Full-color crossovers

The budding yeast *Saccharomyces cerevisiae* has served as an all-purpose model for the study of meiotic recombination. The analysis of recombination mechanisms in higher eukaryotes, however, has been hindered by the lack of a method for rapidly analyzing tetrads. Kirk Francis and colleagues now report an approach that allows the visual identification and quantification of crossover and gene conversion events in pollen tetrads of *Arabidopsis thaliana* (*Proc. Natl. Acad. Sci. USA* 104, 3913–3918; 2007). The authors took advantage of the *quartet* (*qrt*) mutation, which results in the four products of the pollen meiosis remaining attached to each other and accessible for scoring (see Mutant of the Month on p 447). The visual assay was established by generating a series of transgenic *qrt* plants carrying marker genes encoding red, yellow or cyan fluorescent proteins. Pairs of lines carrying differently colored markers on the same chromosome were crossed, and both crossovers and crossover interference were scored by observing the segregation of the two fluorescent proteins. Gene conversion was assessed by scoring fluorescence in the gametes of a line heterozygous for a nonfunctional yellow fluorescent protein. Although this is largely a technical advance, the authors noted an intriguing correlation between developmental position of flowers and frequency of crossing over. ***AP***

Editing microRNAs

RNA editing by the ADAR family of adenosine deaminases is known to create alternate versions of RNA species by editing adenosines to inosines. Now, Yukio Kawahara, Kazuko Nishikura and colleagues report that *in vivo* editing of microRNAs may alter their silencing targets (*Science* **315**, 1137–1140; 2007). The authors characterized tissue-specific A-to-I editing that alters the sequence of the *miR-376* family of microRNAs in both humans and mice. Of particular interest are editing events that alter the functionally important 'seed' sequences. The authors chose the *miR-376a* microRNA for further analyses. Computational algorithms predicted that edited *miR-376a* would target a different set of genes from unedited *miR-376a*, and a luciferase reporter assay confirmed differential targeting of the two species. For example, the assay showed that PRPS1, an enzyme involved in uric acid synthesis, is a target of edited *miR-376a* but not of unedited *miR-376a*. To confirm the functional effects of *miR-376a* editing *in vivo*, the authors made use of mice deficient for ADAR2. As predicted, they detected unedited species of *miR-376a* and higher levels of PRPS1 expression. Interestingly, they also found higher uric acid levels in the ADAR2-deficient mice. Although deficiency for ADAR2 may alter other regulators of PRPS1 or uric acid synthesis, these results suggest a functional role for microRNA editing. *EN*

LRP6 and cardiovascular disease

Genetic studies of rare, familial forms of common diseases provide powerful entry points for identifying underlying disease mechanisms. Richard Lifton and colleagues (*Science* **315**, 1278–1282; 2007) have applied this approach to study a large Iranian kindred in which early coronary artery disease and cardiovascular risk factors such as hypertension, hyperlipidemia and diabetes cosegregated in a pattern consistent with autosomal dominant inheritance. The authors performed genome-wide linkage analysis in this pedigree and found strong evidence of linkage to a 750-kb interval on chromosome 12p. They then sequenced the coding regions and splice junctions of all six annotated genes in the interval and identified a single missense variant in *LRP6* that cosegregated with the disease. The variant, which alters a conserved residue, was absent from 400 Iranian control chromosomes and was found to impair the ability of LRP6 to potentiate responsiveness to Wnt signaling in a cell-based assay. Although the findings do not exclude the possibility that other linked variants exist and contribute to the disease phenotype in this family, they provide a strong indication that defects in the Wnt pathway may be causally implicated in the spectrum of metabolic and cardiovascular traits associated with risk of coronary artery disease. *KV*

Microbial diversity

Recent advancements in large-scale environmental sequencing have offered a wealth of microbial sequence data and opportunities for new types of analyses. In this environment, Peer Bork and colleagues report a new computational method for phylogenetic assessment of metagenomic data–based protein coding markers and demonstrate that this is more quantitative than traditional ribosomal RNA comparisons (*Science* **315**, 1126–1130; 2007). They first mapped a set of 31 protein coding markers from four diverse environmental data sets to a reference tree of sequenced organisms (*Science* **311**, 1283–1287; 2006), using maximum likelihood to find a probabilistic fit for the sequence. With web-based software that makes use of these methods (http://MLtreemap.embl.de), users can input their sequence data and obtain phylogenetic estimates, with branch length and confidence ranges for placements as output. The authors also found that evolutionary rates vary among the four different environments examined, with microbes dwelling at the ocean surface showing the fastest microbial evolution rates, and soil microbes the slowest. In addition, the authors compared habitat preferences of microbial organisms through time and found stability in environments within short to intermediate time frames, suggesting that these microbial lineages maintain relatively low rates of lifestyle change. *OB*

Crohn disease genome scan

Michel Georges and colleagues (*PLoS Genet.*, published online 5 March 2007; doi:10.1371/journal.pgen.0030058.eor) report results of a whole-genome association scan for Crohn disease. Using Illumina's HumanHap300 BeadChip, the authors analyzed 547 Belgian individuals with Crohn disease and 928 healthy controls. In addition to confirming several previously published associations, including risk variants in *CARD15* and *IL23R*, the scan identified a new suggestive association to a cluster of SNPs on 5p13.1. The authors replicated the association with multiple SNPs from the 5p13.1 cluster in independent case-control and family-based studies, both drawn from the Belgian population. Combining the data from the genome-wide association and replication studies yielded a *P* value of 2.1×10^{-12} for the most strongly associated SNP in the region. This peak of association resides in a 1.25-Mb gene desert, with the nearest gene, *PTGER4*, located 270 kb away. Of note, *Ptger4*-null mice are highly susceptible to dextran sodium sulfate–induced colitis. In addition, several SNPs in the 5p13.1 cluster are associated with variation in *PTGER4* expression levels in transformed lymphoblastoid cell lines, suggesting that the associated variants may modulate disease risk through effects on *PTGER4* expression. ***KV***

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