nature genetics

A decade of genome-wide biology

A PubMed search for the term 'genome-wide' identifies 4,325 citations, all but 39 of which postdate 1995, the year that saw the first published application of microarray technology to gene expression. Although whole-genome sequencing obviously provided an essential impetus to genome-wide studies, it could be argued that the microarray, in all its forms, has been equally important in demonstrating the power of a more global view of genetics. For example, consider the impact of the first yeast cell-cycle 'phaseogram,' in which clusters of hundreds of genes are seen to covary in their expression during particular phases of the cell cycle. Patterns once invisible became obvious. The now iconic red-green (or blue-yellow) cluster diagrams, first glimpsed in darkened lecture halls in the mid 1990s, no doubt spurred countless scientists to move beyond the conventional one-gene-at-a-time approach.

To chronicle developments in microarray technology and applications, *Nature Genetics* published the first *Chipping Forecast* supplement in 1999, designed to give readers "a 'nuts-and-bolts' appreciation of the different types of microarray and their manufacture and processing." *The Chipping Forecast II* followed in 2002 and focused on new applications of microarrays, as well as best practice in experimental design and data analysis.

In assembling material for *The Chipping Forecast III*, we note how the microarray arena has changed. Although arrays can be made 'in-house,' there is also a robust, innovative and competitive business in designing arrays for sale to both individual laboratories and to consortia involved in community resource projects such as the HapMap. As the technology has become more widely available and affordable, its uses have multiplied and, as predicted, have expanded beyond applications in genetics. From tissue microarrays to chip-based methods for gene synthesis to enzyme microarrays, the theme is miniaturization, of any kind. For 'old-fashioned' analyses of gene expression, the transcriptome itself now represents a phenotype to be analyzed genetically, as seen in recent studies on the genetics of gene expression. Fortunately, MIAME-based standards for data reporting have made published results useful to an ever-larger number of investigators.

Over the past few years, thick books have been commissioned and published in attempts to keep up with all this activity. The field is now too vast to be covered by a single journal supplement, and so we offer in *The Chipping Forecast III* a series of focused perspectives on those topics likely to be of greatest interest to our readers, with an emphasis on genetic variation, gene expression in cancer and gene function. The first three Perspectives cover the use of microarrays for probing single-nucleotide variation (Ann-Christine Syvänen), large-scale structural variation (Daniel Pinkel & Donna Albertson) and epigenetic marks (Bas van Steensel). Two Perspectives (by Daniel Rhodes & Arul Chinnaiyan and by Daphne Koller and colleagues) highlight the increasing sophistication of bioinformatic approaches for analyzing the vast amounts of microarray data in the field of cancer research. Finally, Douglas Wheeler, Anne Carpenter & David Sabatini describe the integration of cell-based arrays with the most celebrated new tool for assessing gene function, RNA interference. We hope that this combination of topics will provide a provocative update of this maturing technology.

We are grateful to our authors for their insightful contributions, as well as to our referees. In addition, we thank our sponsor Agilent Technologies for their help, not only in producing this supplement and making it freely available online, but also for sponsoring a new feature for this series, an online question and answer page. This FAQ page will be launched on 1 June, and we invite readers to submit questions to the authors of the Perspectives at that time. A select group of questions with responses from the authors will be posted on 1 July, with monthly updates thereafter. Through this page, we hope to encourage an ongoing dialogue that will be of lasting interest to the broad community of microarray users.

Published online 26 May 2005; doi:10.1038/ng1573