Cell Cycle Control; Edited by C. Hutchinson and D.M. Glover, Oxford University Press, New York, 1995. xv + 304 pp. £29.50 (pb). ISBN 019 9634106.

Cdc2 was identified by yeast geneticists nearly twenty years ago. At that time, cell cycle was just an emerging and virgin field of research with no need at all for a textbook. Our field has changed drastically since sisters of cdc2, the 'cyclin-dependent kinases' (CDK), were discovered and a family of cyclin companions was also identified. Cell cycle research is now a multidisciplinary field, and every emerging new question is enlarging the audience of CDKs.

The editors C. Hutchinson and D. Glover conclude the preface of their book with the following sentence 'We are conscious, as we go to press, of the important recent findings that we have been unable to cover as the field moves on, but nevertheless we hope that this book gives a timely overall perspective on current cell cycle research'. To my point of view, the answer is absolutely yes. The major difficulty of writing a textbook in a field that is moving as fast as the cell cycle has during the last decade, is perfectly avoided by the judicious and careful choice of the topics that are covered. The editors, who are leaders in the field, have commissioned chapters that have been written by experts in various aspect of cell cycle research. Indeed, this book not only provides a full coverage of all topics, but is enlightening the most fascinating advances of recent work. In addition, sufficient background is provided with each of the ten chapters to allow the reader to find easily the sources of primary data and to search for supplementary material.

The first chapter is an introduction to cell cycle control written by L. Hartwell, who initiated genetic work on budding yeast cell division cycle mutants in the early 70's. The next one by S. Reed, C. Hutchinson and S. MacNeill is a more technical introduction to the concepts and the experimental models that have made major contributions to cell cycle research. The following two chapters, by S. Reed and by S. MacNeill and P. Fantes are dedicated to the review of our current knowledge of the molecular mechanisms of control at the G1-S phase and the G2-M phase transitions in budding yeast and fission yeast, respectively. Chapter 5, by G. Basi and G. Draetta deals with questions arising from the study of the cdc2 kinase structure-function relationships, and also addresses the role and regulation of this kinase in vertebrate cells. So many kinases, so many cyclins, why? This is one of the most fascinating questions that is addressed in chapter 6 of this book, by J. Pines and T. Hunter. In chapter 7, J. Blow's contribution is an excellent up to date review of the regulation of S-phase. Chapter 8, by A. Zetterberg and O. Larsson, is dedicated to the study of cell growth control in mammalian cells.

One of the major advances of the last few years has been the discovery of several lines of evidence for connecting the molecular mechanisms of cell cycle control and cancerogenesis. This evidence is clearly reviewed in chapter 9 by E. Lees and E. Harlow. The last chapter, by H. White-Cooper and D. Glover beautifully illustrates how useful and powerful multicellular organisms can be to investigate specific aspects of cell cycle control in connection with developmental programs.

These ten chapters are of equal very good quality and have been efficiently compiled, making this a real textbook and not just a juxtaposition of specialized reviews. Scientists who do not follow the cell cycle literature on a daily basis, newcomers to the field and graduate students, all have great difficulty merging and assembling the mass of data that has been accumulated in the recent past. I am very much convinced that they will enjoy and greatly profit reading this book. So, it was time for this new excellent *Cell Cycle Control* textbook.

Bernard Ducommun

Cell Adhesion and Human Disease; Edited by J. Marsh and J.A. Goode, Ciba Foundation Symposium 189, Wiley, Chichester, 1995. ix + 243 pp. $49.95 (hb). ISBN 0-471-95279-6.

Adhesion molecules participate in a large number of cellular functions and activities. They contribute to normal biological processes and disease states such as cancer (invasion and metastasis), inflammatory disorders (rheumatoid arthritis and autoimmune diabetes) and cardiovascular diseases (heart attack and stroke). This Ciba Foundation Symposium volume contains the papers presented at a recent meeting on Cell Adhesion and Human Disease. Each paper is followed by a very interesting discussion. The meeting focused on blood cell (both leukocyte and platelet)-vessel interactions, but also dealt with adhesion molecules in skin and solid tumors. This volume presents current research on selectins and their ligands, immunoglobulin-related molecules, integrins, cadherins and other adhesion molecules. It also considers the therapeutic potential of adhesion molecule antagonists in inflammatory and malignant diseases. It should be of interest to investigators of adhesion molecules, as well as immunologists, hematologists and tumor biologists.

Following a stimulating introduction by R.O. Hynes, chairman of the symposium, adhesion molecules mediating blood cell-vessel interactions are explored in several chapters and discussions spread throughout the volume. Adhesion molecule knockouts, presented in two papers, beautifully demonstrate the biological relevance of these molecules. Wagner presents the P-selectin (CD62P) knockout and demonstrates the importance of this selectin in early leukocyte rolling along vascular endothelium and the subsequent leukocyte extravasation at inflammatory sites. Kwee et al. present E-selectin (CD62E)- and VCAM-1 (CD106)-deficient mice. Participation of E-selectin in neutrophil extravasation was less notorious than that of P-selectin. In contrast to the selectin knockouts, VCAM-1-deficient mice were not viable, indicating the relevance of this molecule during development. A human deficiency of the selectin ligand sialyl Le X (Sle^x, CD15s), known as leukocyte adhesion deficiency (LAD) II, is described by Etzioni et al. As in LAD I ($\beta 2$ integrin-, CD11/CD18- or Leu-CAM-deficiency), these patients suffer from recurrent bacterial infections. Endogenous protein-associated carbohydrate ligands for E-selectin are explored by Patel et al. The authors identify sialyl-di-Lewis X as the endogenous ligand.

Participation of adhesion molecules in detrimental inflammatory reactions is also explored following administration of blocking monoclonal antibodies. Winn et al. concentrate on $\beta 2$ integrins and L (CD62L)- and P-selectins in ischemia/reperfusion injury (stroke, myocardial infarction, hemorrhagic shock, etc.), while Rothlein and Jaeger summarize the effect of anti-ICAM-1 (CD54) antibody in animals and humans (allograft rejection and rheumatoid arthritis). Both groups report protective effect of the antibody treatments. Two chapters describe progress in leukocyte $\alpha\beta 1$ integrin (CD49d/CD29) and its ligands fibronectin and VCAM-1. Elices reviews the protective effect of antibodies to $\alpha 4$ in several animal models of allergy and chronic inflammatory diseases, and introduces a low molecular weight inhibitor of this integrin based on the LDV sequence of fibronectin. Humphries et al. dissect the mechanisms of VCAM-1 and fibronectin binding to $\alpha 4\beta 1$, and particularly the peptide sequences participating in this and other integrin-ligand interactions. Moreover, Hogg explores the binding sites of the integrin $\alpha L\beta 2$ (CD11a/CD18) for its ligand ICAM-1 and describes that, in addition to the I-domain, domains V and VI of αL also bind ICAM-1. Binding of von Willebrand factor to specific platelet membrane receptors and its relevance for platelet adhesion and thrombus formation at sites of vascular injury are summarized by Ruggeri, including the importance of shear forces.

Up-regulation of vascular adhesion molecules in inflamed skin, a process which parallels leukocyte infiltration, is presented by Barker. The skin, because of its accessibility, is an ideal organ to study adhesion molecule expression in inflammatory disorders such as psoriasis and atopic dermatitis. Stanley describes two blistering skin diseases (pemphigus foliaceus and pemphigus vulgaris) as illustrative examples of defective cell-cell adhesion in the epidermis. These patients' autoantibodies to desmogleins, desmosomal glycoproteins members of the cadherin gene superfamily, block adhesion of the epithelial cells.

Adhesion molecules in human solid tumors are explored in three

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-1α (published in 1990) seem not to be known to the authors of the IL-1-chapter (although published in 1990) and also the IL-1β reference is incomplete. In this chapter, too, the homology stated between human IL-1 receptor antagonist and human, murine and bovine IL-1β 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-2γ 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-Ohmann 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