Chromosome Research **13**: 223–224, 2005.

Foreword: From genetic diversity to chromosomal biology: an array of tasks beyond expression

DNA sequencing is revealing the complete genetic information of an increasing number of organisms. Sequencing programmes are providing comprehensive catalogues of protein coding genes and genome databases are now common and invaluable tools for biological research. At the same time it is also evident that sequence information alone is insufficient for understanding the process of gene regulation and genome propagation. While this might reflect in part our limited knowledge of cellular regulation, it highlights the need to obtain more information on how the genome is interpreted in a living cell. Is transcription limited to protein coding genes? What specifies transcription factor binding? How is DNA replication regulated? How are these events modulated by epigenetic modifications of DNA and chromatin?

None of the above questions is new to chromosome biology but thus far they have mostly been tackled by analyzing single gene loci in great detail. The development of DNA microarrays as miniaturized slot blots has enabled researchers to measure thousands of sequence probes in one experiment and thus to perform large-scale and unbiased analyses. Different experimental platforms for arrays exist, most of which have been driven by a need to profile gene expression in order to identify differentially regulated genes. Indeed global expression analyses have moved in a very short time from high technologies that were only available in a handful of laboratories to a standard analysis tool in biological research.

Only very recently has microarray technology been used beyond expression profiling to gain insights into features of chromosomal DNA, such as protein binding or genetic variation. Exciting new approaches have been developed to measure the physiology of chromosomes in unprecedented detail.

The rapid progress in this field led the Editorial Board of *Chromosome Research* to propose a special issue with a focus on genomic microarrays. The goal was to cover many different biological questions that can be addressed with this experimental tool as well as to introduce the different technical approaches. The resulting volume combines up-to-date reviews including original research from leading groups in the field.

Claire Kidgell and Elizabeth Winzeler discuss how genetic diversity at the nucleotide level can be analyzed on oligonucleotide microarrays and how this information can be used in comparative genomics, polymorphism discovery and genotyping. Wan Lam *et al*. report how comparative genomic hybridization is applied to determine genomic instability in cancer, while Heike Fiedler *et al*. introduce how human genomic microarrays can be used to measure chromatin structure and DNA replication.

One surprising observation that was only made possible through the use of tiled chromosomal arrays was the high abundance of transcription outside of open reading frames. Mike Snyder *et al*. discuss how high-resolution tiling arrays are used to identify transcriptional activity outside predicted coding genes and how these observations challenge much of our thinking on regulation of transcription. Identifying sites of transcription factor binding presents another major task in deciphering gene regulation. Alexandre Blais and Brian Dynlacht discuss how this question can be addressed with microarrays representing gene promoters and they also introduce the problems and pitfalls in interpreting the resulting datasets. Modifications of DNA and bound chromatin present key epigenetic modulators of genetic readouts. Martin Lodén and Bas van Steensel discuss different experimental approaches to determine higher order chromatin structure using genomic tools, while Vincent Colot *et al*. review the ways in which epigenomic approaches have shed light on chromosomal regulation in plants. Our knowledge of DNA duplication has benefited from recent genome-wide analyses of replication initiation and timing. In this issue David MacAlpine and Stephen Bell summarize these efforts and, furthermore,

they reanalyze some of the published data. That genome-wide measures can also identify post-transcriptional regulation is nicely illustrated by Jack Keene and Patrick Lager, who propose an intrinsic model of post-transcriptional operons based on global interaction networks of RNA binding proteins with target mRNAs.

I am grateful that leading scientists have agreed to contribute to this issue and I thank Wendy Bickmore for initiating the project and Herbert Macgregor for his enthusiasm and encouragement throughout its development. I also acknowledge the support of Nimblegen in covering the cost of the cover picture of this issue of *Chromosome Research*.

Dirk Schübeler (Guest Editor)
Friedrich-Miescher-Institute
for Biomedical Research
Basel
Switzerland