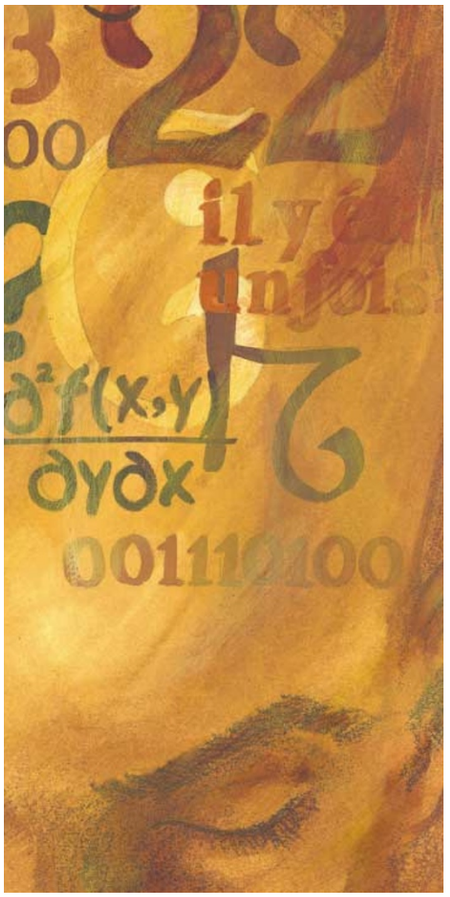

in exon 11 fall into one of these categories. The authors argue that these sites should be the priority for future studies, along with three missense mutations in residues that show signs of recent positive selection in human and primate lineages. Interestingly, these three amino acids lie in the region of BRCA1 that interacts with RAD51— a protein involved in double-stranded break repair.

The authors present a promising approach for prioritizing the study of missense mutations in *BRCA1*, as well as in other genes associated with heritable diseases. Indeed, the authors show that this method can be used to predict the ß-globin amino-acid residues that, when mutated, are associated with various globin pathologies. The true test of this approach, however, will be to determine how many of the 41 missense mutations highlighted by Fleming *et al.* are associated with an increased risk of breast and ovarian cancer.

Catherine Baxter

References and links

ORIGINAL RESEARCH PAPER Fleming, M. A. *et al*. Understanding missense mutations in the *BRCA1* gene: an evolutionary approach. *Proc. Natl Acad. Sci. USA* 16 January 2003 (10.1073/pnas.0237285100)
FURTHER READING Narod, S. A. Modifiers of risk of hereditary breast and ovarian cancer. *Nature Rev. Cancer* **2**, 113–123 (2002)
WEB SITE
Elaine A. Ostrander's lab: http://www.gs.washington.edu/faculty/ostrander.htm

populations but absent from others. On this basis, they suggest that different statistical methods will be needed for association studies in different populations and/or gene regions. They also suggest that, depending on their demographies, different populations might be suitable for different stages of association mapping. The LD debate is far from over, but it is clear that we must be cautious about extrapolating from one gene region, and one population, to another.

Magdalena Skipper

References and links

ORIGINAL RESEARCH PAPER Stumpf M. P. H. & Glodstein D. B. Demography,recombination hotspot intensity and the block structure of linkage disequilibrium. *Curr. Biol.* **13**, 1–8 (2003)
FURTHER READING Ardlie, K. G. *et al.* Patterns of linkage disequilibrium in the human genome. *Nature Rev. Genet*. **3**, 299–309 (2002)
WEB SITE
Centre for Population Genetics and Human Health: http://popgen.biol.ucl.ac.uk/people.html

IN BRIEF

EVOLUTIONARY GENOMICS

Parallel changes in gene expression after 20,000 generations of evolution in *Escherichia coli*.

Cooper, T. *et al. Proc. Natl Acad. Sci.* **100**, 1072–1077 (2003)

Parallel changes in independent evolutionary lineages in response to an environmental challenge are clear indicators of adaptive evolution. Cooper *et al.* used DNA macroarrays to examine the changes in gene-expression in two lineages of *E. coli* in response to a glucose-limiting medium. The authors go on to identify a specific mutation accounting for many of the 59 genes that changed expression in parallel, raising the possibility that this might provide a general strategy for identifying the genes involved in adaptation.

PLANT GENETICS

Direct measurement of the transfer rate of chloroplast DNA into the nucleus.

Huang, C. *et al. Nature* 5 February 2003 (10.1038/nature01435)

We know that plant chloroplast genes can move to the nuclear genome, but how often does this happen? To answer this question, Huang *et al.* engineered tobacco chloroplast genomes with a gene that confers kanamycin resistance only if it is transferred to the nucleus. The authors found 16 out of 250,000 plants with independent nuclear insertions: a rate high enough to significantly impact nuclear genome organization and gene function, and to have implications for the design of genetically modified crops.

GENOMICS

Ringlike structure of the *Deinococcus radiodurans* genome: a key to radioresistance?

Levin-Zaidman S. *et al. Science* **299**, 251–256 (2003)

D. radiodurans can withstand ionizing radiation at doses that are lethal to all other organisms. In this paper, Levin-Zaidman *et al.* describe the unusual 'toroidal' conformation of its genome. This tightly packed structure might confer resistance to ionizing radiation by enabling broken DNA strands to be held together tightly, facilitating template-independent repair.

TECHNOLOGY

A genomics-guided approach for discovering and expressing cryptic metabolic pathways.

Zazopoulos, E. A. *et al. Nature Biotech.* **21**, 187-190 (2003)

Taking advantage of the fact that bacterial metabolic genes are clustered, Zazopoulos *et al.* developed a high-throughput method for identifying metabolic loci independently of their expression. First, using a genomic library, the authors generated 700-bp random genome-sequence tags (GSTs). Second, GSTs of interest were identified on the basis of sequence homology to the biosynthetic genes that are present in microbial databases. Selected GSTs were then used as probes to identify new metabolic genes (and their neighbours) from individual cosmids or BACs.