concepts of DNA science and chart the development of our knowledge of the mechanisms of heredity from the early classification of species through to the elucidation of the genetic code and the amendments to Crick's 'central dogma'. The text is made especially attractive to read by the inclusion of contemporary photographs of some of the major protagonists. The theory behind the techniques of cutting, joining and propagation of DNA molecules is clearly and concisely described in chapters 3 and 4, with chapter 4 concentrating on more advanced technologies for the analysis of complex genomes. One minor criticism would be that I could find no mention of insertional inactivation of an antibiotic-resistance gene as a method for distinguishing between recombinant and non-recombinant plasmid molecules. The remaining four chapters describe in a lucid and practical way how recombinant DNA technology has revolutionized both basic and applied research in the fields of development, cancer, human genetics, agriculture, medicine and industry. Rather than describing technological developments in isolation, experimental theory is combined with succinct summaries of the advances in our understanding that these developments have afforded. This is one of the book's great strengths. Diagrams throughout are attractive and easy to interpret, and each chapter is concluded by useful suggestions for further reading. I think it would have been a useful addition if chapter summaries had also been provided.

The laboratory schedules assume no previous experience, and guide the novice from the basics of micropipetting and sterile technique through to the construction and identification of recombinant plasmid molecules. Extensive prelab notes include useful tips and hints for teachers, technicians and students on the preparation, handling and storage of materials, and clear flow-charts and diagrams ensure that the protocols are easy to follow. Potentially hazardous operations are well flagged throughout. At the end of each experiment the student is presented with a series of questions and suggestions for future research, and likely 'non-ideal' experimental outcomes (such as incomplete restriction enzyme digestion or overloading of electrophoresis gels) are discussed. The laboratory section is followed by appendices detailing reagents and restriction site data, and the book is concluded by a comprehensive glossary/index. If necessary, the relevant materials may be purchased from the Carolina Biological Supply Company. From a purely practical point of view I would question whether it is appropriate for the laboratory schedules to be bound together with the eight theory chapters: perhaps thought could be given to publishing the schedules separately.

In conclusion, I believe that readers of this book will find it engaging and enjoyable to read. The authors (one a science educator, the other a practising molecular biologist) have broken new ground here and have produced a very valuable resource for students and teachers alike.

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Genes and Phenotypes: Genome Analysis Volume 3. Edited by KAY E. DAVIES and SHIRLEY M. TILGHMAN. Cold Spring Harbor Laboratory Press. 1991. Pp. 174. Hardback $40. ISBN 0 87969 402 5.

This is the third of a series of short single-theme review books, designed to keep us up to date with fast-moving areas of molecular genetics. Its title, *Genes and Phenotypes*, is a little uninformative, but the contents, whether or not they can be bracketed under a single theme, are well worth inspecting. Of the six chapters, three (nos. 1, 4 and 6) are concerned with the genetic analysis of human diseases genes, chapter 2 brings us well up to date on the mouse *t*-complex responder locus, chapter 3 describes cloning the mammalian sex-determining gene, TDF, and chapter 5 the molecular biology of the *W* and *Steel* loci of the mouse. A main theme in the book is 'reverse genetics', later called 'forward genetics' and still more recently renamed 'positional cloning', a relatively new approach which has been of particular value in running down genes responsible for major single-gene disorders in man.

Taking first the studies on human genes, Tsui and Estivill give an overview of identifying the genes responsible for single-gene disorders, starting with their chromosomal localizations. They discuss the successful cases of chronic granulomatous disease (CGD), Duchenne/Becher muscular dystrophy (DMD/BMD), retinoblastoma (RB), cystic fibrosis (CF), choroideraemia (TCD), neurofibromatosis type 1 (NF1) and Wilms' tumour (WT). Progress with CGD and DMD was made much easier by the discovery of a patient affected by both these conditions and also retinitis pigmentosa, whose X chromosome had a cytogenetically detectable deletion responsible for these defects. The molecular genetic techniques applied in these studies, described in some detail with adequate references, are complex, varied, highly ingenious and, I imagine, difficult to grasp fully by anyone not working in one of the large teams involved with them, but this chapter should certainly help the enthusiast. Tsui and Estivill remark:

> There has been tremendous competition in the field of disease gene cloning... It is difficult to describe the feelings of performing repeated searches for clone after clone without an open reading frame, constructing and screening genomic and cDNA libraries one after another, watching the come and go of a candidate gene, and working under the fear that the gene has perhaps been identified by another group.

And this, it should be noted, is only the first and easiest step in elucidating the function of the disease gene and the basis of the disease.

Pelletier, Munroe and Housman on the molecular genetics of Wilms' tumour leads on directly from the above chapter, taking the analysis of WT more or less up to date. This nephroblastoma is the most common renal tumour in children, with a remarkably constant rate of occurrence among diverse population groups of about 1 in 10000 children under 15. The cure rate: 5·7% in 1938, 50% in 1950 and nearly 90% in 1989, due to progress in surgical, radiotherapy and chemotherapy techniques, makes a dramatic success story. Of particular interest, several other disease conditions are often associated with Wilms' tumour, giving the so-called WAGR syndrome which includes aniridia, genito-urinary anomalies and mental retardation. These have been jointly located in chromosome 11p13 by a visible deletion. From these beginnings, more than 325 markers have been mapped to the short arm (p) of chromosome 11, making it one of the most densely marked of all the human autosomal regions. Concentration on 11p13 has suggested a candidate gene for WT containing four zinc fingers of the Cys–His variety at the carboxyl terminus, with other characters of a DNA-binding protein.

Ghosh and Todd consider mutlifactorial disease, with lessons from type-1 diabetes (IDDM). Schizophrenia, Alzheimer's disease, hypertension and atherosclerosis are other examples in which presumed genetic and environmental influences contribute to both onset and progression of the disease, with the number of genes and their types of interaction to be sought out. A mathematical approach using likelihood, comparative mouse–human mapping where similar diseases are found in the mouse, use of large numbers of markers in both species, and other approaches suggested by the much easier search for QTLs (quantitative trait loci) in plants and animals of agricultural interest are promising, but we are evidently at an early stage in this very important field. Ghosh and Todd's article, with its many references, is well worth study.

Goodfellow, Hawkins and Sinclair give an excellent account of their many problems and final success in cloning TDF, the mammalian sex-determining gene on the Y chromosome. This article brings out the unexpected difficulties that can be experienced in the supposedly straightforward tasks of constructing maps of the human Y and pinpointing the position of TDY, chromosome walking and searching the cloned sequences for likely candidate genes, and proving equivalence between target and a candidate gene. This must have been rather like climbing Everest with under-tested apparatus, and I was relieved to find the climbers had got down again. Do not miss this chapter, especially if you intend to embark on chromosome walking and even jumping.

Reith and Bernstein fill us in on the molecular biology of the *Dominant white spotting (W)* and *steel (Sl)* loci in the mouse. Both loci lead to defects in haematopoiesis, melanogenesis and gametogenesis, and *W* is allelic with *c-kit*, a proto-oncogene that encodes a receptor tyrosine kinase (RTK), while *Sl* encodes the ligand for the Kit receptor. Much new work on these two classic mammalian developmental loci is described, which I have not the space to summarize here. Rather, I want to draw the reader's attention to the article by Snyder and Silver on the mouse *t*-complex responder locus.

This transmission ratio distortion system, as is well known, consists essentially of several distorter (D) genes and one responder (R) gene, all in a 20-cM region of chromosome 17, containing a number of other irrelevant loci. Research by several groups has not, until recently, approached an explanation of how the transmission distortion is produced. The R, not the D genes, has the central role in this system: males heterozygous for both D and R genes transmit a very high proportion of R sperm to their progeny, whether R and D are on the same or opposite chromosomes, while R heterozygous on its own is only transmitted in 10–30% of sperm instead of around 90%. Snyder and Silver describe how the search among candidates for the Responder gene has identified the previously known gene *Tcp-10b*^{t}. This gene contains 10 exons and generates two transcripts whose expression differs, during spermatogenesis. The full-length transcript comes from the total of exons, while a novel transcript (only produced in the round spermatid stage, not in the pachytene spermatocyte) splices out exon VIII and uses a cryptic splice donor in exon IX to join with the acceptor of exon X, out of frame. The authors' model to explain transmission ratio distortion on the basis of this amazing discovery may tax those who find the rest of the book too easy to follow, though no other model yet seems more feasible.

From my brief discussion of the contents of the six chapters in this book, the reader may well conclude that it should at least be in his departmental library, and would stimulate his molecular genetic students. One would like to see it in soft covers with a lower price so that it could find its way to a number of laboratory shelves. The authors are all to be congratulated on making their chapters so absorbing to at least one reader.

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Major Genes for Reproduction in Sheep (2nd International Workshop, Toulouse, July 1990). Edited by J. M. ELSEN, L. BODIN and J. THIMONIER. (Coll. les Colloques no. 57.) 1991. Pp. 462. 250.00 FF. ISBN 2 7380 0337 0.

Although major genes are by no means unknown in

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