Monkeyflower adaptation mechanism

Chromosomal inversions are thought to contribute to adaptation and speciation, as they can lead to hybrid sterility. Now, David Lowry and John Willis report an adaptive inversion polymorphism in the yellow monkeyflower *Mimulus guttatus* (*PLoS Biol.* 8, e1000500, 2010). They initially observed suppression of recombination at a large effect, pleiotropic quantitative trait locus in crosses between inland-annual and coastal-perennial populations. In-depth genotyping of more crosses between geographically distinct inland-annual and coastal-perennial populations showed evidence for a chromosomal inversion linked to ecotype. This inversion contributes to adaptive flowering time differences between annual and perennial populations. To test if this inversion polymorphism affects adaptation in the wild, the authors introgressed alternative inversion arrangements into outbred annual and perennial backgrounds and performed reciprocal transplant experiments. Fitness was measured as survival to flowering and number of flowers produced per plant, and the effect of the inversion was significant. For example, at the inland field site, survival to flowering in plants with the coastal genetic background and the inland annual inversion was eight times greater than that of coastal plants with the coastal perennial inversion. The authors suggest that this inversion may directly contribute to reproductive isolation between annual and perennial ecotypes, consistent with the theory that local adaptation can facilitate the maintenance of chromosomal rearrangements and promote speciation. ***PC***

Mosquito vector pathogenomics

Culex quinquefasciatus, or the southern house mosquito, is geographically widespread and is a vector for a range of pathogens, including West Nile Virus, St. Louis encephalitis virus and the nematode-causing lymphatic filariasis. Peter Atkinson and colleagues report the genome sequence of *C. quinquefasciatus*, providing a reference genome for comparisons with the previously sequenced *Anopheles gambiae* and *Aedes aegypti*, which together represent the three major taxonomic groups of disease-vector mosquitoes (*Science* **330**, 86–88, 2010). They identify 18,883 protein coding genes in *C. quinquefasciatus* and find that the increase in gene number compared to *A. gambiae* and *A. aegypti* is partly explained by an expansion of gene families, including those for olfactory receptors and immune-related genes. In an accompanying study, Marc Muskavitch and colleagues report a comparative genomic analysis of these three mosquito species (*Science* **330**, 88–90, 2010). Using whole-genome microarray analysis, they identify infection response genes as those showing changes in expression after mosquito infection with an arbovirus, parasite or bacteria. In infected mosquitoes, there were changes in only a small proportion of immune-related genes, and there were no observed changes in RNAi or programmed cell death pathways, suggesting the pathogens may have evolved mechanisms to evade the host immune response. *OB*

Asthma susceptibility

William Cookson and colleagues (*N. Engl. J. Med.* **363**, 1211–1221, 2010) report results of a large genome-wide association study of asthma. They combined genome-wide genotyping data from 23 studies comprising 10,365 asthma cases and 16,110 controls, all of European ancestry. In the overall analysis, six loci showed genome-wide significant association with asthma. These included previously reported risk loci at 2p12 near *IL1RL1* and *IL18R1*, at 6p21 near *HLA-DQ* genes, at 9p24 near *IL33*, and at 17q21 near *ORMDL3* and *GSDMB*, as well as newly discovered risk loci at 15q21 near *SMAD3* and at 22q13 near *IL2RB*. Stratified analyses showed that the 17q21 locus is specifically associated with childhood-onset cases, whereas the 6p21 locus is more strongly associated with later-onset cases. Conversely, their well-powered study provided limited support for several other previously reported asthma susceptibility loci. They also observed limited overlap between loci associated with asthma risk and those associated with variation in serum immunoglobulin E levels, suggesting that these two traits are under distinct genetic control. Collectively, these findings highlight an important role for adaptive immunity and inflammatory pathways in asthma etiology. *KV*

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Tolerating aneuploidy

Aneuploidy inhibits proliferation in normal cells but is found in a high percentage of tumors. The molecular mechanisms that enable cancer cells to tolerate aneuploidy are not well understood. Now, Angelika Amon and colleagues report the identification of evolved isolates of aneuploid yeast strains that display increased proliferative abilities (*Cell* **143**, 71–83, 2010). The authors used tiling arrays or deep sequencing on 14 strains and identified 43 non-synonymous SNPs and 4 synonymous SNPs present in the evolved isolates but not the parental strain. Each evolved isolate had several SNPs and there was little overlap between strains, which indicates that different SNPs led to improved proliferation in each strain. Mutations were found in genes involved in chromatin remodeling, stress response, protein folding and ribosomal RNA processing, as well as in proteasomal degradation. The authors found premature stop codons in *UBP6*, which encodes a deubiquitinating enzyme, in two independently evolved isolates. Competition assays showed that inactivation of *UBP6* led to an increase in fitness for some but not all aneuploid yeast strains and did not influence the growth of wild-type cells under the conditions tested. The authors further found that loss of *UBP6* function appears to improve fitness by increasing the degradation of proteins that are in excess due to aneuploidy. *PC*

Activating RNAs

It is now well accepted that genome transcription produces RNAs with repressive regulatory functions. Now, Ramin Shiekhattar and colleagues report the identification of endogenous regulatory RNAs that have enhancer functions (*Cell* 143, 46–58, 2010). The authors used transcriptome annotations of a third of the human genome generated by the ENCODE project to identify a curated set of 3,019 long non-coding RNAs (ncRNAs). They used custom microarrays to profile expression of these ncRNAs in three different human cell lines, which together showed expression of 1,167 of them. They used small interfering RNAs (siRNAs) to knock down a small set of endogenous ncRNAs in expressing cell lines and measured expression of neighboring genes. In total, they tested 12 ncRNAs and found evidence that 7 ncRNAs have an activating effect on specific neighboring genes. Further, reporter assays showed that three different ncRNA loci can act as enhancers for a heterologous reporter gene in an orientation-independent manner. The enhancer activities were abrogated by siRNAs that knockdown expression of the ncRNAs. These experiments suggest an RNA-dependent *cis* mechanism of enhancer function for these ncRNAs, yet interestingly, the ncRNAs act independently of the sequence of the target promoter. ***EN***