

chapters. Birchmeier et al. report the loss of E-cadherin expression and reduced intercellular adhesion in carcinomas, concluding that E-cadherin acts as an invasion suppressor. The role of CD44 splice variants in metastatic cancer is presented by Sleeman et al. Interestingly, the CD44 variants form homomultimeric complexes at the cell surface, which may increase their affinity to ligands such as hyaluronate. Finally, Pantel et al. describe expression of cell adhesion molecules in early metastasis. The authors conclude that down-regulation of desmosomal proteins and neo-expression of ICAM-1 or

MUC18 are important determinants of the metastatic capability of individual malignant cells.

In summary, this volume presents recent advances in adhesion molecule research. The excellent overviews, contributed by leading scientists in the field, are complemented with fascinating discussions. The book constitutes a most valuable resource in a biomedical research library.

Manuel Patarroyo

Cytokines in Animal Health and Disease; Edited by Michael J. Myers and Michael P. Murtaugh, Marcel Dekker, Inc., New York, 1995. ix + 465 p. \$175.00 (hb). ISBN 0-8247-9435-4.

The scope of this book is the growing field of cytokines in veterinary important animals (domestic and companion animals). Whereas cytokines have been studied extensively in man and in rodents, the investigation of cytokines in domestic animals has only recently started to take pace, fuelled by the growing realization of the importance of cytokines in immunological and inflammatory processes. The aim of the editors as stated in the preface of the book is not only to 'review the current status of cytokine biology in domestic animals' but also to 'establish an improved foundation for future research'.

In the first part of the book, background on cell sources, biological effects and receptors, structure and molecular biology of interferons (IFN) (I.R. Tizard), interleukin-1 (IL-1) (J.R. Lederer and C.J. Czuprynski), IL-2 (M.A. Morsey), tumor necrosis factor (M.J. Myers and M.P. Murtaugh) and IL-6 (C.D. Richards and colleagues) are described in man and mouse in addition to a summary of comparative aspects especially in the bovine, porcine, and ovine species (equine, canine, feline, and lapine species are also covered in some of the chapters). Generally for these cytokines, wide-spread species-species cross-activity is seen (although the IL-1 chapter concludes otherwise). The important general conclusion on the therapeutic use of cytokines is that they may be more toxic than they are beneficial. In the chapter on IL-1, there is no discussion of the more interesting possibility of the therapeutic use of natural cytokine inhibitors as e.g. interleukin-1 receptor antagonist. For some reason dissociation constants are called affinity constants in the IFN-chapter. Curiously, sequence data for porcine IL-1 α (published in 1990) seem not to be known to the authors of the IL-1-chapter (although published in 1990) and also the IL-1 β reference is incomplete. In this chapter, too, the homology stated between human IL-1 receptor antagonist and human, murine and bovine IL-1 β is clearly exaggerated, and the chapter is marred by the regular occurrence of nonsensical dissociation constants (around 10^{-1} M). The IL-2 chapter does not mention that the IL-2 γ receptor also binds IL-4 and IL-15, there is not much cross-species information, and there is no discussion on measuring IL-2 in animals. In the chapter on TNF there is a good discussion of assays, covering the principle of using cross-species reacting reagents. The three-dimensional structure of IL-6, contrary to what is claimed, is not known.

In the second part of the book H.P.A. Hughes and L.A. Babiuk reviews potentiating the immune response by administering cytokines in a vaccine formulation and D.J. Weiss discusses the use of drugs to modulate cytokine actions. The authors of the first chapter are quite optimistic, even though most of the data deal with IL-2 only. The application examples are superficially referred to (in some, the species immunized is not even mentioned) and toxic side effects are not mentioned. This chapter has a strong point in its good overview of the complex interactions taking place between cytokines during a natural infection. The drug chapter is short but quite to the point; the concern is to limit the adverse effects of cytokines.

In the third part of the book specific applications are described in which cytokines play major roles or can be used as drugs. There is some repetition of facts in this part of the book, e.g. concerning the division of T_H-cells into T_{H1} and T_{H2} subsets and the concept of a cytokine network. N. Mathialagana and R.M. Roberts describe interferons and their role in recognition of pregnancy and fecundity in ruminants. A practical use of trophoblast IFN (IFN- τ), being the messenger molecule in cattle and sheep may be confined to special cases like embryo transfer methods for sheep as only adverse effects have been observed with the homologue IFN- α in cattle. M.J. Myers and J.C. Kawalek summarize

the effects of cytokines on the drug-metabolism of the host. Exogenously added cytokines can decrease the drug-metabolizing capacity of the body. IFN- α , IL-1, IL-6 and TNF- α are directly involved in cytochrome P450 down-regulation, which is of clear relevance considering the widespread use of antibiotics. T.H. Elsasser and colleagues present data on the involvement of cytokines in an animal's management of stress, a syndrome characterized by changes in nutrient use and catabolic delivery and therefore significant for the economically important growth rate parameter. The practical relevance of the cytokine involvement is not clear. H. Bielefeldt-Olmann and M.J. Wannemuehler describe in two separate chapters both pathogenetic and therapeutic aspects of cytokines in microbially induced respiratory diseases and in intestinal diseases respectively, stressing the detrimental effects of out-of-balance cytokines and generally judging therapeutic uses of cytokines as less encouraging. Inhibitors (antibodies and soluble receptors and antagonists) are expected to be better therapeutic candidates, although the problem of timing is a major concern. In some contrast to these two economically important diseases, M.B. Tompkins and W.A.F. Tompkins summarize the pathology of retroviruses in the cat. Cytokine therapy in these viral diseases is hampered by the fact that the two viruses (FeLV and FIV) reside in the immune system itself. Specifically, the lack of tools for lymphocyte subtyping blocks further research. The chapter by L.M. Sordillo and M.J. Daley returns to the economically important diseases. It reviews the possibilities for involvement of cytokines in the prevention and therapy of mastitis. The therapeutic use of recombinant G-CSF and GM-CSF, IFN- γ and IL-1 and IL-2 administered in monstrous doses is presented. The results are characterized as 'extremely encouraging' but prone to be regulatory/politically sensitive. There is no reference to the potential risks of this approach or to the costs associated with it. The authors seem to view cytokine therapy as a means of cleaning up the mess left by inefficient antibiotics.

The last two chapters deal with future directions, the first one by E. Atac and others discussing relating cytokine expression to disease resistance and, by mapping the corresponding genes laying the foundation for the selective breeding of preferred cytokine genotypes. Knowledge is scarce; cytokines with similar biological effects generally map closely on the same chromosome. Only 10 cytokine-related genes have hitherto been mapped in the bovine and in cattle and pigs, respectively. While selective breeding is a most cost-effective and preferable way to combat infections, it is not discussed that with a complex system, selecting for a favorable trait may co-select for another, unfavorable one. The concluding chapter summarizes that cloning of cytokines has primarily been done in swine, cattle and sheep; curiously, equine cytokines are not mentioned (genes for IL-1, IL-2, IL-4 being sequenced and IL-10 being partly sequenced before time of print). Methods are pivotal and their application to new species non-trivial. There is a highly readable and important description of the various types of assay systems used for the measurement of cytokines. With both immunoassays and biological assays there is a need for specific antibodies against cytokines. There is also a great need for antibodies to define specific subpopulations of e.g. lymphocytes in different species. A major future theme is the biological complexity of regulation of the cytokine network. Important applications will include vaccine technology while the potential of cytokines as therapeutics is less obvious. Alternative applications include the use of cytokine inhibitors for the restriction of inflammatory reactions, and the monitoring of health status by either direct measurement of specific

cytokines or through the measurement of the more robust, cytokine-induced acute-phase proteins.

The book is not without flaws; there is a fair share of typographical errors and the outline and content of the individual chapters differ widely. There are many directly opposing conclusions, as well as overlaps and omissions, and a general lack of cross-referencing between chapters. A substantial proportion of the chapters contain no references after 1992. There is no list of abbreviations (which are widely used in the cytokine and immunology fields). Some chapters contain factual errors, some mentioned above. This all points to a lack of editing that decreases the readability of the book. Concerning the contents, the background/cytokine chapters generally fail to familiarize the reader with any feeling of the cytokine network; molecular details of cytokines from the most investigated species (man and mouse) are described, instead of concentrating on useful generalizations. A small introductory review, simply introducing cytokines and relating their actions in a physiological setting in a general way would have aided the non-specialist reader (of which some should be expected with a multi-discipline text like this). One does also miss an introductory, critical and comprehensive chapter on methodology, as methodological development has been implicitly linked to the advance in cytokinology and as methodological knowledge is crucial when applying cytokine assays to a new species. Finally, this reviewer finds it frustrating that none of the numerous descriptions of recombinant therapeutics provide

a single warning on the inherent dangers of using heterologously expressed proteins for therapy (abnormal bioactivity with respect to levels and side-effects, reactions with antibodies (either preformed or induced)). There is one example given in which the bioactivity of the same IL-2 seemingly differs 200-fold with two different expression systems, but this goes largely unmentioned upon.

This said, the volume quite accurately reflects the state of affairs in the veterinary cytokine field and presents a very interesting plethora of application examples. The book is timely, as the research on infectious diseases and health surveillance in domestic animals increases in sophistication and is becoming the occupation for molecular biologist and immunologists as well as for biochemists and veterinarians. And it is the only comprehensive volume on the subject available at this time. The big number of references and the inclusion of titles in the references add to the usability of the book. The index is quite good, and makes the otherwise not so homogeneous book quite usable for the general reader and for the critical veterinary clinician as a reference handbook compiling data from many different areas in veterinary cytokinology at least up to 1992. The book clearly meet a demand in this field. Investigators concerned with human and/or rodent systems only may also find it useful both concerning inter-species cytokinology and the increased number of animal models becoming available.

Peter M.H. Heegaard

In Situ Polymerase Chain Reaction and Related Technology; Edited by Jiang Gu, Birkhauser, Boston, 1995. 143 pp. \$29.00 (hc). ISBN 3-7643-3870-9.

This book consists of 8 invited chapters ranging in size from 8 to 34 pages. Most chapters have 1–3 figures. Two of the 8 chapters provide detailed protocols. Ten color plates are provided at the end of the book.

The strength of this book is that it demonstrates to the reader that many groups have achieved success with in situ PCR. Several of the 8 groups that have written a chapter for the book have also published in situ PCR data in peer review journals. This is especially true of Bagasra et al., whose group has published extensively in peer review publications on their data with in situ PCR, primarily as it relates to HIV-1 related disease. It is not surprising, perhaps, that Bagasra et al. also provide the most detailed protocols and illustrations.

This book has two main weaknesses: (1) as would be expected for any book in a rapidly emerging field, some important information is omitted and (2) its small size and multi-author format does not allow for a discussion of the theoretical foundation of in situ PCR. With regards to the first point, a thorough discussion of the various DNA synthesis pathways that may be operative inside a cell during in situ PCR is not well covered. This information, in my opinion, is very important especially to the newcomer in this field in understanding and interpreting his/her data. This book also perpetuates the misconception that diffusion of the amplicon is a serious problem with in situ PCR and that the robustness of the reaction inside the cell is poor. Under proper

conditions of fixation (cross linking) and protease digestion, amplicon migration is strikingly limited inside the cell. Also, a 200-fold amplification inside a nucleus 4 μ in size is equivalent to a 10^6 fold amplification in a 100 μ l reaction chamber, and easily visualized under the microscope. With regards to point 2, a beginner to in situ PCR is presented in this book with a variety of protocols, with no discussion of the pros and cons of these different methodologies. A section comparing different protocols (e.g., different fixatives, +/- protease, DNase digestion, etc.) would have aided this book for the person wishing to start doing in situ PCR.

In summation, this book is useful for the person who wishes a single source to see how this important new field -- PCR in situ hybridization (for DNA) and RT in situ PCR (for RNA) is now being used. The chapter by Bagasra et al. is the most comprehensive for those wishing to do in situ PCR. However, in general the book will not be of much utility to the person who wishes to begin doing the technique, as the various, non-integrated protocols and lack of a strong theoretical discussion on in situ PCR, including the various synthesis pathways, use of Dnase and protease digestion, and effect of different fixatives, are not well covered, due to the book's brevity.

Gerard Nuovo
