Flower power

Not all mutations are forever. Epimutations, heritable changes in gene expression without a corresponding change in primary DNA sequence, have been associated with the presence of transposons and DNA methylation in maize. Methylation can alter the expression of at least one endogenous gene in *Arabidopsis thaliana*: epimutant alleles of *SUPERMAN* are normal in sequence, but heritably hypermethylated, producing a floral phenotype (which includes an increased stamen number and a distorted fourth whorl) similar to that induced by true mutant alleles. But whether *SUPERMAN* epialleles are unique or represent a more common phenomenon is not known. We do know, however, that *SUPERMAN* is no longer alone; Enrico Coen and colleagues have revealed in a recent issue of *Nature* (vol. **401**, 157–161; 1999) that some mutant alleles of *Lcyc*, a gene controlling floral symmetry in *Linaria vulgaris* (toadflax), also result from epimutation. They found that, in contrast with the wild-type flower, the mutant plant carries a hypermethylated *Lcyc* allele that correlates with loss of gene expression.

Wild-type (left) and epimutant flowers of *Linaria*, which show bilateral and radial symmetry owing to differences in methylation state.

As pointed out by En Li in September's issue of *Nature Genetics* (vol. **23**, 5–6; 1999), the mechanisms that govern epimutation onset are obscure. Coen and colleagues propose that aberrant activation of a silencing process in the meristem, the pool of stem cells from which plant tissues are derived, might be the cause. Both the *Lcyc* and *SUPERMAN* epimutations affect genes expressed only in floral development, a relatively late event; it may be that a common aspect of genes that are expressed at a comparatively late stage of development conditions them to epimutation. Curiously, introduction of a demethylating transgene does not decrease methylation of *SUPERMAN* epialleles, and late onset of *SUPERMAN*-like floral phenotypes is seen in a demethylated background. It is possible that a compensatory mechanism might initiate localized hypermethylation in response to genomic hypomethylation or deficiency of methyltransferase. So the next time you contemplate flower power, you might ponder whether it's what's in the DNA, or what's on the DNA, that makes the difference.

—Michael Ronemus

Incriminating gene suspects, Prader-Willi style

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It is not often that consecutive reports in the scientific literature read like chapters of a good thriller novel, yet such a story is now unfolding around the genetics of Prader-Willi syndrome (PWS), a condition associated with developmental and neurobehavioural deficits. A study on page 199 of this issue, by Matthieu Gérard and colleagues[1], represents the latest episode of a seat-gripping saga with telling lessons for geneticists.

Setting the scene

Infants with PWS first present with a failure-to-thrive phenotype, characterized by hypotonia (poor muscle tone) and respiratory distress. At two to four years, they tend to hyperphagia (an inability to stop eating), which, without modifications to diet or feeding behaviour, leads to severe obesity. Other clinical features include short stature, small hands and feet, mild mental retardation with learning disabilities and obsessive-compulsive disorder, and small gonads. The genetics of PWS is complex, involving large deletions, uniparental disomy and imprinting mutations of chromosome 15q11–q13 (ref. 2), but all involve loss of paternal gene expression in this region. Inheritance patterns of PWS establish it as a classic example of a human disorder involving imprinted genes, in which one allele is functional (paternal in PWS) and one silent (maternal in PWS). The finding that a number of contiguous genes in this region are expressed only from the paternal chromosome (see figure), coupled with the fact that loss of expression of these genes accompanies PWS, has led to the prediction that PWS is a multigenic disorder[2]. As orthologous genes are arrayed in a parallel fashion—and imprinted—in the mouse[2–4], perhaps valuable mouse models of PWS could be obtained. Indeed, mutant mice with equivalent failure-to-thrive phenotypes (resulting in death 2–7 days after birth) result from large chromosome deletions[5], uniparental disomy[6] and imprinting mutations[7] of the kind observed in people with PWS.

Weighing the evidence

The study carried out by Gérard *et al.*[1] suggests that abrogation of the necdin gene (*Ndn*) is critical in the failure-to-thrive aspect of PWS. But this finding contrasts with that of Ting-Fen Tsai and colleagues[8], who recently reported that mice deficient in *Ndn* have no abnormal phenotype. Gérard *et al.* observed postnatal respiratory distress and lethality, depending on the strain of mouse, and determined that neither reactivation of the maternal allele nor an imprinting defect occurred. The mice that survived 30