Monoclonal Antibodies. Production Engineering and Clinical Applications; Edited by M.A. Ritter and H.M. Ladyman, Cambridge University Press; Cambridge, 1995; xv + 480 pp. $39.95. ISBN 0521 42503 4

The generation of hybridomas and monoclonal antibodies is certainly one of the most powerful inventions of the past 20 years. Monoclonal antibodies are useful reagents for the identification and purification of molecules and cells, both in basic research and in many areas of clincial medicine. Among numerous other applications, they have raised new hopes for Paul Ehrlich's old idea that targeted antibodies can be used as 'magic bullets' against infectious diseases and cancer. For inventing monoclonal antibodies, Georges Köhler (1946–1995) and César Milstein received the Nobel Prize in Physiology and Medicine in 1984. Monoclonal antibodies have an important and wide-ranging role in most areas of biomedical research and this volume is among the first to attempt to combine both the technical and clinical aspects of the subject. Monoclonal antibodies have continued to provide highly specific and versatile reagents with which to identify, analyze, quantitate and manipulate molecules, both in solution and in the solid phase, as for instance on the cell surface. The aim of the book is to provide a unique source of information concerning the production of antibodies, both by hybridoma and other cellular techniques, as well as by more recent techniques based on molecular biology. These technical descriptions are followed by discussions of the different analytic, diagnostic and therapeutic applications in clinical medicine including histopathology, oncology, transplantation, infectious diseases, rheumatology, haematology and dermatology. The initial chapters include a brief introduction to the basic aspects of the immune response to generate antibodies (Chapter 1 by M.A. Ritter), the use of cellular and molecular techniques for the generation of mouse and human monoclonal antibodies (Chapter 2 by H.M. Ladyman and M.A. Ritter; Chapter 5 by A. Sa'adu and A. Zumla) as well as the production of antibodies by phage display techniques (Chapter 7 by A.J.T. George), genetic manipulation of monoclonal antibodies (Chapter 8 by N.S. Courtenay-Luck), the generation and applications of bispecific monoclonal antibodies (Chapter 6 by S. Songsivilai and P.J. Lachman), mapping of epitopes recognized by antibodies and the generation of peptide antibodies (Chapter 4 by K.M. Price), and the use of monoclonal antibodies in novel and enhanced diagnostic immunoassay systems (Chapter 9 by D.B. Cook and C.H. Self). To complete this aspect of the book, Chapter 3 by R.J. Morris provides an important and 'user-friendly' introduction to antigen–antibody interactions and how affinity and kinetics affect assay design and antibody selection procedures. The second part of the book contains a series of chapters (Chapters 10 to 16) covering most of the many clinical areas in which monoclonal antibodies are currently used, both for routine applications as well as for experimental purposes. Chapters 10A (by A. Colfor and P.A. Hall) and 10B (by A. Bamias and A.A. Epenetos) discuss the uses of monoclonal antibodies in oncology, in diagnostic pathology and for in vivo targeting for immunoscintigraphy and therapy of human malignancies. As pointed out before, the idea of targeting human tumors with antibodies is by no means a new one, and monoclonal antibodies have already now been tested in connection with diagnosis and/or therapy in vivo for more than 15 years but due to limited success have so far not been established as a routine in the clinic. Several more recent developments, especially in the recombinant DNA area and in the generation of human antibodies, might raise new hopes that after all the 'magic bullets' might be within reach in a foreseeable future. Chapters 11A (by T.G. Wreghitt and J.J. Gray) and 11B (by J. Cohen) discuss the applications of monoclonal antibodies in the important area of infectious diseases, for diagnosis and in prophylaxis and therapy, respectively. Monoclonal antibodies have already found important applications for diagnosis of infectious diseases, but similarly to the cancer area in vivo applications have been more problematic as exemplified by the variable results obtained in treatment of Gram-negative sepsis with monoclonal antibodies. A further important application area is the use of monoclonal antibodies in connection with transplantation and for immunosuppression, where the immunohistological applications are discussed in Chapter 12A (by M.L. Rose), the experimental uses of monoclonal antibodies in Chapter 12B (by N.M. Parish and A. Cooke), prophylaxis and treatment og graft-versus-host disease after bone marrow transplantation in Chapter 12C (by L. Boström and O. Ringdén), and the clinical uses in organ transplantation in Chapter 12D (by M. Giral et al.). The use of monoclonal antibodies in further clinical areas are discussed in the following three chapters: monoclonal antibodies and the skin (Chapter 13 by A.C. Chu and E. Tsele), monoclonal antibodies in endocrinology (Chapter 14 by E. Hillhouse and C.H. Self), and finally a discussion of monoclonal antibodies in rheumatology (Chapter 15 by J.D. Isaacs). A final technical appendix (Chapter 16 by H.M. Ladyman and M.A. Ritter) summarizes the basic methods and recipes used in the generation, production and characterization of mouse monoclonal antibodies (introduced in Chapter 2) and in addition gives a number of practical hints which are useful for the beginner in this field. A similar technical appendix containing the basic protocols for conjugation of peptide antigens is included separately in Chapter 4.

All these chapters include extensive bibliographies which makes this book an excellent source for primary reference material.

All in all the editors and the individual authors have succeeded in realizing their intentions in producing yet another volume on the principles, methods and uses of monoclonal antibodies as well as recombinant antibodies. The book is extremely well suited as an introduction to monoclonal antibodies for clinicians from different areas of clinical medicine. After reading the book, it should be possible for even beginners in the field to raise their own monoclonal antibodies and to obtain some appreciation of the advantages and disadvantages of these reagents. Even if some readers do not go on to produce their own antibodies, nearly everybody in some area of biomedical science are confronted with monoclonal antibodies as reagents and for this reason it is highly relevant with a single source for information on the advantages and potential pitfalls of using these unique reagents. The book is well organized though it is necessary for the reader to get acquainted with how its put together to use it to its full advantage. A final plea is caused by the abbreviation 'mabs' for monoclonal antibodies which is used throughout this volume: it is high time for a consensus in this area, we already have 'MAbs' and 'mAbs', what is next?

Jesper Zeuthen

Peptide Antigens. A Practical Approach; Edited by G.B. Wisdom, Oxford University Press; New York, 1994; xix + 252 pp. $50.00. ISBN 019 963452 1

This volume is another fine addition to The Practical Approach Series (series editors D. Rickwood and B.D. Hames). The book lives up to the consistently high quality of this series whose place is in the laboratory rather than in the library. The specificity by which antibodies recognize and bind to proteins and peptides has been a major subject of immunochemical research and the use of peptides to produce antibodies, to affinity-purify antibodies, and to map epitopes has been essential in advancing our comprehension of antigen-antibody reactions. The topics covered span a wide range of techniques helpful to the use of peptides in the study of antibodies. After a short introductory resumé (G.B. Wisdom) of the application of peptides as antigens and immunogens follows the only chapter of the book which is of a more theoretical nature: 'Epitope prediction from the primary structure of proteins' (J.-L. Pellequer, E. Westhof, M.H.V. van Regenmortel). The large body of information about epitopes on proteins of known three-dimensional structure combined with results from epitope mapping with peptides have been used to develop prediction methods for antigenic sites on proteins. The prediction algorithms are valuable to design peptides having a higher probability of inducing protein-reactive antibodies and, thus, are useful in the production of antibodies against proteins whose sequence has been derived only from DNA or which are otherwise unavailable for

immunization. The chapter gives a critical and well balanced overview about the many algorithms in current use to predict B cell and T cell epitopes. A new algorithm, developed in the authors' own laboratory and based on the apparent preponderance of β-turns in protein epitopes, is presented. In spite of all their sophistication, the success rate of the prediction methods remains modest.

The ever increasing use of peptide antigens has been fostered by tremendous improvements in automated solid-phase peptide synthesis and by new and ingenious methods to rapidly and simultaneously synthesize large numbers of peptides in small amounts and in forms suitable for different immunological applications. Three chapters are related to the chemical synthesis of peptides. In chapter 3, B. Walker gives a concise and clear presentation of current synthetic procedures, covering the pros and cons of Boc and Fmoc protection strategies as well as of the attention that has to be given to the proper choice of side chain protection. Peptides are generally poor immunogens and a recurrent task is to render them immunogenic, which in the past has been achieved mainly by coupling the peptides to a high molecular weight carrier that helps to improve immunogenicity and to enhance T cell help. A purely synthetic approach has been taken by J.P. Tam. His multiple-antigen peptide system is presented in chapter 4 and discussed together with the more traditional carrier approach.

Also dealing with new methods of peptide synthesis is chapter 7 on 'Epitope mapping using synthetic peptides' (J. Worthington and K. Morgan). Practical aspects of Geysen's 'Pepscan' technology in which hundreds to thousands of short peptides are synthesised onto plastic pins and directly used in immunoassays are surveyed and the use of this astonishingly simple method for the mapping of B cell and T cell epitopes is illustrated by examples from the authors' own work. Multiple peptide synthesis has had a strong influence on the way epitopes are conceived by many researchers. This is unfortunate as epitope mapping with peptides is necessarily limited to the detection of sequential epitopes, that is, epitopes of proteins that can be successfully mimicked by a short synthetic peptide. Although I do not share the minority view of those who doubt that peptides are at all useful for epitope mapping, I find that the problems with the peptide approach of epitope mapping have not been sufficiently considered in this chapter. The allusion given that all possible epitopes of a particular protein can be identified by the peptide approach is a misconception of what epitopes are and of the very disparate nature of epitopes: Epitopes are not an intrinsic property of a protein per se but exist only by virtue of a connection with complementary antibodies, hence it is conceptually impossible to identify 'all possible epitopes' (p. 81), not even all possible sequential epitopes. The reaction of antisera with peptides cannot disclose the majority of epitopes on a native protein as these are mostly discontinuous and often cannot be mimicked by short peptides. The situation is simpler for monoclonal antibodies, but also here the peptide mapping approach is restricted. The same applies to 'Epitope mapping using libraries of random peptides displayed on phage', the title given to the chapter by W.J. Dower and S.E. Cwirla. Unfortunately, I also could not find a reference of caution about the limits of this otherwise most elegant and highly proficient technique. Chapters on the use of peptides for preparative immunoaffinity chromatography (M.R. Price and K. Beyzavi) and on the different immunoassay procedures currently in use to analyze anti-protein and anti-peptide antibodies round up this useful small volume which deserves to become a good companion to the scientist at the bench.

Hans Rudolf Bosshard

Immunocytochemical Methods and Protocols. Methods in Molecular Biology, Vol. 34; Edited by L.C. Javois, The Humana Press; Totowa, 1994; xiv + 435 pp. $64.50. ISBN 0 89603 285x

Immunocytochemistry is important to many disciplines that need to evaluate the distribution and cellular heterogeneity of antigens. A vast number of techniques are available today and the novice will need guidance through the many complicated steps involving cell and tissue fixation, pretreatment, staining and evaluation.

Immunocytochemical Methods and Protocols consists of 48 chapters divided into sections dealing with antibody preparation, tissue preparation for light microscopy, light microscopic immunocytochemical detection systems, fluorescence-activated cell sorting (FACS), colloidal gold detection systems for electron microscopy, photomicrography, and special applications including immunocytochemical detection of non-radioactive in situ hybridizations, confocal microscopy and laser microbeam applications. This volume, hence, has a big scope and guides the reader through many different techniques in many chapters. A few of these, like some of the FACS chapters, have nothing to do with immunocytochemistry but nevertheless represent fascinating reading.

The book contains some outstanding contributions. Particularly chapter 8 by Melissa A. Melan gives a competent and critical overview of cell fixation and permeabilization which successfully balances the subsequent chapters 9–11. These chapters take the everyday problems of a pathology department as their starting point, including the practical compromises that are necessary in such a setting. They may therefore not be entirely relevant to a more experimental setting. Mark C. Willingham has contributed two excellent treatises on immunocytochemistry of tissue culture cells and Lorette Javois writes about the important aspects of whole-mount stainings. Gary Bratthauer describes well the use of different immunoenzymatic detection procedures and Robbert Cunningham and associates treats the important aspects of immunofluorescence and FACS. Good descriptions of colloidal gold methods are provided by Constance Oliver and Liana Harvath provides a nice overview of confocal microscopy. Treatment of non-radioactive in situ hybridization (unfortunately termed 'nucleic acid immunocytochemistry') is restricted to chromosomal hybridizations. This is a pity as many workers today want to combine mRNA in situ hybridization and immunocytochemistry. Information about these methods will have to be sought in specialized volumes on in situ hybridization methods.

Although generally good, there are some sad omissions from this volume. First and foremost one lacks an overview of the limitations and pitfalls of immunocytochemistry as well as an in-depth discussion of the necessary control procedures. The short chapter 1 on overview of antibody use in immunocytochemistry is too brief and ignores many of the major pitfalls. Other omissions include lack of descriptions of double- and triple-staining methods as well as the vast area of quantitation, model systems and auxiliary techniques like Western blotting. Perhaps these omissions can be rectified in forthcoming updates. This book is a useful, sometimes beautiful, compilation of protocols and methods, which, however, lacks the critical overview that allows it to stand by itself as the text on immunocytochemistry.

Lars-Inge Larsson

Guidebook to Cytokines and Their Receptors; Edited by N.A. Nicola, Oxford University Press; New York, 1994; xx + 261 pp. £22.50. ISBN 0 19 859946 3

In the field of cytokines a guide is as important as on the way to the Matterhorn. Guides should show the way and prevent false steps (which are much more frequent, but less deadly in the cytokine field).

The book begins with color diagrams of the 3D structure of prototypic cytokines and schemes of cytokine receptors, and two introductions (to cytokines and cytokine receptors), which are very useful as they emphasize common structural and functional features, and ends with tables listing the chromosomal location of the