genes is the one on mutagenesis and gene disruption. Inclusion within this chapter is the use of the powerful technique of polymerase chain reaction in site-directed point mutation generation.

Unfortunately, these books suffer from some of the problems associated with multi-author volumes. There is inevitably a duplication of information and in this respect section III, vol. 217, 'screening libraries and identifying genes' should probably have been omitted as this topic is covered in earlier volumes. Despite this small quibble, these multi-author volumes will not only be a useful acquisition for libraries but will be found very useful to molecular biologists in small research groups.

Stephen Heath


The separation of the chromosomes from the rest of the cell by the nuclear envelope is a fundamental, perhaps the fundamental, eukaryotic characteristic, but exactly why this separation occurs is more the subject of speculation than proof. There is the argument that in large eukaryotic cells with large genomes, the capacity to concentrate relevant soluble components like enzymes, transcription factors and deoxynucleotides in the vicinity of the DNA is favoured. However, we humans tend to prefer an explanation implying more sophistication than this, so there has long been an assumption that the nuclear membrane is a fundamental, bi-directional control point in cellular trafficking, and hence genetic control. Unfortunately it is difficult to point to much hard evidence that this is the case. For example, in their inactive state several transcription factors (e.g. steroid hormone receptors and NF-κB) are present primarily in the cytoplasm and it was originally thought that nuclear translocation was their critical control point. However this is now seen to be simplistic: for example, IκB, the inhibitory subunit of NF-κB responsible for the cytoplasmic anchoring of the transcription factors, and in vitro it is capable of dissociating DNA-bound active NF-κB from DNA. Since it would appear to be quite capable of continuously regulating a nuclear pool of NF-κB, it is quite possible that NF-κB could be adequately controlled in the absence of a nuclear envelope. In general, our appreciation of higher order structure-function relationships throughout the whole nucleus are remarkably rudimentary, a fact equally well shown by the nuclear skeleton; it is clear that it exists and that replicating and transcribing DNA has special associations with it, but why is a matter of guesswork.

H.R. Woodland

Corticotropin-Releasing Factor (CIBA Foundation Symposium 172); edited by Derek J. Chadwick, Joan Marsh and Kate Ackrill, John Wiley; Chichester, 1993; x + 357 pages. £45.00. ISBN 0-471-93448-8.

The symposium which forms the basic of this volume took place only just over 10 years after Vale and his colleagues finally characterised CRF as a 41-residue straight-chain peptide. In that decade, its known and putative functions have been extended beyond the control of ACTH in such diverse directions as would have been hard to predict. Vale himself summarises them in his introduction: modulation of growth and reproductive hormones; induction of fever and loss of appetite; actions on the autonomic nervous system which influence cardiac function; behavioural effects on arousal, influencing fear, anxiety and depression. All these can be fitted without much difficulty into the familiar theoretical framework of CRF as a central mediator of the diverse responses to stressfull stimulation.

The greatest surprise to me was the revelation that the effects of CRF are not exclusively central. Wei et al. in a chapter on its anti-inflammatory effects and Lowry in his chapter on CRF binding protein show that CRF is both produced, and active in the periphery. The latter chapter and the discussion which follows tell us how the dramatic fall of CRF-BP in late pregnancy of primates, including humans, leaves surprisingly high levels of plasma-free CRF which are thought to be important in parturition.

The opening chapters deal with the central localisation of this neuropeptide, its control and some first information on its receptors. In the chapter by Plotsky et al. on feedback regulation of CRF is embedded some fascinating data on the effects of neonatal experience on the hypothalamo-pituitary system. Studies on the effects of the early environment - in vogue thirty years ago - are rather out of fashion, but this is important work deserving of wider recognition.

Interactions between CRF and the immune system are covered in two chapters: the first by Rivier and Rivest deals with the route by which cytokines - specifically interleukin 1 - inform the brain of activation of the immune system, thereby stimulating CRF and independently inhibiting GnRH and LH secretion. A.J. Dunn's chapter on infection as a stressor continues this theme, and implicates CRF in the production of fever and the defensive - withdrawal spectrum of
behaviour characteristic of sick animals. Koob and colleagues’ contribution is a review of the role of CRF in other behavioural stress responses, and in the following chapter Nemeroff and Owen consider its part (cause or effect?) in depressive illness and anxiety states.

The symposium was a timely event, given the burgeoning interest in CRF and this volume, with its detailed reports of the discussion which followed the presentations makes one disappointed to have missed the live meeting. It is hard to fault this well-produced, efficiently indexed book. As always, some contributors to discussion tended to use it to present their own uninvited results, but that is a small price to pay to have such a wealth of information between two covers, in an accessible form.

Peter Chevins

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This book is part of the NeuroMethods series. As such, its emphasis is methodological, and the neurotrophic factors of the title are the glue that holds the chapters together. The outcome, therefore, is a wide-ranging review of methods that includes the purification and sequencing of the factors, the screening for related genes using low stringency hybridization, the production of recombinant protein, the transfection of the factors and their receptors, as well as the use of in vivo models and axonal regeneration.

Consequently, the book cannot hope to be comprehensive; the whole of protein purification and sequencing is covered in 20 pages, whilst each topic may be found as the subject of a complete book elsewhere. Similarly, because each method is described as it has been applied to the study of neurotrophic factors, the text is a curious mixture of methods (including protocols) and results, with different chapters leaning in different directions. The result is that the coverage of the literature is partial, and the methodology is more of the ‘tested methods’ variety than the ‘secrets’ as proclaimed on the jacket.

Having said that, this book contains within one volume a good enough review of the literature in the field of neurotrophic factors, and enough help in the protocols to launch a researcher into a new area of interest. I suspect that this volume will have parts that prove useful to most workers or potential workers in the field.

J.A. Smith

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**Tumor Necrosis Factor: Molecular and Cellular Biology and Clinical Relevance**, edited by W. Fiers and W.A. Buurman, Karger; Basel, 1993; x + 256 pages. SFr 323.00, DM387.00, £161.50, $258.50. ISBN 3-8055-5676-4.

This book contains papers presented at the 4th International Conference on Tumor Necrosis Factor and Related Cytokines held in Veldhoven, The Netherlands in May, 1992. It contains 35 articles ranging from 5 to 10 pages in length, covering the nature of the two Tumor Necrosis Factors (TNFs), their genes and sections on the TNF receptors, the cellular mechanisms of action of TNFs, their involvement in pathophysiological phenomena, in auto-immune and infectious diseases, and finally in cancer and their potential in cancer therapy.

Although the original interest in TNF lay in its potential as an anti-tumour agent, it is now clear that it is a major component of the cytokine network, involved in immune and inflammatory responses, in combatting viral, bacterial and parasitic infections, and apoptosis as well as diverse other normal processes. TNF overproduction is implicated in septic shock, arthritis, graft–host disease and many other diseases.

From the papers presented here, it is evident that the precise details of the regulation of TNF gene expression, release of membrane bound forms of TNF and interaction with the receptors are well characterised, and the significance of shedding of ligand binding domains of TNF receptors from the cell surface is beginning to be unravelled. However, the signal transduction mechanisms activated by TNF remain far from clear, with tantalising hints (but no more) that phospholipases C or A₂, and protein kinases and phosphatases are implicated at some stage.

Indeed, as the reader proceeds through the book the articles become increasingly phenomenological with only rare definitive clues to mechanisms underlying the physiological and pathological events described.

The early promise that TNF held out as an anti-tumour agent has been denied by its toxicity when systematically administered at therapeutic doses. However, some interesting contributions monitor progress with modified forms of TNF and other strategies which might widen margins between toxic and therapeutic doses, and others announce encouraging success with clinical trials with TNF in combination with interferon and chemotherapeutic agents in isolated limb perfusion.

The book is a very useful guide to the state of progress in the TNF field in mid-1992, although the multiple contribution format generates a niggling repetition of redundant background information. The quality of articles is reasonably uniform for such a text, but the level of experimental detail given is variable. Despite a frustrating number of typographical errors, the standard of reproduction of the text and paper quality are excellent, but at that price they should be! Nevertheless, unless I was working in the broad TNF field, I would find a chapter on TNF in a current review journal better value for time and money.

Mike Billett