TECHNOLOGY

A wide (micro)array of options

Gone are the days when oligonucleotide microarrays were used only to study gene expression; their function in genotyping studies, for example, has arguably overtaken their original application. Two recent reports now stretch their uses further: Ronald *et al.* show that microarrays can be used to simultaneously study gene expression and perform genotyping, and Barrett *et al.* demonstrate their usefulness in comparative genomic hybridization studies.

Traditionally, it is DNA that is hybridized to microarrays in genotyping experiments. Using mRNA instead allowed Ronald *et al.* to combine genotyping with expression studies, to fully exploit the genetic information that is present on the array. The authors intially needed to refine the new design. For example, a low hybridization signal could reflect a mismatch between the probe and mRNA (a polymorphism) or simply low gene expression, so several probes per ORF were used to distinguish between the two possibilities. The authors identified polymorphic loci between two strains of *Saccharomyces cerevisiae*. Although the mRNA-based method is less sensitive than the DNA-based version, the authors obtained ~1 marker per 4 cM, which is sufficient to provide much of the linkage information.

The strength of this new method lies in its ability to detect allele-specific expression. Ronald *et al.* identified 70 ORFs with allele-specific expression in a diploid hybrid of the two yeast strains: they followed the probes that, in the diploid, indicated that one or the other strain-specific allele was expressed more strongly, and they confirmed their results by quantitative PCR.

The combination of gene expression and genotyping will facilitate identification of candidate genes. Importantly, with its ability to identify ORFs with allele-specific expression, it is set to become a useful tool in the study of the genetics of gene expression.

In the second study, Barrett *et al.* devised microarrays to detect copy-number variations at multiple loci in the genome — a task that is usually performed using array-based comparative genomic hyridization (CGH), which is based on PCR clones that are present in BACs or as cDNAs. The authors improved on conventional CGH by hybridizing genomic DNA to carefully designed microarrays. Using 60-mer oligonucleotide arrays, which were specifically optimized for CGH measurements, they successfully detected single copy and homozygous deletions, and complex rearrangements in human cancer cell lines.

An important advantage of this method lies in the fact that it can be used to study copy number variation in any region of the genome, unlike the traditional approach, which is limited to expressed sequences or those cloned into BACs. As with the method of Ronald *et al.*, which has a rather high false-positive rate, microarray-based CGH will benefit from being further optimized. Nonetheless, microarrays are rapidly becoming something of a 'Jack of all trades'.

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References and links

ORIGINAL RESEARCH PAPERS Ronald, J. *et al.* Simultaneous genotyping, gene expression measurement, and detection of allele-specific expression with oligonucleotide arrays. *Genome Res.* 1 February 2005 (doi:10.1101/gr.2850605) | Barrett, M. T. *et al.* Comparative genomic hybridization using oligonucleotide microarrays and total genomic DNA. *Proc. Natl Acad. Sci. USA* **101**, 17765–17770 (2004)