

all free-living amoebae. However, the author may be referring only to small free-living amoebae since the methods described are not to the reviewer's knowledge easily applied to the large amoebae.

Despite the shortcomings noted, the volume is a valuable reference that is comprehensive in its coverage of a wide range of living materials. Collecting the expertise of the authors into one ease-to-use manual

designed for direct laboratory application is attractive. The volume offers easy access to a variety of useful protocols without the need for a cumbersome search of the voluminous and scattered literature on low-temperature preservation, as the editors aptly point out.

Frank P. Simone

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**Human Basophils and Mast Cells: Biological Aspects; Chemical Immunology, Vol 61;** Edited by G. Marone, Karger, Basel, xi + 242 pp. \$ 228.00. ISBN 3-8055-6127-X

This volume is one of two; the other deals with clinical aspects of mast cells and basophils. There are a number of recent publications dealing with both basic and clinical aspects of these cell types. Although unlike the present volume, most represent conference proceedings, this account differs in one important way; it attempts to deal with mast cells in a wide range of organs and systems of the body, areas often neglected in other treatises.

The first chapter on ultrastructural morphology of human mast cells and basophils describes results using a modified immunogold technique for localising enzymes involved in the eicosanoid pathways and histamine secretion. This, together with a chapter on the portfolio of cytokine and other receptors expressed by mast cells and basophils by P. Valent provide a useful structural and molecular basis to the functional studies which come later. One of the major advances in understanding of the growth and differentiation of mast cells and basophils and the importance of the micro environment in the phenotype of mast cells had been the discovery of the role of Stem cell Factor (SCF) (C-kit ligand) derived from fibroblasts and certain other cell types. The importance of synergy of SCF with other cytokines in enabling culture of mast cells *in vitro* is mentioned although the important role of interleukin-6 (IL-6) and of TH1 and TH2 cytokines might have received more emphasis.

The present state of knowledge on signal transduction following FCεRI cross-linking in mast cells and basophils is well reviewed by Scharenberg, Kinet and MacGlashan. However the opportunities for therapeutic intervention offered by insights into the stimulus - secretion coupling events seem limited. The human mast cell as a source of immuno regulatory cytokines is well reviewed by M. Church and colleagues. Students of the pathogenesis of human disease in which mast cells appear to be involved (asthma, psoriasis, atopic eczema chronic arthritis) may well feel that the pathogenetic importance of these cells in the aforesaid diseases has received insufficient attention. The authors also make the important point that the tissue micro environment of the mast cells may have a major influence on the pattern of cytokines produced by mast cells. Whilst the arachidonate

transformation pathways in mast cells and basophils are quite well covered in the chapter by Marone and colleagues, the reader is left wondering about the role of cytokines as described in earlier chapters and including IL-10, on modulation of these important pathways as previously described elsewhere by Austen and colleagues.

One of the two most important chapters in the book is that by Grant and Alam dealing with histamine releasing factors. Although the chemokines as histamine releasing factors are described in some detail, presumably because the authors themselves have been involved in their evaluation, there is a surprising omission of mention of other workers' findings in this field including histamine releasing cytokines (Claveau and colleagues (Quebec) and anti FCεRI auto antibodies (discovered by Hide and colleagues (London)). The modulating role of stem cell factor on mast cell activation is also not discussed.

The second important chapter is on the neuro immune connection. Most people believe there is an important functional relationship between the nervous system and the tissue mast cells but no one seems to have a clear idea of exactly how it works. Bienenstock makes a worthy attempt to clarify this fascinating area beginning with evidence on the close relationship between tissue mast cells and peripheral nerve endings. He also emphasises the role of neuropeptides and nerve growth factor in mast cell regulation; the former acting via the axon reflex flare and the latter leading to mast cell proliferation. However the crucial pathways whereby information from higher centers can feed down to tissue mast cell populations, leading to activation remains to be elucidated.

Overall this book can claim to be the most comprehensive treatise currently available on the rapidly developing topics of the biology of mast cells and basophils. Individual chapters integrate together well enough to give the reader a feeling of a continuous and logical journey through this complex field. The volume should form an excellent introduction to the more clinically oriented second volume.

Malcolm W. Greaves

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**Oncogenes (2nd. edn.);** Edited by G.M. Cooper. Jones and Barlett Publishers, Boston, 1995. xiv + 384 pp. \$ 52.50. ISBN 0-86720- 937-2.

The author was one of the pioneers in isolating activated oncogenes from human cancers in the early 80ies. He presents an overview mainly aimed at advanced undergraduates, medical student, doctors and scientists. Out of the vast literature he has selected what he considers as highlights and has concentrated this in short descriptive chapters follow by an extensive list of references. These are organized after topic making it easy to find relevant papers.

In a brief introduction basic concepts of cancer research are presented in order to create a background for the following chapters. Thereafter follow a description of tumorvirus where the general theme for DNA tumor virus is the interference between viral proteins and p53 and pRb disturbing the control of the cell cycle. In contrast to these stand the retrovirus where the understanding of retroviral oncogenes gave the first understanding of disorders in cell proliferation related to cancer as summarized in chapter 4.

Chapters 5 to 8 relate to the cellular oncogenes. How they were identified showing that all of those isolated from cancer cells carried mutations in contrast to their normal counterpart the protooncogenes.

How they could become targets for viral integration or insertional mutagenesis. Finally how many of these were involved in chromosomal translocation or amplifications in tumors. In each chapter clear tables help to provide the overview out of which comes the general picture that several of the oncogenes have been activated by several different mechanisms in different tumors and therefore show a gain of function in tumors.

The tumor suppressor genes are exemplified by the discovery of the retinoblastoma gene. It started with somatic cell hybridization where the normal counterpart dominated over the tumorigenic cell. This was followed by the recognition that when hybrids lost some chromosomes they regained tumorigenicity. Combined with the occasional loss of chromosome 13 in retinoblastomas lead step by step to the identification and cloning of the retinoblastoma gene. This in turn showed loss of function in many common types of tumors and not only in the rare hereditary disease in children. This has lead to the general concept that tumor suppressor genes show loss of functions in cancer. Table 10.1 and 10.2 give a summary of the most common tumor

suppressor genes identified in tumors. Most of these are both involved in rare hereditary cancer syndromes as well as sporadic occurring tumors.

The concept of multistep carcinogenesis was originally based on statistical evidence from cancer registration and later supported by evidence from chemical carcinogenesis in animals. The identification of the genes involved in tumorigenesis has substantiated this hypothesis and current research are now directed against the functional aspects of the individual mutations. This is therefore dealt with in the second half of the book. In individual chapters the following topics are treated in relation to malignant growth and disease. Growth factors and protein tyrosine kinases including growth factor receptors. Guanine nucleotide binding proteins and serine/threonine kinases. Transcription factors, mitogenic signals and regulation of cell cycle.

Consistent with the normal functions controlled by oncogenes and

tumor suppressor genes the development, differentiation and programmed cell death has also in recent years been shown to be affected. This has also led into insight in non malignant diseases such as Hirschsprungs disease where mutation in one protooncogene lead to defective development of the enteric nervous system.

In the last chapter the author deals with new prospects for cancer prevention and treatment. He points rightly at the fact that our present rather detailed understanding of processes driving tumorigenesis have not yet guided us to specific treatments. But he lists a number of possibilities including prevention and possibilities for specific treatment directed against the now recognized somatic mutations causing the cancers.

All in all a very good overview of a rapidly expanding research area.

Jes Forchhammer

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**Peptide Synthesis Protocols. Methods in Molecular Biology, Vol 35;** Edited by M.W. Pennington and B.M. Dunn, The Humana Press; Totowa, New Jersey, 1994. xii + 321 pp. \$ 64.50. ISBN 0-896-03273-6

This monograph forms part of a series aimed at providing a range of practical guides for molecular biologists. However, those expecting to find a logical approach to presenting the various steps associated with peptide synthesis will probably be disappointed. Somewhat surprisingly, for example, there is no chapter dedicated to standard procedures against which the various modifications discussed within this book can be judged. The book comprises 15 chapters that cover topics such as procedures to improve difficult couplings, effect of solvent compositions on solid phase peptide synthesis and cleavage of protecting groups (both Fmoc/t-butyl and Boc/benzyl strategies), through to the more specialised areas of site specific modification, phosphorylation, disulphide bridge formation, fragment synthesis and condensation strategies and asymmetric chemical synthesis of conformationally constrained amino acids. Attention is focused mainly on the solid phase approach with both Fmoc/t-butyl and Boc/benzyl methodologies being covered.

The opening chapter discusses problem couplings. These arise through the association of peptide chains, via the formation of  $\beta$ -sheet type structures, within the peptide-polymer matrix. Significant advances have been made in this area in the last 3 years and it is unfortunate that these are not included within this chapter. The contribution to secondary structure formation from amino acid composition, side chain protecting groups and solvent composition are now more widely understood. The approaches advocated in this chapter to improve such difficult couplings, elevation of temperature, addition of excess tertiary amine or the use of more powerful carboxyl activation, should be viewed with caution as side reactions may also be promoted. In particular, the generation of epimerized products from the incautious use of tertiary base may lead to disastrous consequences for the unwary and should only be considered if all else fails. The development and application (1993) of a reversible protecting group for backbone amide bonds is likely to provide a general solution to the problem of aggregating sequences.

The next four chapters form the main peptide synthesis content of the book. Methods for removal of the Fmoc group (both solid phase and in solution) are extensively covered by G. Fields and includes sections on monitoring and useful comments on side reactions. The subsequent chapter (G. Fields and C.G. Fields) discusses the effects of solvent composition on peptide-polymer solvation, particularly

relevant to the discussion on difficult sequences of the first chapter. Extensive, detailed instructions for the use of the hazardous hydrogen fluoride, for final deprotection and peptide-polymer cleavage in the Boc/benzyl methodology, are presented by M.W. Pennington. This includes both the standard protocol and the 'low-high' procedure developed by Tam. In comparison, a much shorter presentation follows, by F. Dick, on trifluoroacetic acid based deprotection and peptide-polymer cleavage conditions as the final step in Fmoc/t-butyl synthesis, with useful description of scavengers employed to prevent side reactions at sensitive residues. The only significant omission is the use of tert-butoxycarbonyl protection for the indole side chain of tryptophan that has had a significant impact on the ease of synthesis of peptides containing this potentially troublesome amino acid.

The remaining 10 chapters include detailed experimental procedures for preparing modified peptide structures, in particular the chapter, by G. Barany, F. Albericio and co-workers, on disulphide bridged peptides is outstanding. The chapter, consisting of almost a quarter of the whole book, gives a wide-ranging discussion on the strategy for preparation of intra and inter (both symmetrical and unsymmetrical) disulphide-bridged species. The extensive literature cited (over 350 references) illustrates the different chemical approaches possible. The final chapters on preparation of peptide fragments (M. Mergler) and fragment condensation (R. Nyeffer) describe the situation up to about 1993). Since then, significant advance has been made through the use backbone amide bond protection. This technique eliminates the unpredictable insolubility problems associated with protected peptide fragments leading to dramatically improved procedures for preparation, purification, analysis and their subsequent use in assembly of small proteins. Equally, protein synthesis can also be effected through site-specific ligation of fully deprotected peptides. Significant protein targets have been prepared from this technique by Kent and co-workers.

On the whole this is a good laboratory manual containing experimental protocols for a range of useful peptide techniques. Though some of the chapters are suitable for a more general audience, many will be appreciated more by peptide chemists.

Tony Johnson