

## Back to basics in Berlin

**At this year's quinquennial International Congress of Genetics, human genetics provided only a fascinating minority of the content of this conference dedicated to illuminating fundamental biological systems and their evolution.**

In his keynote lecture, Oliver Smithies revisited the lab notebooks that led to his prizewinning work on homologous gene replacement ([http://nobelprize.org/nobel\\_prizes/medicine/laureates/2007/smithies-lecture.html](http://nobelprize.org/nobel_prizes/medicine/laureates/2007/smithies-lecture.html)). Soon after he had made the gel system to visualize protein polymorphisms, he came upon the processes of nonhomologous and homologous recombination that generate copy number variation in the human haptoglobin genes, early (1955–1962) instances of phenomena that are only now being investigated on a genome-wide scale.

Evan Eichler presented evidence from comparative genomics of the great apes of the ancestral configuration and surprising evolutionary history of the 17q21.31 inversion (p 1076). The structure and configuration of segmental duplications promotes recurrent inversion of a chromosomal segment that can both re-create the structural polymorphism in a population and sponsor recurrent deletions with associated genomic disorders.

The five-year spacing of the conference is well suited to looking back over whole areas of basic biology the operation of which we once never even suspected. Elizabeth Blackburn originally posed a question about the replication problems presented by the ends of linear chromosomes and picked a model organism that had more chromosome ends than most. She has now followed this line of enquiry right through many experimental systems to assays that measure ways in which environmental stress takes a quantitative toll on human health. The remedy may even be close at hand, as telomerase remains present in a surprising range of adult tissues. Equally broad in its impact on biology is one of the major degradative modes utilized by all eukaryotic cells. Yoshinori Ohsumi presented a comprehensive tour of the enzymology, protein networks and ubiquitin-like tags involved in autophagy in yeast and serum-starved mammalian cells. This process has also been demonstrated to underpin quality control of protein folding, important for neurological function in mammals. But genetic analysis can cut deeply as well as broadly: Richard Axel and colleagues have now identified four levels of neuronal connections from antenna to muscle in the sexually dimorphic *cis*-vaccenyl acetate pheromone response in *Drosophila* courtship behavior.

The way in which our understanding of epigenetics and stem cell biology has developed from phenomenology, via genetic screens, to universal mechanisms was exemplified by a talk from Gunter Reuter. In his lab, the classical phenomenon of position-effect variegation was unraveled by screening for modifier mutants, loci which now identify heterochromatin proteins, histone methylases and other 'epigenetic' regulators of gene expression and transposable element

silencing. Also at this meeting, Azim Surani reexamined the determination and identity of primordial mammalian germ cells in the era of somatic nuclear reprogramming and the generation of induced pluripotent cells. Allan Spradling explained, using the well-characterized *Drosophila* ovary with clonal marking of cell lineage, how many of our preconceived ideas about stem cell biology are wrong. Stem cells are not necessarily long-lived, rarely dividing cells with stable identity. Rather, cells de-differentiate under the right dynamic confluence of signals (the stem cell 'niche'), cells can compete for the role of stem cell, and stem cell populations in adjacent developmental compartments are able to coordinate their proliferation and differentiation. Spradling's work raises the questions of how many more proteins of the cell surface and cell-cell interaction (for example  $\beta$ -catenin and Notch) also have a signaling role in the nucleus, and how many more of these 'structural signallers' remain to be found in key stem cell roles.

Whereas genetics once grew out of agriculture, here, with a preponderance of molecular cell biologists of model organisms in attendance, it is just possible that the possibilities of genomic agricultural genetics might have gone underappreciated. The potential is enormous, as Edward Buckler emphasized when he presented the results and ambitions of the maize diversity project. Quantitative traits such as yield and flowering time are being mapped in millions of plants from among thousands of inbred lines of the world's largest and most diverse crop.

With all the meeting's emphasis on lifetime achievement and the mature analysis of fundamental biological processes, there was still plenty that was breaking new ground. Yijun Ruan laid out some of the new applications of high-throughput paired-end tag sequencing, particularly as it can be applied to copy number variation and epigenetic mapping of transcriptional regulatory regions that form looped and clustered regions of the genome. Michael Axtell made the point that we are no longer limited by DNA sequencing, and is using deep resequencing to mine the cell's pool of degraded mRNA for the targets of evolutionarily conserved microRNAs that directed their degradation. Augustine Kong presented a long-range haplotyping method that promises to be useful in pinpointing the origin of (deleterious and therefore short-lived) founder effect mutations and copy number variations by genotyping only a proportion of the population (p 1068).

It is of course impossible in a meeting report to cover more than a few of the highlights of an event of this kind, and it will be most exciting to know what the next five years will bring. ■