Book Reviews

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DNA Microarrays: A Molecular Cloning Manual. Edited by David Bowtell and Joseph Sambrook. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 2003. Pp. 712. $135 paperback, $195 hardcover.

This first edition of the book on DNA microarrays is a welcome addition to a series of laboratory manuals published by the Cold Spring Harbor Laboratory Press over the past two decades. It perpetuates a tradition of practical laboratory guides, which started with the famous guide by Maniatis on *Molecular Cloning* in the mid-80s, followed by volumes dedicated to other subjects, such as *Antibodies* (1988), *Genome Analysis* (1997), and several model organisms.

DNA microarrays have gained the reputation of being one of the leading and most powerful technologies available for investigating a broad range of questions related to functional and structural genomics. These microfabricated devices consist of thousands of spotted features covalently linked to a solid and impermeable support, each feature being a unique nucleotide sequence. Depending on their design, tiling, and layout, microarrays offer the opportunity to interrogate, through a hybridization process, either the integrity of nucleic acid sequences or the differential level of gene expression in biological samples. Microarrays are used to detect point mutations and single-nucleotide polymorphisms, to monitor site-specific methylation patterns, to estimate gain (amplification) and loss (deletion) of entire chromosomes or chromosomal regions, or to determine the relative abundance of specific ribonucleic acids expressed in different cells or under different physiological states. By far, the most extensive application of DNA microarrays has been in the comparative analysis of transcriptomes and global gene-expression profiling, whereas applications to genotyping and assessment of sequence variations have been reported less abundantly. Some recent examples of the impact that DNA microarrays had in the field of human genetics are studies of the pathogenesis of inherited disorders, such as Rett syndrome, trinucleotide-repeat expansions, fragile X syndrome, hereditary breast and ovarian cancer, craniosynostosis, Duchenne muscular dystrophy, dysferlinopathies, Sandoff disease, autosomal trisomies, and the 17q23 amplicon.

The book is intentionally devoted to very technical and experimental aspects of DNA microarrays. It comes at a time when the foundations, the concepts, and the fundamental aspects of the microarray technology have been reviewed in many articles and in two supplements to *Nature Genetics* (in 1999 and 2003, respectively) but when a guide to practical approaches was felt desirable. How to fabricate reliable microarrays, design and carry on experiments, use the associated instruments, and generate, store, analyze, and interpret data sets is the main concern of this book, which is prefaced by none other than Edwin Southern. Neither the utilization of microarrays nor the interpretation of the data is a simple task. The technology is complex and at the convergence of several disciplines. The editors, David Bowtell and Joseph Sambrook, succeeded in coordinating the contributions of more than 90 experts, from academia and the private sector, who gathered at a meeting hosted by Cold Spring Harbor Laboratory. This collective experience is condensed in a thick (700-page) but easily readable and extremely valuable manual.

Each of the eight chapters in this book is divided into an introduction, in which a specific topic is presented in its context, together with the underlying principles; one or several parts, each including several experimental protocols, with relevant "materials" and "methods" subsections; and, at the end, a list of literature references and, often, a list of Web sites. Each chapter is well illustrated with colored photographs, graphics, diagrams, and tables. There are four appendices dedicated to the construction of cDNA libraries, reagents and recipes, and suppliers, all very helpful in assisting in the preparation, storage, and handling of the chemicals and solutions required at each step of microarray processing. Biohazards, an important consideration, are included in the fourth appendix.

The first two chapters may appear less interesting or attractive to users of ready-made microarrays, as they cover the *in silico* domain of the technology: the intricacies of producing and depositing probes, robotics and microfluidics, glasses and glass coatings, spotting and printing. They will be best appreciated by managers of core facilities, by those inclined to customize their chips and adopt new designs, and by those inclined to establish preferred quality assurance standards and to reduce operational costs. Genomic DNA, cDNA, and ESTs, as well as synthetic oligonucleotide microarrays, are all described in detail, together with protocols specific to handling libraries. Commercially available liquid-handling systems, arrayers, and their specs are listed and critically evaluated in large tables. Likewise, the source and composition of clone sets (human, mouse, rat, *Drosophila,* and *Arabidopsis*) and oligo sets (mammalian, bacterial, and parasite genomes) are listed in separate tables.

Techniques are not limited to expression analysis of RNA, dual fluorescently labeled targets, and glass microarrays (chapter 3). Membrane-spotted microarrays and phosphorimaging (chapter 4); tissue microarrays (chapter 5); genomic microarrays used for comparative genomic hybridization (CGH), mutation detection, and SNP genotyping, as well as microarrays designed to map DNA-protein and DNA-chromatin interactions (chapter 6) are also thoroughly treated. There are no fewer than 10 different protocols to isolate and purify RNA from various

sources. It is also to the credit of the authors that they have inserted sections on the isolation and amplification of minute amounts of RNA, as such approaches are essential to the success of experiments aimed at analyzing manually and micro-(laser-) dissected biopsies, or even single cells.

An entire section (part 2) in chapter 3 deals with perhaps the most critical steps in DNA-microarray experiments (the labeling of targets, hybridization, and posthybridization), and one will find all that is required to achieve the best outcomes. A trouble-shooting section is particularly well illustrated, with two dozen scanned images, which provides an immediate visual aid to diagnostics.

One part of the DNA-microarray experiment is done in the wet lab. The next parts, scanning and data acquisition, are instrument-based processes. The last part is the analysis, interpretation, and comparison of unusually large data sets. All three phases involve complex biophysical and statistical principles, which are explained in sufficient details to allow one to get properly (and progressively) educated in often-arcane subjects. Accordingly, a very good and not-too-overwhelming chapter 7 introduces the reader to microarray bioinformatics. In this chapter, the questions of experimental design, image capture, normalization and filtering, data management, and analysis are abundantly covered, critically assessed, and, again, well illustrated. The authors elected to present only some of the approaches available to extract meaningful information from large data sets. Clustering analyses and commonly used softwares, multidimensional scaling, and self-organized maps are all described in detail, whereas the so-called supervised methods of analysis, more complex and still evolving, were left for a future edition.

DNA Microarrays is a compendium. It deconstructs each step of the microarray analytical process and offers a vast repertoire of techniques that represents a collective expertise. For all these reasons, the clarity of its style, and the elegance of its presentation, it is highly recommended. It is destined to be in the hands equally of the novice and of the already-experienced investigator.

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Babyface: A Story of Heart and Bones. By Jeanne McDermott. Bethesda: Woodbine House, 2000. 261 Pp. $22.95.

Rereading chapter 1 of *Babyface,* I am moved by how far this family has come during 8 years of Nate's lifetime and by their view of how far we still have to go toward creating a more comfortable world for those with "visible imperfections." The author, Jeanne McDermott, was a science journalist, married to Ted, with a son in nursery school, when she gave birth to their second son, Nathaniel, in 1990. Nathaniel was 1 of 14–60 babies born that year in the United States with Apert syndrome: a visibly unusual child with fused fingers and toes; a "towering skull"; bulging brow; and eye, ear, mouth, and respiratory problems because of premature fusion of the skull bones. The book, which is based on McDermott's journal, recounts in detail the events of Nathaniel's first year of life. These include harrowing times in the intensive-care unit; multiple surgeries; second, third, and fourth opinions from specialists of many varieties about how to manage this rare craniofacial condition; periods of parents' agonizing uncertainty about Nathaniel's mental development; and times when even his survival was in question. The narrative, at times gripping, is filled with vivid anecdotes that capture the ups and downs of daily life for the family during this exhausting year.

Every anecdote, as now written, illustrates an ethical stance: that disability or "deformity" does not define an individual's worth. One wonders whether each event had that clear import at the time. Yet, the vignettes are anything but simplistic; they are as complex as daily life. Although Nathaniel "had no clue that he was physically different, and, for years to come, he would not," his mother started worrying on the way home from the hospital, 4 days after his birth, about how others would treat him. "The fact that Nathaniel was born with observable imperfections meant that we lost the social anonymity that members of the able-bodied, physically 'normal' majority take for granted. People paused, stared, and noticed." On the first day, Jeanne "grieved for the dreambaby who had died and loved the one who had been born." From then on, she focused first on his survival, made possible by tertiary-care medicine, and then most fiercely on seeing that his world gave him the affirmation he would need to develop as a full human being. Still, she lets us glimpse the mind games that even committed parents play to banish the guilt of having given birth to a child with a serious congenital condition: "Pretend he's adopted," she said to her husband. "That way, I don't feel like we failed every time I look at him."

"Studies show that in the first five seconds of meeting a person, we make a decision about his character and moral nature based on how we see his face." In the light of this socio-biological fact, McDermott asks herself,"Could I really see beauty in every face?…Could I get past the barriers of my own fears and prejudices? Was beauty entirely a matter of the heart, wholly independent of flesh and bones?" Could I "look with such transcendent love that it changed the way others saw…?" She and her husband focus their parenting on allowing their son's identity to become manifest, not as different or "disabled," but as human. Each chapter is preceded by a small "box" in Nathaniel's own printing, describing daily happenings of ordinary life: a powerful, concrete way of assuring the reader of Nathaniel's individuality and ability now, years later, to participate in the typical life of a child and to express himself.

There is much here of universal interest to families whose children have special needs or congenital conditions, to anyone advocating for them, and to professionals who care for these