Pigmentation in flies

A major goal of evolutionary genetics is to understand the molecular basis of phenotypic change within and between species. Patricia Wittkopp and colleagues report that alleles near the pigmentation genes *tan* and *ebony* contribute to intra- and interspecific differences in pigmentation phenotypes (*Science* 326, 540–544, 2009) between *Drosophila americana*, which is dark brown, and *Drosophila novamexicana*, which is yellow. Introgressing the *ebony* and *tan* alleles from *D. americana* into *D. novamexicana* showed that these regions recapitulated 87% of the pigmentation differences between the two species. Using fine-scale genetic mapping, the authors showed that noncoding changes in *tan* contribute to pigmentation divergence. The authors also investigated whether pigmentation differences within wild populations of *D. americana* were due to alleles at *tan* and *ebony*. The authors found that in two *D. americana* populations, alleles at either *tan* or *ebony* contributed to pigmentation differences, whereas in two other populations, alleles at both *tan* and *ebony* explained pigmentation variance. Sequencing of the *tan* and *ebony* alleles in some of the lighter *D. americana* lines revealed that there is probably shared ancestry with the *D. novamexicana* alleles, suggesting that standing genetic variation that was present before speciation is responsible for divergent pigmentation both within and between these *Drosophila* species. *PC*

Open chromatin and recombination hot spots

Investigations at targeted loci have revealed an association between open chromatin and the placement of double-strand breaks (DSBs) and crossovers during meiosis. Now, Jason Lieb and Gregory Copenhaver and colleagues report a genome-wide investigation of the relationship between meiotic recombination hot spots and chromatin conformation in *Saccharomyces cerevisiae* (*Genome Res.* published online 2 October 2009; doi:10.1101/gr.096297.109). The authors used formaldehyde-assisted isolation of regulatory elements (FAIRE) to generate genome-wide maps of nucleosome-depleted open chromatin during the period in meiosis when DSBs are generated. They compared these profiles to published maps of meiotic DSB hot spots in *S. cerevisiae*, defined as sites of enrichment for single-stranded DNA. This analysis revealed an association between open chromatin and DSB hot spots, although a proportion of DSB hot spots occurred within closed chromatin. As expected, euchromatic regions adjacent to subtelomeres, which are known to have high crossover rates, showed high levels of open chromatin during meiosis. Interestingly, centromeres and pericentromeric regions, which have low crossover rates, had higher-than-expected levels of open chromatin. Finally, the authors identified a 15-bp sequence motif frequently located downstream of tRNA genes that is over-represented in meiotic open chromatin. *EN*

Personal microbiomes

The healthy human body plays host to approximately 100 trillion microbial cells. Rob Knight and colleagues surveyed microbiota in 27 body 'habitats' in several healthy adults (*Science* published online 5 November 2009; doi:10.1126/science.1177486). Body habitat was the primary variable that determined the composition of these bacterial communities and also influenced the amount of intracommunity variation. Communities in the oral cavity displayed the least variation, both between individuals and within individuals over time. Gut communities were highly variable between people, but showed minimal variation within individuals. Skin, hair, nostril and ear communities also differed between people, and they also varied greatly within individuals. Sites on the skin showed striking differences in community composition: for example, the forearm, palm and index finger had high levels of diversity, whereas the forehead showed low levels of diversity. To investigate community assembly on the skin, the authors disinfected plots on the foreheads and forearms and inoculated them with defined microbiota. Forearm plots inoculated with tongue bacteria were more similar to tongue communities than to native forearm communities. Forehead plots showed the opposite results, as those inoculated with tongue bacteria grew biota more similar to native forehead communities than to tongue communities. The authors suggest that human microbiota show systematic differences across body habitats, although each microbiome is personalized. *PC*

Written by Orli Bahcall, Pamela Colosimo, Emily Niemitz and Kyle Vogan

IL10R and inflammatory bowel disease

Common variants in *IL10* were recently shown to confer increased risk of ulcerative colitis in humans, and mice deficient in subunits of the interleukin-10 (IL-10) receptor have severe enterocolitis, demonstrating an important role for this pathway in controlling gut inflammation. Building on these findings, Christoph Klein and colleagues (*N. Engl. J. Med.* published online 4 November 2009; doi:10.1056/NEJMoa0907206) now report finding homozygous mutations in the genes encoding two different subunits of the IL-10 receptor (*IL10RA* and *IL10RB*) in three families with early-onset inflammatory bowel disease. The authors used genome-wide marker sets to identify regions of homozygosity that segregate with disease in two consanguineous families. Sequencing of candidate genes within the disease-linked intervals revealed a nonsense mutation in *IL10RB* in one family and a missense mutation in *IL10RA* in the second family. Sequencing of these genes in six additional subjects with severe early-onset colitis identified a third individual with a homozygous missense mutation in *IL10RA*. Functional studies revealed that the mutations impair IL-10 signaling. Considering the established role of IL-10 signaling in restricting excessive immune responses, the authors propose that the disease phenotype results from deficient negative-feedback signaling following exposure to bacteria in the gut. *KV*

Rolling out genomes

Bringing us closer to the $1,000 genome, Complete Genomics reports the sequencing of three new individual human genomes using their nanoarray technology, at an average materials cost of $4,400 per genome (*Science* published online 5 November 2009; doi:10.1126/science.1181498). They sequenced two individuals from the HapMap (a CEPH male at 87× coverage and a Yoruban female at 63×) and a participant in the Personal Genomes Project (PGP1, male, at 45×). Their method begins with synchronized synthesis using rolling-circle replication at a uniform temperature to obtain hundreds of tandem copies of the sequencing substrate in coils of single-stranded DNA, forming self-assembling DNA nanoballs (DNBs). These DNBs are placed onto a patterned array with individual DNB binding sites, and sequencing is performed using combinatorial probe anchor ligation (cPAL) chemistry. The base reads were mapped to the human genome reference assembly with an alignment algorithm and then assembled into diploid sequence using Bayesian and de Bruijn graph methods. The authors identified ~3 million SNPs per genome for the two individuals of European descent and ~4 million SNPs in the Yoruban genome. In comparisons with HapMap datasets, they found 99.03% concordance in SNP calls. *OB*