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Book reviews

Functional Analysis of the Human Genome. Farzin Farzaneh and David N. Cooper (eds). Bios Scientific Publishers, Oxford. 1995. Pp. 296. Price £60, hardback. ISBN 1 872748 46 5.

As the title indicates, this is a book about methods and approaches to studying the functions of the human genome rather than a review of our current knowledge of what these functions might be. As such, it is informative and the gathering of material from several different disciplines is helpful. The explosion of data about genes and the genome being generated in the Human Genome Project, which now must be made meaningful at a functional level, also makes it timely.

Chapter 1 gives an overview of the human genome. Although the chapter structure separates somewhat artificially various aspects of genes and their regulation, it provides a good introduction to the subject matter of the rest of the book. The point is well made here that the function of the genome is not simply the function of its component genes and that considerable effort is also needed (and is being made) to understand the organization, functions and constraints of extragenic DNA and the genome itself within the nucleus. Chapter 2 provides a clear overview of the international effort to map the human genome, both physically and genetically. Having set the scene, the book then moves on to three chapters which deal with how to find genes. Chapter 3 is a general account of how to construct cDNA libraries, screen them and identify full length transcripts. Gene identification by differential display and various *E. coli* and eukaryotic expression systems are also covered briefly. In Chapter 4 the use of retroviral insertion as a means of identifying genes of interest, i.e. genes whose ablation or alteration in expression cause a detectable phenotype, is discussed. In Chapter 5 this is taken a step further with the description of gene trap vectors and their use *in vitro* and *in vivo*. In both chapters the material is dealt with very readably and clearly.

The next two chapters would not, I think, be automatically included in another book of the same title. However, the background to gene transfer by transfection and the details of the experimental procedures and considerations given in Chapter 6 are very interesting and useful, particularly as this technology may be of increasing importance in the assessment of gene function. It would also have been helpful, either in a new chapter or as part of this one, to discuss additional cell-based techniques for studying the expression of transfected genes. Following from this, Chapter 7 deals with the process of foreign DNA integration into genomic DNA and the *de novo* methylation response which it is thought to evoke from the cell. The intriguing suggestion is made that alterations in DNA methylation may occur both at and at a distance from the site of integration. This implies that DNA integration may have wide-ranging and unforeseen consequences even in the case of homologous recombination.

Chapter 8 outlines very well the production of transgenic animals (except by homologous recombination which is dealt with in Chapter 9) and the kinds of studies on gene regulation and gene function which they make possible. It clearly illustrates that this is a very powerful means of analysing gene function and has much future potential, particularly with the possibility of creating double (or more!) mutants. It only touches briefly, however, on the problems which differences between humans and rodents create in extrapolating the expression patterns and phenotypes seen in transgenic mice to human development or disease. Chapter 9 deals with homologous recombination and it too is a clear exposition of the background, mechanism and uses of this method.

Complementation analysis is discussed in Chapter 10 and both the fusing of different types of whole cells as well as whole cell to microcells, containing only one or a few chromosomes, are outlined. Examples of various experiments are given to illustrate that this technology is applicable to studies in many fields; cancer, development and gene mapping are mentioned. For the examples given, it is largely the phenotypic effects of the fusions which are discussed. This was tantalising as these experiments must increasingly enable gene expression patterns to be analysed directly and so yield much more detailed knowledge of the gene interactions which have been disrupted or invoked by the fusion process. The last chapter (Chapter 11) outlines the uses of antisense oligonucleotides. It gives some detail of the considerations important to targeting and design of the oligonucleotides as well as, in discussing the various modifications which are being tried, introducing its significant limitations. It ends with a discussion of the therapeutic potential of this technology which, like the rest of the chapter, gives a clear account of both its advantages and disadvantages concluding, however, that there is great potential in this area of research.

This book carries the usual caveat of all books dealing with aspects of molecular genetics, and particularly human molecular genetics, that it is a very fast-moving field and so, inevitably already has elements that are out-of-date or missing. Having said this, it is still a very worthwhile attempt to draw together the various technologies involved in analysing the function of the human genome. It is not a 'how to' manual but describes the prinicples behind the techniques and the problems, pitfalls and successes encountered. With the rapid advances being

made with these technologies, there shouldn't be too long to wait for what should be the very exciting sequel (or series!): 'Functions of the Human Genome'.

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In the Blood. Steve Jones. HarperCollins Publishers, London. 1996. Pp. 302. Price £20.00, hardback. ISBN 0 00 255511 5.

One of the factoids that university lecturers rapidly learn is that students have an attention span of about 20 minutes. The problem, then, is to find a way of filling the remaining half-hour of a notional one-hour lecture slot. Most of us do this by acquiring a collection of slides, overheads and anecdotes, related, or more often tangential, to the lecture topic, in order to keep the students entertained. In this book, Steve Jones has taken this process to its logical conclusion in that the bulk of the book is devoted to exactly the 'lecture-filler' material that experienced lecturers hoard like magpies, and the 'hard stuff' is relegated to 'boxes', that the less demanding reader can skip without losing the thread of Jones' arguments. The difference here, however, is that with the resources of researchers commensurate with a TV series, there is a lot more really good quality 'filler' than most lecturers could accumulate in a lifetime of sabbaticals, or rained-off field-work.

Although the book is primarily concerned with genetics, Jones' approach is that of contrasting scientific enquiry with religious belief (mostly Christian). I am in no position to question the theological veracity of some of Jones' contrasts, but for me the approach seems to work. Throughout the book, Jones' laconic style shines through — one can almost hear him speaking, particularly with his speciality of pithy throw-away lines.

Jones does not duck the social implications of modern genetics, especially where they impinge on legislation, often created for solid liberal reasons. Many of his genetic examples will be familiar but his style of presentation puts them in a new light. For example, the case of haemophilia in the royal houses of Europe is usually consigned to a pedigree (and sometimes a photograph of Queen Victoria) in most textbooks, but Jones puts the case in a different perspective with a narrative which describes the mores and conventions of the aristocracy of the period.

If I have a criticism it is that too often the 'boxes' of subsidiary information are too long (often several pages) and one has to search for where the main text resumes.

This is a ripping good read, well written and beautifully illustrated. Although I thought that I was fairly well equipped with genetic anecdotes, there were plenty of new things in the book to hold my attention and even old friends were cast in a new light. There is plenty of material to fill out your lectures for years to come. At whatever your next festival is when gifts are exchanged, ask for a copy, you won't be disappointed, but keep it out of the hands of your students - they might just end up with too much stuff to pad out essays and examination answers.

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Nucleic Acids and Molecular Biology (vol. 9). Fritz Eckstein and David M. J. Lilley (eds). Springer-Verlag, Berlin. 1995. Pp. 376. Price £112.00, hardback. ISBN 9 783540 588245.

The problem (I imagine) with editing a series of books like this one is that you have to find new and exciting developments to fill 300 or so pages on an annual basis. Eckstein and Lilley have been lucky (or more likely far-sighted) in choosing an area of research where new and interesting things are not too hard to find. The title *Nucleic Acids and Molecular Biology* allows them to capture topics covering a pretty wide area, although in this volume (number 9) the topics are mainly limited to a fairly restricted definition of these terms. These include DNA structure (2 chapters), recombination (2 chapters) and a lot of coverage on DNA-protein interaction, including 3 chapters on DNA topoisomerases, 3 chapters on HMG-box proteins and 3 chapters on proteins involved in chromosome structure. The only 2 chapters which don't fit with this definition are one on ribonucleotide reductase and one on RNA splicing.

Although for most readers it does not matter, I found that the order of the chapters was not entirely logical. For example, it jarred a little to have a chapter on parallel-stranded guanine tetraplexes sandwiched between one on the unlinking of DNA by topoisomerases and one on DNA gyrase. Similarly the chapter on ribonucleotide reductase found itself between one on cyclic AMP receptor protein and one on the HMG box. However, this is probably only relevant if you read the book from cover to cover (like a reviewer has to!).

With a book of 18 chapters it is probably pointless (and dull) to go through each chapter and comment on it, so, at the risk of being unrepresentative, I will comment on selected chapters. I think the value of books such as these is that they can serve to summarise for the non-expert recent developments in a particular field. A good example of this is the chapter on chromatin structure and transcription by Hayes and Wolffe. This presents a clear account of nucleosome structure and how this can influence transcription, and is illustrated with clear explanatory figures. The 2 chapters on recombination, one on branch migration and one on the RuvAB and RecG proteins,