

Book Reviews

Nucleases, 2nd edn. Edited by STUART M. LINN, R. STEPHEN LLOYD and RICHARD J. ROBERTS. Cold Spring Harbor Laboratory Press, 1993. 507 pages. Price Cloth \$75.00. ISBN 0 87969 426 2.

The second edition of *Nucleases* presents a series of reviews of various aspects of the cleavage of DNA and RNA, giving the reader a good introduction to each subject, and an extensive bibliography. It is the result of a Keystone Symposium held in mid-1993 and is a complete rewrite of the first edition published in 1982, with several extra chapters being added to cover new areas of research.

The book clearly shows the spectacular progress made in the last few years on the study of nucleases, particularly when structural and physical biochemical methods have been able to complement genetic and molecular biological approaches. This is apparent in excellent chapters on type II restriction enzymes, DNA recombination, repair and proofreading during replication, DNA topoisomerases and ribonuclease H.

Significant progress is reported on the recognition of DNA sequences by the multifunctional type I and type III nucleases, but unluckily the discovery of potential type I nucleases outside the confines of enteric bacteria was too late for inclusion. There are also chapters on homing endonucleases, fungal and mitochondrial nucleases (including the secreted S1 and P1 single-stranded nucleases), RNA maturation nucleases and ribozymes.

More chemical aspects of nucleases are well represented in the opening chapter on the chemical mechanisms of phosphodiester cleavage and a chapter on the artificial nucleases formed by coupling a sequence-specific targeting molecule to a nonspecific DNA cleavage molecule. Their use as rare sequence cutters in genome mapping projects and as therapeutic agents are discussed.

The text concludes with four appendices comprising the known target sequences of restriction enzymes, known DNA repair nucleases and glycosylases, commercially available nucleases and a list of the daunting number of nucleases required to keep even a simple organism, such as *Escherichia coli*, alive.

Overall the book is well presented and well written; the editors and authors have done a good job. It

introduced me to many new, fascinating nucleases and each chapter clearly indicated where I could find further information. This edition of *Nucleases* will serve as a valuable reference book for quite a few years, despite the rapid pace of research, and I recommend it, not only to those people working on nucleases, but to anyone with an interest in the interactions between proteins, DNA and RNA.

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Blastogenesis: Normal and Abnormal. Edited by J. M. OPITZ; Wiley Liss. 1993. 403 pages. Price £124.00. ISBN 0 471 59789 9

This book contains papers from a workshop on human foetal pathology held some 3 years ago under the auspices of the March of Dimes. It contains 28 papers, most of which review or present data on human foetal pathologies, although there is a sprinkling of chapters that cover case studies, theoretical views and karyotypic work. These papers can be as short as six pages (a case study) to as long as 42 pages (a review on conjoined twinning). While coverage is not exactly comprehensive (little attention is, for example, paid to pathologies of the reproductive system) there is no doubt that anyone in the general area of foetal pathology will find something of interest in this book, be it the series of papers on cranial malformations or the various articles on twinning. For me, however, the major advance that the book highlights is the increasing use of 3D reconstructions of sectioned material to illuminate the structural basis of pathological states.

That said, I was unimpressed by every other aspect of the book. The chapters lack summaries to highlight their contents, while the editor seems to have made no attempt to impose any order on chapter organization so that the book seems a formless hodgepodge of articles. One particularly odd choice was the decision to call the book *Blastogenesis*, a term that the editor defines as development up to the end of gastrulation. Leaving aside the fact that the great majority of the papers deal with pathologies that clearly develop after gastrulation, most embryologists take the view that

blastogenesis ends at the beginning of gastrulation and, indeed, the indexer agrees with this opinion. I cannot see the intended audience selecting this book on the basis of its title to browse through in a bookshop so, if the publishers want to sell it, I hope that they are publicising it in other ways.

The price of the book is £124, an amount far in excess of its value and I can see no reason why it should be so expensive other than it has a few colour plates (of 3D reconstructions). It seems to me that the March of Dimes would have served the field better had they chosen a cheaper publisher and provided a degree of subsidy to enable foetal pathologists to buy the book. As it stands, I suspect that the book will merely be found in a few rich libraries and in the offices of participants and reviewers. While the original topic of the workshop, human foetal pathology, merited support by the March of Dimes, I feel that this charity has been let down by its editor and publisher.

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Physician to the Gene Pool. By JAMES V. NEEL. Wiley, New York & Chichester. 1994. 457 pages. Price £18.95. ISBN 0 471 30844 7.

Human geneticists know Jim Neel very well, and will already have bought his autobiography knowing that it will be a stimulating and provocative read, as it surely is. Other geneticists are advised to study it for the insights it throws on their trade, and many will want to lend it to their friends for the knowledge it gives of how a geneticist thinks and works – and how often have we wanted just such an exposition to save us from embarrassment?

Neel started as a *Drosophila* geneticist working on the effects of environment on gene expression, and this nature-nurture thread runs through the whole book. Typically, the mutation *polymorph* appeared spontaneously in his flystocks, for Neel is one of those people who finds four aces in every hand of cards he picks up: serendipity he calls this, but you have to spot the mutation before you use it and Neel rarely misses his opportunity. One of the charms of the book is following the interplay of chance and the author's preparedness to exploit it. Lucky Jim!

But flies are not all, and Nazi plans for eugenics experiments during World War II, better understood in Europe than in America, turned Neel's interest towards human genetics. While working at Cold Spring Harbor he had seen the Eugenics Record Office established there by Davenport, and a glance at the terrifyingly inaccurate data accumulate for the benefit of American race-cleansers showed that there was a whole world of genetics waiting to be explored.

Neel decided to get a medical qualification to prepare himself to study this subject. As a third year student he identified a case of Cooley's anaemia (Thalassemia) and recognized that haemoglobin mutants were good 'clean' genes to work with. He found a second, Sickle Cell Anaemia, and this became the focus of his studies when he moved to Ann Arbor where he worked out the significance of the polymorphism through relative resistance of the heterozygote to malaria. This is now all standard textbook material, but at the time there were other plausible hypotheses and the need to decide among these sent Neel to Africa to measure gene frequencies in relation to malaria incidence – gene-environment interactions on a population scale – and it also introduced him to primitive societies.

Between the first and last of his haemoglobin studies Neel was called-up to do his military stint as a first lieutenant in General Hospitals, although the war was over by then. There he suggested to a fellow intern that he would be interested in studying the genetic consequences of the Hiroshima and Nagasaki bombs. Surprisingly, for the word got through, he found himself posted to Japan with the remit to advise the National Academy on the delayed effects of the atomic bombs. Four chapters are devoted to the studies which derive from this assignment, and they update the earlier report of Neel and Schull (but a more comprehensive summary of the genetic effects of radiation on man is given in *The Children of Atomic Bomb Survivors*, 1991, National Academy Press, ISBN 0 309 4537 1, which includes that classic paper). The unexpectedly high level of radiation (about 2 Sv) needed to double the mutation frequency, gonadal and somatic, and its implications for the 'normal' mutation rate in man are again textbook topics. What will interest more is how Neel overcame the difficulties of data collection in a foreign, defeated country, and how he (and his associates) coped with the problems and advantages of Japanese social structure, including its high levels of consanguinity. Despite its complexity this part of the story is clearly and amusingly told.

More stories follow. Neel recognized that his studies had given him no insight into the nature and organization of the human gene pool. He decided to establish a base line for exploring this by starting with a simple, primitive community since this might also expose some of the selection-genetic systems under which we have evolved; the maturing gene pool. After a serendipitous hold-up in Venezuela (the Brazilian revolution of 1964) he chose the Yanomama to work with; a tribe of about 15000 forest dwellers in the upper reaches of the Orinoco. This did not simplify the problems of logistics; but it is as well that it was done since such of these peoples as have survived 'civilization' are now dispersed among the entrepreneurs seeking to take over their mineral rights, etc. No-one will again be able to study such a simple, untouched community, the story of whose future will depend on the emergence of a new B. Traven.