Genet. Res., Camb. (1991), **57**, *pp.* 283–289 *Printed in Great Britain*

Book Reviews

Biology of Mammalian Germ Cell Mutagenesis, Banbury Report 34. Edited by J. W. ALLEN, B. A. BRIDGES, M. F. LYON, M. J. MOSES and L. B. RUSSELL. Cold Spring Harbor Laboratory Press. 1990. 461 pp. illus. indexes. $95.

A significant revitalization of interest in the germ line and in germline mutagenesis has come about in recent years owing to the realization of the role of mutation in human heritable disease. It is therefore timely and appropriate for a conference to be held on germ cell mutagenesis and this volume records the proceedings of such a meeting, held at the Banbury Center on 12-15 November 1989. Bringing together experts, several of whom carried out pioneer mutagenesis work on the mammalian germline in the 1950s when the major investigations into chemical and radiation effects on germ-cell sensitivities commenced, the book provides a comprehensive account of current knowledge in the field. The topic areas for discussion, subdivided into six sections, ranged from properties affecting the induction and recovery of mutations, variables affecting their rate and nature, aberrant chromosome structure and behaviour, non-mutational effects on early development and the untilization of DNA techniques to detect germinal mutations. There was also a session on genetic risk estimation for human populations and individuals, in which W. L. Russell, one of the pioneers of mammalian germ-cell mutagenesis, gave an illuminating account of the deliberations of committees who, over the last 40 years, have grappled with the problems of risk estimation of genetic hazard from radiation.

Although there appears to be no direct evidence for induction of germinal mutations in man by chemical exposure, the consistency of mutagenicity test results in a wide range of experimental organisms leaves little doubt that humans will likewise be susceptible to their effects. A number of papers thus dealt with the mutagenic effects of chemical treatments on rodent germ cells (I.-D. Adler, M. J. Moses, J. W. Allen) while L. B. Russell emphasized the importance of germ-cell stage of induction (rather than chemical) in determining the nature of any genetic lesion. She also pointed out the paucity of information which exists concerning mutation induction in females compared with males. From the work of L. B. and W. R. Russell have come the 'supermutagens' ethylnitrosourea (ENU) and chlorambucil (CHL), the former acting mainly on differentiating spermatogonia, the latter on early spermatids. Contributions concerning the mechanisms of ENU mutation in the mouse germline came from J. Favor and J. Peters, while J. D. McDonald emphasised the possibility to produce animal models for human disease using this mutagen. Both of these mutagenic chemicals were seen as providing a valuable resource for in-depth molecular, genetic and cytogenetic studies of mutation.

Among the fewer papers devoted to germinal mutation in man, B. Brandriff presented data on human sperm cytogenetics and studies in the 1-cell embryo, A. Wyrobek described the detection of specific locus mutations in human sperm, and B. Kovacs covered work on germinal mutations at human hypervariable loci. There were also interesting contributions on the use of molecular technology in the detection of mutation arising in the human germline, as for example by the use of PCR to analyse sperm DNA sequences (N. Arnheim).

The overall wide range of expertise available at this conference is fully reflected in the lively discussions which follow each of the 33 presentations, and which are extremely well documented in the book. These I found most valuable, as many points not covered in the papers emerged during these exchanges.

As a final comment, W. R. Russell drew attention to the change in attitude over the past three decades regarding the relative importance of the risk from mutagenesis and the risk for carcinogenesis. In Russell's view, the current relative inattention to genetic risk may be out of balance since germ cell mutations can act from conception to old age to cause major disorders in every bodily function while cancer is a group of related diseases occurring predominantly in later life. This imbalance, the meeting organizers have obviously tried to redress, and as J. W. Allen points out in the book's Preface, this is a view which many now share, as a growing number of geneticists are turning their attention to the special problems of germ-cell mutagenesis. Much of the vital research has already been accomplished and with molecular technology now available, the detection and characterization of mutations and assessment of their transmission and expression, in rapidly advancing. This book should be considered a 'must' for every

https://doi.org/10.1017/S001667230002944X Published online by Cambridge University Press

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DNA Topology and Its Biological Effects, Monograph 20. Edited by NICHOLAS R. COZZARELLI and JAMES C. WANG. Cold Spring Harbor Laboratory 1990. 480 pages. Price $97. ISBN 0 87969 348 7.

This book is the newest addition to the high quality series of monographs published by the Cold Spring Harbor Press and is no exception to this standard. The first half of the book deals with DNA structure and supercoiling and the second half with the enzymes that change its topology, the topoisomerases, and their effects. The subject area is central to the understanding of almost all DNA interactions (e.g. transcription, replication, recombination and chromosome organization) a pivotal role that is underlined by the effectiveness of topoisomerase inhibitors as anti-cancer drugs. The chapters are written by widely respected experts in the field and the book as a whole constitutes a welcome resource for many whose work impinges upon this area and a window into a marvellous world of coils and supercoils for anyone who just finds this subject fascinating. In the preface, the editors state that 'The organisation of this volume was designed to provide a structured introduction to the uninitiated ... and that the authors had been asked to write their chapters 'in a didactic style, operating on the assumption that the average reader would have little prior knowledge of the subject'. This is rather a tall order when also attempting to make each chapter 'a separate unit for the more advanced' in an area as intellectually challenging as this. From my point of view as a geneticist with an interest in this area I was interested to see how well they had succeeded in their goals and this review can be viewed as 'a geneticist's perspective'.

The book starts by introducing the structures of DNA, emphasising the knowledge that we now have from a variety of methods of the effect of sequence on structure. I found this section fascinating but not easy to follow and I would have appreciated a more gentle introduction to the definitions of twist, roll and slide at an earlier stage in the first chapter. The book then goes on to discuss the bending of DNA in nucleoprotein complexes and in loops that regulate gene expression. These chapters interweave the experimental evidence with theoretical work and illustrate the subject with examples to produce a clear picture. The only part that I had difficulty with was the 'linking number paradox' which was clarified in the later chapter on the topology and geometry of DNA supercoiling. To my mind, the chapter dealing with the topology and geometry of DNA supercoiling was the high point of the book. This chapter takes the novice through the intricacies of linking number, twist and writhe to newer parameters such as surface twist and surface linking number without assuming any prior knowledge or advanced mathematical skills. I do not want to imply that the chapter makes for easy reading; it is very challenging. But to retain rigour while making the subject accessible is a superb achievement; congratulations. Unfortunately I cannot say the same thing about the chapter on DNA supercoiling and unusual structures. Here the theoretical treatment is not accessible without specialist knowledge outwith the coverage of the book, and the treatment of the experimental work on cruciforms and Z DNA is rather limited. The chapters of the book that cover the topoisomerases are more descriptive and therefore not so intellectually challenging. Type-I and Type-II topoisomerases of prokaryotic, eukaryotic, archebacterial and viral origin are described in eloquent detail as are their effects on replication and illegitimate recombination; and the book ends with a section on the natural modification of topoisomerases and the effects of drugs that interact with topoisomerases and their use in the treatment of cancer. An appendix giving the nucleic acid and encoded amino-acid sequences of topoisomerase genes completes the picture.

As a whole I believe that the book succeeds very well and will allow the non-specialist to enter into the world of coils and supercoils but also does not sacrifice the rigour required to be of value to the scientist working in this area. Because of my own interests I would have liked to have seen a section on site-specific recombination where such remarkable applications of topological principles have been made to understand the organisational level of the reaction mechanisms. But as the editors say in the preface they have not been 'exempted from the usual perils associated with the publication of a book on a rapidly evolving subject'. In fact they have done remarkably well in avoiding these perils and have put together a book that I can recommend very highly.

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In Situ Hybridisation: Application to Developmental Biology and Medicine. Society for Experimental Biology Seminars Series 40. Edited by N. HARRIS and D. G. WILKINSON. Cambridge University Press. 1990. 288 pages. Hardbound Price £35.00. ISBN 0 521 38062 6.

This volume presents 14 articles based on talks given at a meeting on '*In situ* hybridization' in Edinburgh in April, 1989. *In situ* hybridization uses labelled nucleic acid probes to detect specific RNA or DNA sequences within chromosomes, cells and tissues. This powerful

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