

Book Reviews

Superantigens: A Pathogen's View of the Immune System. Edited by BRIGITTE T. HUBER and ED PALMER. Current Communications in Cell and Molecular Biology, 7. Cold Spring Harbor Laboratory Press. 1993. 180 pages. Paperback. Price \$55. ISBN 0 87969 3983.

Superantigens were originally described as viral or bacterial products which induced MHC non-restricted proliferation of all T lymphocytes expressing specific T cell receptor (TcR) V β regions, eventually leading to anergy and deletion of reactive clones from the T cell repertoire. However, intensive research over the last 5 or 6 yr has revealed many examples of apparently anomalous 'superantigen-like' phenomena where T cell activation is apparently MHC-restricted or limited to a subset of those T cells which express the relevant V β gene. At the same time, the evolutionary significance of superantigens – to both the pathogen and the infected host – has been questioned. This book, which addresses these questions, and more, is thus both timely and thought-provoking.

Superantigens have been convincingly demonstrated in a number of bacterial pathogens (streptococci, staphylococci, mycoplasma, yersinia) and in the mouse mammary tumour viruses (MMTV's); chapters in the book critically review the more recent, and admittedly rather indirect, evidence for superantigenic effects of rabies virus nucleocapsid proteins (Lafon *et al.*) and HIV-1 (Posnett *et al.*, Soudeyns *et al.*). The molecular basis for the interaction of staphylococcal enterotoxin A (SEA) with MHC Class II antigens and the TcR is reviewed by Fraser *et al.* Blackman *et al.* review evidence that V α sequences of the TcR and polymorphic residues of MHC molecules can influence the affinity of superantigen binding. They propose that, for viral superantigens at least, high affinity interactions may lead to T cell deletion, medium affinity interactions may lead to T cell anergy (but not deletion) and low affinity interactions may have little or no effect. This would go a long way to explaining the anomalous data referred to above.

Following an initial proliferative response, superantigen-activated cells eventually become anergic and are deleted. This can result in loss of T cell reactivity to specific antigens ('holes in the repertoire'). In the case of endogenous superantigens, such as

those encoded by the *sag* genes of MMTV's – which are stably integrated into the mouse genome and which are expressed during foetal development – superantigen activation of thymic T cells can lead to deletion of more than 90% of T cell specificities. It remains to be seen whether such endogenous superantigens have been incorporated into the human genome. However, it is clear that superantigens can play a profound role in shaping the T cell repertoire. How, then, did superantigens evolve, how do they benefit the organism that produces them and is there any benefit for the host? To quote Fraser *et al.* (p. 26), '...how and why have such widely divergent proteins as the MMTV and bacterial superantigens converged on a complex biological activity involving the simultaneous binding to two highly polymorphic proteins such as MHC Class II and the TcR?'

A cogent argument for the role of MMTV-encoded superantigens is put forward by Ross *et al.* They propose that superantigen activation of T cells is necessary to generate a reservoir of susceptible cells in which the virus can replicate and in which infectious virus can be transported to the mammary glands. Since the activated cells will eventually become anergic or be depleted, the adult mouse will be immunologically tolerant to MMTV-infected cells. In the case of endogenous superantigens, deletion of reactive T cells *in utero* will render mice resistant to horizontal infection by similar viruses, thus reducing viral load, reducing the incidence of mammary tumours, increasing lifespan and reproductive potential and thus increasing germline transmission of the integrated gene. Convincing evidence in support of this theory is presented, including evidence for selection of exogenous viruses expressing mutant superantigen genes in the face of T cell deletion by endogenous superantigens. Bacterial superantigens may play a similar role, promoting immunological suppression or tolerance through deletion of reactive T cell clones (Lafon *et al.*, p. 133).

Although much remains to be discovered about the impact of superantigens on the immune system, I suspect that Soudeyns *et al.* are correct in stating (p. 156) that the viral superantigens 'play a role in the life cycles and associated pathogenic processes of their respective viruses, a role significant and dynamic

enough to warrant their genetic conservation throughout evolution'.

This is a clearly written, very readable, well referenced volume with good use of original data. It is also bang up-to-date; much of the data referred to as 'in preparation' is only now appearing in the primary literature. Individual chapters are complete in themselves, allowing them to be read as single review articles. However, this does lead to an inordinate amount of repetition of the generally accepted facts. An expanded introduction, covering the common ground, would have minimized repetition and highlighted those areas where the consensus has yet to emerge. The main emphasis of the book is on viral superantigens rather than bacterial superantigens. The editors do not comment on whether this is simply a reflexion of levels of activity in the two areas, or an indication that the role of viral superantigens is more profound – or more controversial – than that of bacterial superantigens. On the plus side, the editors have clearly encouraged the contributors to hypothesize and to spell out the links between their own work and the rest of the field. It is gratifying to find that questions raised in one chapter are seriously addressed in subsequent chapters. In summary, this is a stimulating journey through the rapidly unfolding superantigen saga which will be a rewarding read for anyone interested in the ontogeny of the immune system, the immune response to infection or the evolution of host–pathogen relationships.

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Transcriptional Regulation. Two volumes. Edited by STEVEN L. MCKNIGHT and KEITH R. YAMAMOTO. Cold Spring Harbor Laboratory Press. 1993. 1334 pages. Price Hard cover \$160. ISBN 0 87969 4106. Soft cover \$95 ISBN 0 87969 425 4.

The vectorial process of gene expression, which can be described in terms of four main stages, DNA transcription, RNA processing, RNA translation, and protein processing, is the sole means by which the genetic information contained within nucleic acids is realized. It is a truism, but one worthy of repetition, that this multifaceted process is by no means passive: It is by responding to different stimuli – whether internal or external – that both unicellular and multicellular organisms (and their genetic elements) in nature are able to survive. Gene regulation, in short, is the 'stuff of life'.

A primary target in such regulation, but by no means the sole one, is transcription by the DNA-dependent RNA polymerase(s). There are two main forms of this essential enzyme, one is multisubunit in composition and is present as a single species in

eubacteria, archaea, and chloroplasts, and as three species in the nuclei of eukaryotes; the other form is a single polypeptide chain as exemplified by the T3/T7/SP6 bacteriophage-encoded enzyme and that found in mitochondria. Given the strong conservation and widespread nature of the multimeric RNA polymerase, it is particularly fitting that this new publication from Cold Spring Harbor should attempt to consider transcriptional regulation in a single monograph (number 22 in the series). Note that in addition to the hardback there is a competitively priced paper edition.

Transcriptional Regulation comes from a long line of excellent monographs, and it is by no means surprising to find that the standards of this pedigree are maintained. Indeed, a veritable wealth of information is packed into this two-volume set, ensuring that both the pundits and lay people are well catered for. It is impossible to do justice to such a *magnum opus* and the following description is intended as a 'snap-shot', summarizing the basic details.

As with other CSH monographs, *Transcriptional Regulation* is written by key figures in this large field; it is very much a North American affair.

The topics covered in *Transcriptional Regulation* can be separated into three major areas: RNA polymerase itself, transcription factors, and regulatory networks, and although the emphasis is on eukaryotes, there is generally a healthy proportion of eubacterial material. (I was somewhat surprised to see no coverage of eubacterial RNA polymerases *per se*, especially bearing in mind its role as a simple paradigm for the more complex eukaryotic counterparts; the archaeal enzymes are also not considered.)

Let us look at the contents of the monograph in a little detail. For this purpose, given the eukaryotic bias, it is convenient to separate the topics on a species basis (chapter numbers are given in parenthesis).

Eukaryotic RNA polymerases. Other than an extensive review of the current status of the genetics and biochemistry of the three yeast enzymes, the focus is on RNA polymerase II (2), including, in addition to the general details, the intriguing CTD and its phosphorylation (3–5), and information on the three-dimensional structure at 15 Å (3).

Eubacterial transcription. Here we have both sigma factors and rho (6, 14), the termination cycle in quantitative and topological terms (7, 46), and the control of termination through antitermination mechanisms and various forms of attenuation (8, 15, 16). A number of individual transcription factors are considered separately in some detail: repressors – LacI, TrpR, lambdaoid (23, 18, 17); activators – AraC, Crp, signal transduction response regulators (24, 19, 25).

Eukaryotic transcriptional initiation. In addition to considering the role of chromatin structure (47, 48), there are several chapters describing the well-characterized initiation factors acting on the three different RNA polymerases: TFIIs, TFIIIs, TATA-