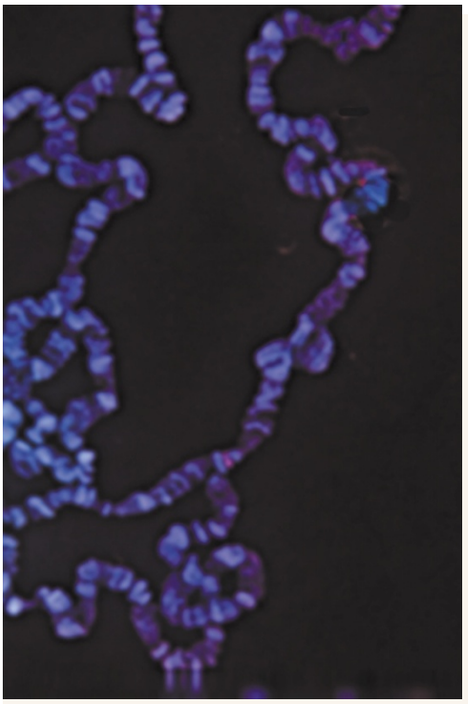

characteristic of this mutant is that it silences the wild-type allele *in trans* — hence the 'dominant' name. This is thought to occur because the heterochromatin causes both *brown* alleles to be located in a heterochromatic compartment of the nucleus, leading to stochastic silencing of the wild-type allele, and the variegated phenotype. Feeding these flies with a drug that binds specifically to the satellite repeat within the bw^D allele led to a range of defects during development. These defects did not occur when wild-type flies were treated, and so were dependent on the presence of the bw^D allele. After much detective work, the explanation was found — opening of the bw^D heterochromatin exposes the GAGAA satellite repeat, which can soak up a certain transcription factor (GAF, a GAGA factor encoded by a *Trithorax*-like gene), and produces a phenotype that resembles a hypomorphic mutation in GAF. It had been shown previously that GAF moves from a euchromatic distribution (in interphase) to centric heterochromatin during mitosis, suggesting that the reversible association with satellite DNA might be a normal form of GAF regulation.

By opening up chromatin, these new polyamide drugs render satellite DNA more open to scrutiny. Their effects on PEV mutants in *Drosophila* will stimulate new ideas about this and other non-coding components of the eukaryotic genome.

Mark Patterson

References and links

ORIGINAL RESEARCH PAPERS Janssen, S. *et al*. Chromatin opening of DNA satellites by targeted sequence-specific drugs. *Mol. Cell* **6**, 999–1011 (2000) | Janssen, S. *et al*. Specific gain- and loss-of-function phenotypes induced by satellite-specific DNA-binding drugs fed to *Drosophila melanogaster*. *Mol. Cell* **6**, 1013–1024 (2000)
WEB SITE Ulrich Laemmli's lab

date-gene approach. Reasoning that the sitosterolemia locus might be regulated by a nuclear hormone receptor (LXR) that mediates cholesterol homeostasis, the researchers used microarrays to search for mouse transcripts that were upregulated in response to an LXR ligand. One such transcript encoded a novel ABC transporter, ABCG5, that mapped to the human sitosterolemia locus. Its gene turned out to be adjacent to another locus, transcribed in the opposite direction, that contained a second transporter gene, *ABCG8*. Sitosterolemia patients were found to have mutations in either gene.

Sitosterolemia sufferers accumulate large amounts of plant sterols in their tissues that are not normally absorbed. Or so it was thought. Berge *et al*.'s findings indicate that plant sterols, such as sitosterol, are absorbed by intestinal cells but are then pumped back into the gut lumen by ABC transporters, such as ABCG5 and ABCG8. It remains to be investigated whether subtle defects in these proteins or in their regulation underlie our varied responses to high-cholesterol diets.

Jane Alfred

References and links

ORIGINAL RESEARCH PAPER Berge, K. E. *et al*. Accumulation of dietary cholesterol in sitosterolemia caused by mutations in ABC transporters. *Science* **290**, 1771–1775 (2000)
FURTHER READING Allayee, H. *et al*. An absorbing study of cholesterol. *Science* **290**, 1709–1711 (2000)

IN BRIEF

POPULATION GENETICS

The genetic legacy of paleolithic *Homo sapiens sapiens* in extant Europeans: a Y chromosome perspective.

Semino, O. *et al*. *Science* **290**, 1155–1159 (2000)

By typing 1007 Y chromosomes from 25 European and Middle Eastern regions for 22 biallelic markers, this study found that 95% of these Y chromosomes could be classified by just 10 key mutations, which reveal the history and origins of European populations. Two mutations, for example, have been present in Europe since Paleolithic times, and the remaining mutations probably entered Europe during independent migrations from the Middle East and the Urals. The study also shows that Y-chromosome variation patterns have been less influenced by natural selection than by migration, particularly during the last ice age.

EVOLUTION

Adaptive amplification: an inducible chromosomal instability mechanism.

Hastings, P. J. *et al*. *Cell* **103**, 723–731 (2000)

According to the Darwinian view of genetic change, natural selection selects the fittest organism among pre-existing variants. However, it has also been shown that some organisms undergo adaptive mutation, whereby mutations arise in response to, rather than before, exposure to a changing environment. The traditional explanation for adaptive mutation invokes a rise in genetic mutation rates, which increase an organism's adaptability. The amplification of the *lac* operon in *E. coli* under selective conditions, as shown here, provides evidence that DNA amplification, like hypermutation, can be an adaptive process. Cells use adaptive point mutation and amplification as two independent mechanisms, to confer a permanent or reversible response to stress, respectively.

GENOME MANIPULATION

Illegitimate Cre-dependent chromosome rearrangements in transgenic mouse spermatids.

Schmidt, E. E. *et al*. *Proc. Natl Acad. Sci. USA* **97**, 13702–13707 (2000)

The Cre–*Lox* system is a popular way to generate conditional mutations in the mouse (see Highlight on page 7). Activating the expression of the *Cre* recombinase gene at a particular time or place causes mutations by catalysing recombination between *Lox*P sites introduced into the genome. But there might be a problem. Schmidt *et al*. show that Cre can induce recombination in the mouse in the absence of *Lox*P sites. In their study, the expression of *Cre* in the male germ line caused 100% male sterility as a result of chromosomal rearrangements that produced inviable embryos. It is not known whether Cre can mediate such recombination in somatic tissue but, to limit unwanted recombination in conditional transgenesis experiments, it might be wise to switch *Cre* off once its job is done.