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Book Reviews

Apoptosis: The Molecular Basis of Cell Death. Current Communications in Cell and Molecular Biology 3. Edited by L. D. TOMEI and F. O. COPE. Cold Spring Harbor Laboratory. 1991. 321 pages. $44.00. ISBN 0 87969 366 5

At last, an affordable book which brings together an informative collection of articles on a theme which, in recent years, has received an enormous upsurge in interest. Whilst most biologists (understandably) have tended to concentrate their efforts on getting to grips with the mechanisms by which cells live, only a few, until recently, focused their attention on how cells die. To the life scientist death often means failure, and to many who study living cellular processes the importance of understanding how cells die can be a difficult concept to grasp. For most who rely upon *in vitro* models, experiments in which cells die are failed experiments, usually put down to inadequacies in the particular cell system under investigation. But to some this is not so, the important question being '*How* did they die?' In the first two chapters of this book, the concepts of cell death are set out, the second chapter by Kerr and Harmon providing clear definitions in a historical perspective. Here, as well as in several other chapters, the significance of cell death in the development and normal functioning of multicellular organisms is underlined: death of cells is by no means always accidental, that is, it does not solely occur as a result of living processes going wrong. Rather cell death is, more often than not, suicidal in nature, the suicide processes constituting an important part of cells' normal physiological make-up, being activated or suppressed according to the requirements of the organism as a whole. The sixteen chapters in this book define the cell suicide process(es) and their importance in cellular homeostasis in a variety of cell and organ systems, and discuss mechanisms of regulating cell death.

Apoptosis, a widely mispronounced process, is accepted by many as synonymous with 'programmed cell death'. Historically, the term 'apoptosis', describes a series of morphological features, beautifully illustrated and contrasted with the features of necrosis in chapter 2 of this book, characteristic of cells undergoing physiological death. The term 'programmed cell death' is distinguished from apoptosis by some, however: Lockshin and Zakeri in chapter 4 of this volume suggest that 'programmed cell death' implies a relationship to death in development rather than control against a potentially dangerous situation. Indeed, they distinguish between apoptosis and the morphological features of developmental ('programmed') cell death. Perhaps a unifying view is that cells have an in-built, genetically controlled suicidal program which when activated will, in some but not all cell types, cause the features originally defined as apoptosis. Of course, such a view does not distinguish between different forms of cell suicide and different cellular responses to a single suicide mechanism.

Several of the chapters deal with the significance of apoptosis in cancer, both from the point of view of oncogenesis and in relation to drug treatment. In their chapter on 'Apoptosis and hepatocarcinogenesis', Ledda-Columbano and Columbano introduce the concept of 'compensatory cell death', suggesting that apoptosis could be important in the removal of preneoplastic cells from an initially hyperplastic lesion. Growth of tumours is a balance between proliferation and cell loss. Chemotherapeutic strategies for removal of tumour cells have been largely aimed at the proliferating component; new strategies should take account of the capacity of drugs to induce programmed cell death, perhaps, as proposed by the Columbanos, even through their ability to stimulate proliferation and subsequently trigger compensatory cell death. The APO-1 antigen, as described in Chapter 6, also has implications for tumour therapy. Ligation of this antigen by specific monoclonal antibodies results in the induction of apoptosis in a variety of cell types which express the molecule on their surface.

Excellent chapters dealing with cell death induced by cytotoxic lymphocytes and radiation are provided by Duke and Umansky, respectively. The central issue of cellular signalling pathways for apoptosis features in a number of chapters, the role of oncogenes and the relationship with the cell cycle receiving particular attention. A full chapter devoted to the second-messenger pathways involved in thymocyte apoptosis is provided by McConkey and Orrenius. Their findings pave the way for elucidating the nature of the signalling pathways operating in other cell systems. It will be of particular interest to many in the field to determine to what extent the sustained elevation of intracellular

calcium promotes, whilst increased PKC prevents, apoptosis in different cell types.

The genetic control of programmed cell death provides a central thread to the theme of this book. The term 'programmed' implies ultimate regulation from within the cell, and several of the chapters refer to experimental evidence of genetic control of cell-death processes. However, two of the most important genetic systems of relevance to cell death, although occasionally referred to, are sadly missed from this volume: death genes in the nematode *C. elegans* and the mammalian cell survival gene, *bcl*-2. It is likely that this area of cell death research will develop particularly rapidly over the forthcoming years.

In their introductory chapter, Tomei and Cope state the objective of this book: 'to provide graduate students and scientists an introduction to the concept of apoptosis and an opportunity to consider how scientific hypothesis functions'. In my view they achieve both of this objectives and, in so doing, will probably also succeed in convincing some of the sceptics that there is more to cell death than downhill thermodynamics.

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The Molecular Pathology of Alcoholism. Molecular Medicine Series. Edited by T. NORMAN PALMER. Oxford University Press, 1991. 293 pages. Paperback £22.50. ISBN 0 19 261903 9.

Bleuler's classic work on psychiatry (1923) devoted only 13 of its over 600 pages to the causation of mental disease. Until recently few more modern textbooks could justifiably claim that our factual knowledge allowed a greater ratio to be given, although hypotheses as to aetiology are as legion as they have always been. Of the psychiatric illnesses the anatomy of alcoholism, with its multifaceted social and medical dimensions, has always led it to be the most difficult to dissect. By far the most commonly used stimulant of man is also his most common poison and a *sine qua non* of one of his most common diseases. Attempts to cover the subject in depth have not always therefore been successful.

It was a pleasant surprise then to receive a jolly good book devoted to telling us what is known of the molecular aspects of alcoholism. I have read many of the chapters several times over and the softback covers of the review copy are in a rather sorry state, surely the hallmark of something well worth perusing. The first two chapters of the book, taking up nearly 50% of the total, both involve the part or whole authorship of Charles Lieber. After a brief social introduction the first chapter gives a comprehensive review of alcohol-related pathology and pathophysiology by human organ system. Not only are the primary toxic effects of alcohol discussed, but also the cascading series of events leading to clinical phenotypes as far as these are known. The following chapter on the liver is equally lengthy, reflecting the pivotal importance of this organ in the metabolism of alcohol. Current views on all aspects of the biochemical events leading to hepatocyte injury are presented, and not just the part that the various systems of alcohol-degrading enzymes have to play. The effects of drugs on these systems and the reciprocal effect these systems have on drug metabolism are covered, as are ideas about how alcohol may be involved in carcinogenesis. There follow two chapters on the alcohol and aldehyde dehydrogenases. The first describes the basic biochemistry of these enzymes, although I am not convinced that printing pages of full amino acid sequence data (nor the cDNA sequence data found in the next chapter) for the variant types serves a useful purpose in this sort of volume. Bleuler himself noted that the susceptibility to the intoxicating effects of alcohol was far from uniform and noted that 'whoever gets drunk on small quantities will hardly ever become an alcoholic'. Yoshida covers the genetics of the ADH and ALDH systems, including their role in the alcohol sensitivity of those of Oriental extraction, which is associated with a low risk of developing alcoholism. There is a deal of overlap here with Agarwal and Goedde's rather more detailed chapter on this very subject, which might have been avoided. The direct neurotoxicity of alcohol is not neglected and Littleton discusses ideas of ethanol's interaction with inhibitory (γ-aminobutyric acid) systems and touches also on excitotoxic (NMDA) systems in the brain, his main postulate being the modulation of voltage-dependent calcium channels as a common denominator in the development of tolerance, dependence and toxicity. Finally, and unusually, the book deals with the foetal alcohol syndrome, which serves to remind us that alcohol can unfortunately severely damage other lives by a direction action as well as by its social and economic ill-effects.

So here at last is a useful book on the molecular aspects of alcoholism. Criticism can only be minor, and the book would be worth buying for the chapters by Lieber alone. There are few typographical errors and the reference lists are comprehensive and mostly up to date to 1990. The Molecular Medicine series now has several excellent volumes to its credit, though by the nature of the field some already need to be brought up to date. This reasonably priced paperback should suit the pocket and minds both of clinicians who want to learn more about the molecular aspects of one of the diseases they most commonly treat, and of scientists who want to learn how the molecular aspects can be integrated with and be explanatory for the huge variety of clinical manifestations.

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