination.

Reich and colleagues identified SNPs at various distances away from the core cSNP in 44 unrelated individuals of N. European descent and measured the distance at which LD drops away (the half length). By comparing the 19 regions, Reich *et al.* found that LD has an average half length of 60 kb, indicating the presence of blocks of LD, larger than previously estimated. However, they also found great variation in LD between different genomic regions. For example, LD extends for 155 kb around the *WASL* gene, but for only 6 kb around *PCI*. These regional variations emphasize the value of a global view.

So why do large blocks of LD exist? The simplest explanation is that an extreme population bottleneck occurred — according to the authors' simulations — ~27,000–53,000 years ago. But could differing recombination rates also account for this pattern? If so, these regions should show long-range LD in all populations. To assess this, the authors analysed LD in 48 Swedes and 96 Yorubans from Nigeria — the Swedes had an identical pattern of long-range LD but in the Yorubans the half length was dramatically reduced to ~5 kb. These results strongly indicate that N. European populations indeed underwent a bottleneck after their divergence from Africans — one of such enormous proportions that only a handful of chromosomes gave rise to most of the N. European gene pool. This population contraction might have occurred during the migration from Africa, or perhaps more recently during the colonization of Europe or the last Ice Age.

The authors advocate that geneticists should make good use of these differing LD rates between populations for finding disease genes — their long-range LD makes European populations ideal for gene-mapping studies but not for finer mapping, which could be done in populations with less extensive LD, such as the Yorubans.

Jane Alfred

References and links

ORIGINAL RESEARCH PAPER Reich, D. E. *et al.* Linkage disequilibrium in the human genome. *Nature* **411**, 199–204 (2001)

FURTHER READING Wright, A. F. *et al.* Population choice in mapping genes for complex diseases. *Nature Genet.* **23**, 397–404 (1999)

WEB SITE Human SNP database